SECOND EDITION

Traumatic Brain Injury

Rehabilitative Treatment and Case Management

Edited by

Mark J. Ashley

CRC PRESS

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Preface

Interventions for traumatic brain injury (TBI) at the acute level have changed relatively little in the last decade, particularly in comparison with changes seen in other fields such as cardiology. There have been few clinical advances made in emergency or intensive care management, most probably due to poor public awareness of TBI and poor research funding. At the same time, managed care has resulted in tremendous changes in hospital lengths of stay and access to care for people with TBI. While it may be argued that managed care has had a beneficial impact on the management and costs of some health conditions, catastrophic diagnoses like TBI are not well addressed within the managed care environment. Consequent to both of these points, people with TBI face substantial levels of disability with relatively little recourse in the form of treatment. Treatment which is rendered must be succinct and the most effective possible. There are certainly limitations to what can be expected, however. We must question whether it is possible to provide fast, inexpensive, and effective rehabilitation for people with TBI. A determination of whether such a goal is attainable is dependent upon one's definition of "effective rehabilitation" and the extent of recovery that is to be achieved.

It can be argued that far too little is offered to people with TBI and their caregivers, in general. Our societal disposition is away from provision of rehabilitative care, perhaps because the field has been slow to properly document the financial benefits of disability reduction. Be that as it may, there is evidence that both postacute and late rehabilitation can be effective in reducing disability, improving quality of life, enhancing life satisfaction, and reducing the long-term financial expenditures associated with TBI. The population of persons with TBI is maturing, and support systems, which were in place for many years in the form of nuclear family members, are reaching the point where they can no longer be relied upon. Lifestyle changes in the last 20 years call into question the willingness and/or ability of families to bear the burden of caring for an injured family member. Depression rates and life satisfaction are abysmal among persons who have suffered TBI and their families. Rehabilitation can be an effective means of combating both and contributing to improved long-term financial benefits in healthcare management of this population.

This text is intended for a broad audience of professionals involved in treating and caring for people with traumatic brain injury. Injury to the brain produces a wide array of deficits which must be addressed during rehabilitation of the person with TBI. Recovery can extend well beyond the period of time most individuals have access to rehabilitative services, particularly those which are hospital-based.

Deficits seen following TBI can include physical, cognitive, psychological, communicative, educational, vocational, social, and medical domains. In general, severity of injury bears on the nature and number of deficits seen, though this is not always the case. TBI occurs frequently, but it is the rare professional who sees enough people with TBI to develop ready expertise in the area. It is difficult, at best, to develop expertise due to the fact that TBI presents so uniquely in each person and many settings restrict either the severity of injury treated and, therefore, encountered by the practitioner, or length of stay due to financial constraints imposed by funding sources. Professional turn-over rates vary from setting to setting, but clearly impact the level of institutional knowledge available to benefit the person with TBI.

This text attempts to address a number of deficits which are prevalent and persistent following TBI. The text does not attempt to be absolutely comprehensive in this pursuit, however. The goal is to provide therapists, case managers, and physicians with information about the longer-term issues faced by this population. The second edition has been enlarged with the addition of eight new chapters. The book's purview has been substantially broadened to address some of the issues faced by people with TBI and their caregivers over a lifetime. These include medical, environmental, social, financial, and legal arenas. All readers will be intrigued by the discussion of ethical issues in relation to treatment and living life after TBI. Chapters have been added to address some of the needs of the educator, discharge planner, and neuropsychologist. The importance of cognitive function following TBI is underscored by the addition of a third chapter on the topic. The case manager should derive a great deal of new information from chapters on audiological issues, discharge planning, and neuromedical issues of aging in TBI.

Reader reaction to the first edition indicated that the text was educational for the inexperienced clinician and served as a reference tool for the experienced clinician. This text is designed to allow its use both for education about TBI treatment and as a reference tool for the practitioner. Each chapter begins with an outline to allow quick access to specific material. Specific diagnostic and treatment interventions are provided and, in some cases, the theoretical constructs upon which they are based are included. Some chapters are largely treatment oriented, some will be used both as a source of information about treatment and as a reference tool, and others will be largely used for clinical reference.

The reader is encouraged to use the information contained herein for treatment of the person with TBI, education of that person and his/her caregivers, and advocacy for all people with TBI. The TBI population is somewhat unique in that our job as rehabilitation professionals is to work to return control over their lives to those injured. The sequelae of TBI are so pervasive as to make this difficult, at best, if not impossible. The person with TBI faces a daily struggle to survive and return to preinjury functioning levels. They and their caregivers can exhaust personal energy and financial reserves in a seemingly never-ending stream of day-to-day challenges following TBI. To that end, it is encumbent upon us all to advocate for ongoing rehabilitative treatment for specific individuals with TBI as well as for all people with TBI.

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Contributors

Sam S. Andrews, B.S.
Craig Hospital
The Rocky Mountain Regional Brain Injury System
Englewood, Colorado

Mark J. Ashley, Sc.D., CCC-SLP, CCM
Centre for Neuro Skills
Bakersfield, California

Susan M. Ashley, M.S., CCC-SLP, CCM
Centre for Neuro Skills
Bakersfield, California

Juan J. Bermejo, Ph.D., FAAA
Bakersfield, California

Amy Berryman, OTR/L
Centre for Neuro Skills
Bakersfield, California

Phillip J. Best, Ph.D.
Department of Psychology
Miami University
Oxford, Ohio

Ronald A. Browning, Ph.D.
School of Medicine
Department of Psychology
Southern Illinois University
Carbondale, Illinois

Velda L. Bryan, PT
Centre for Neuro Skills
Bakersfield, California

Charles D. Callahan, Ph.D.
Memorial Medical Center
Springfield, Illinois

Steven J. Cloud, Ph.D.
University of Southern Mississippi
Hattiesburg, Mississippi

Fofi Constantinidou, Ph.D.
Speech Pathology and Audiology
Miami University
Oxford, Ohio

Roberta DePompei, Ph.D.
University of Akron
School of Speech-Language Pathology and Audiology
Akron, Ohio

Christie Byrd Depner, MSPT
Centre for Neuro Skills
Bakersfield, California

William L.E. Dussault, P.S.
Seattle, Washington

Debbie Eaton, M.D.
The University of Texas Southwestern Medical Center at Dallas
Department of Otolaryngology
Dallas, Texas

Douglas E. Garland, M.D.
Director, Neuro-Trauma Division
Department of Surgery
Rancho Los Amigos National Rehabilitation Center
Downey, California
and
Department of Orthopedics
University of Southern California Keck School of Medicine
Los Angeles, California

David A. Gelber, M.D.
Springfield Clinic NeuroScience Center
Springfield, Illinois

Prudence Gensman, OTR, MBA, CCM, CEAC
Centre for Neuro Skills
Bakersfield, California

Kenneth A. Gerhart, P.T., M.S.
Craig Hospital
The Rocky Mountain Regional Brain Injury System
Englewood, Colorado

Karen Goodwin, OTR/L
Centre for Neuro Skills
Bakersfield, California

Stephanie Hanson, Ph.D., ABPP (Rp)
College of Health Professions
University of Florida
Gainesville, Florida

Theresa D. Hernández, Ph.D.
Associate Professor
Associate Chair and Director of Graduate Studies
Department of Psychology, UCB 345
The Center for Neuroscience
University of Colorado
Boulder, Colorado

Kenneth R. Hosack, M.A.
Craig Hospital
The Rocky Mountain Regional Brain Injury System
Englewood, Colorado

Thomas Kerkhoff, Ph.D., ABPP (Rp)
College of Health Professions
University of Florida
Gainesville, Florida

Rose Leal, M.S., CCC-SLP
Centre for Neuro Skills
Bakersfield, California

Robert P. Lehr, Jr., Ph.D.
Emeritus, Department of Anatomy
School of Medicine
Southern Illinois University
Carbondale, Illinois

Paul M. Levisohn, M.D.
Associate Professor of Pediatrics and Neurology
University of Colorado Health Sciences Center
Medical Director
Children's Epilepsy Center
The Children's Hospital
Denver, Colorado

Zenobia Mehta, M.A., CCC-SLP
Centre for Neuro Skills
Bakersfield, California

Ronald L. Morton, M.D.
Associate Professor
Jules Stein Eye Institute
University of California
Los Angeles, California

John R. Muma, Ph.D.
University of Southern Mississippi
Hattiesburg, Mississippi

Dean K. Naritoku, M.D.
Departments of Neurology and Pharmacology
Southern Illinois University School of Medicine
Springfield, Illinois

Joe Ninomiya, Jr., M.A., CRC
Centre for Neuro Skills
Bakersfield, California

Erik Otto, P.T.
Oldenzaal, Netherlands

Chris H. Persel, B.A.
Director of Behavior Programming
Centre for Neuro Skills
Bakersfield, California

Craig S. Persel, B.A.
Director, Department of Research
Centre for Neuro Skills
Montreal, Quebec, Canada

Peter S. Roland, M.D.
The University of Texas Southwestern Medical Center at Dallas
Dallas, Texas

Penelope S. Suter, O.D., F.C.O.V.D., F.A.B.D.A., F.N.O.R.
Vision Laboratory, Department of Psychology
California State University, Bakersfield
Bakersfield, California

Robin D. Thomas, Ph.D.
Department of Psychology
Miami University
Oxford, Ohio

Janet Tyler, Ph.D.
University of Kansas Medical Center
Department of Special Education
Kansas City, Kansas

Jay M. Uomoto, Ph.D.
Emory University School of Medicine
Department of Rehabilitation Medicine
Division of Rehabilitation Neurophychology
Atlanta, Georgia

Arousiak Varpetian, M.D.
Adult Brain Injury
Department of Neurosciences
Rancho Los Amigos National Rehabilitation Center
Downey, California
and
Department of Neurology
University of Southern California Keck School of Medicine
Los Angeles, California

Alan Weintraub, M.D.
Craig Hospital
Englewood, Colorado

Jan Wood, CRC, CDMS, CCM, RTC, CLCP
State Compensation Insurance Fund
Monterey Park, California

Contents

Part 1 Medical Themes

Part 2 Allied Health Themes

Part 1

Medical Themes

1

The Neurologic Examination of the Patient with Traumatic Brain Injury

David A. Gelber and Charles D. Callahan

CONTENTS

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Introduction

The neurologist often has a key role in the evaluation and management of patients with traumatic brain injury (TBI), especially in the emergent and acute phases of care delivery. As rehabilitation commences, the neurologist may be involved as a consultant or may play a more active role overseeing the rehabilitation process, depending on the nature of his or her practice, and the degree to which physiatric services are available. The role of the neurologist in the rehabilitation of the patient with TBI includes defining the extent of neurologic damage, reviewing pharmacological issues as they impact central nervous function, identifying and managing neurological complications such as posttraumatic seizures, and presenting information in a manner which is of maximal use to allied health professionals, family members, and the patient. This chapter provides a review of the neurologic examination, which will foster effective interaction between the neurologist and other rehabilitation professionals.

The brain and supporting structures are extremely vulnerable to traumatic injury. Patients with TBI are often left with significant physical, cognitive, and behavioral sequelae requiring prolonged hospitalization and the need for postacute rehabilitation programs. In the postacute setting, it is the physician's role to perform an adequate patient evaluation, including detailed history, physical, and neurologic examination and, in conjunction with the rest of the rehabilitation team, develop a comprehensive rehabilitation program to address each patient's particular needs.

The extent of brain injury and residual deficits varies from patient to patient, depending upon the nature of the insult and localization of brain injury. Penetrating or open head wounds due to skull fracture or gunshot wound, for example, most often cause focal brain injury at the site of impact due to contusion, laceration, hemorrhage, or necrosis of underlying brain tissue.[1] Closed head acceleration/deceleration injuries typically cause coup or contrecoup insults to the brain, resulting in polar injuries to the frontal, temporal and, occasionally, the occipital lobes. Diffuse axonal injury also commonly occurs as a result of shearing of axons within myelin sheaths, leading to injury to the subcortical white matter.[2] Brain structures most vulnerable to this type of injury include the corpus callosum, superior cerebellar peduncles, basal ganglia, and periventricular white matter.[3] In addition to direct traumatic injury, the brain may also be damaged as a result of complications of head injury, including edema, hypoxia, posttraumatic infarction, and hydrocephalus.[4]

Generally speaking, the severity of brain injury is predictive of functional outcome. Poorer functional outcomes are associated with increased patient age, presence of intracranial hemorrhage, abnormal motor responses, impaired eye movements or pupillary responses, hypotension, hypoxemia, hypercarbia, and increased intracranial pressure.[5] With the most severe injuries, patients may have prolonged coma, severe cognitive and behavioral sequelae, and marked motor and sensory deficits, leading to profound functional impairments. At the other end of the spectrum, mild brain injuries may result in the

"persistent postconcussion syndrome," marked by concentration, memory, and behavioral manifestations, as well as headache and vertigo, but without sensory or motor deficits.[6,7]

The neurologic examination is a key element in the evaluation of the patient with traumatic brain injury. The focus of the examination, however, differs depending on the stage of patient recovery. In the acute patient, the neurologic examination serves to localize the site and extent of brain injury, allowing the physician to develop a plan of acute medical and surgical management. In addition, serial neurologic examinations performed in the first few days or weeks following injury provide useful information regarding prognosis for recovery.

The purpose of the neurologic examination in the postacute rehabilitation setting is different from that performed in the acute stages following traumatic brain injury. The most important aspect of the examination in the postacute setting is to identify the specific physical, neurologic, cognitive, and behavioral deficits that will potentially limit the patient from a functional standpoint. Hemiparesis, for example, may affect a patient's ability to perform independent transfers, ambulate safely, or dress without help. Spasticity may impede nursing cares, limit bed mobility, and cause difficulty with wheelchair seating and ambulation. Identifying these deficits and related functional impairments allows the rehabilitation team to set appropriate functional goals and to develop a comprehensive rehabilitation program to address the patient's needs. It is also important for the rehab team to be able to identify specific deficits and potential limitations to patients' family members and caregivers, to allow them to adjust to these changes and make adequate plans for the patient's return to home and reentry into the community.

In the postacute setting, the physician must also be able to distinguish deficits that are a direct consequence of the traumatic brain injury from those that are due to medical complications. These potential complications include heterotopic ossification, posttraumatic hydrocephalus, posttraumatic epilepsy, intracranial and systemic infections, and medication side effects. Failure to identify medical complications will delay appropriate treatment and could place the patient at risk of permanent impairments.

This chapter will detail the neurologic examination of the patient with TBI in the postacute recovery period. Emphasis will be placed on identifying neurologic deficits that are commonly associated with TBI. Functional impairments, particularly as they relate to rehabilitation, will be reviewed. Finally, medical complications that are commonly encountered in TBI rehabilitation will be briefly discussed.

Evaluation of the Traumatic Brain Injury Patient in the Postacute Setting

The initial evaluation of the patient with TBI should include a detailed history. Since most of these patients have some cognitive impairment, the history may need to be obtained from medical records and from family members. Important details of the injury include the nature of the head injury (open or closed), whether the brain injury was focal or diffuse, the presence and duration of coma and posttraumatic amnesia, complicating conditions (hemorrhage, hypoxia, hypertension, posttraumatic seizures), associated systemic injuries (including spinal cord or peripheral nerve injury), the presence of intoxicants (drugs or alcohol),[8] and prior history of brain illness or injury.

One of the most important factors in assessing patients with traumatic brain injury is the patient's premorbid cognitive and behavioral status. Assessment should include a history of substance abuse or psychiatric illness. Level of education and employment

TABLE 1.1

Components of the Neurologic Examination in the Patient with TBI

Mental status
Level of consciousness
Orientation
Attention and concentration
Memory
Calculations
Speech and language
Spatial orientation/perception
Affect, mood, and behavior
Cranial nerves
Motor
Muscle bulk
Muscle tone
Muscle strength
Abnormal movements
Sensation
Primary sensory modalities
Cortical sensory function
Coordination
Reflexes
Posture and gait

status should also be obtained. Younger patients will have school records, often including results of previous formal cognitive testing, which can provide some objective picture of premorbid cognitive skills. Additional information can be sought from family members or employers.

A physical examination should be performed on all patients. General observation should include assessment of patient's level of consciousness, posture in bed, and presence of any external catheters or tubes (tracheostomy, gastrostomy tube, Foley catheter). The skin should be carefully examined for signs of breakdown (decubitus ulcers) or rash. Since concomitant skeletal injuries are common, a thorough musculoskeletal examination should be performed, with careful attention to any abnormal posturing of limbs, skeletal deformities, or limited range of motion at joints. Careful examination of the lungs, heart, and abdomen should also be performed to rule out infection or other pathological processes.

Finally, a detailed neurologic examination should be performed. This should include a detailed assessment of mental status, cranial nerves, motor system, sensory system, reflexes, coordination, and posture and gait (Table 1.1).

The Neurologic Examination

Examination of Mental Status

Cognition and behavioral deficits are typical of traumatic brain injury and often are the features most related to chronic functional disability. Manifestations include disorders of attention, learning and memory, language, perception, and executive functions. Although a formal detailed cognitive assessment is usually performed by the neuropsychologist and speech pathologist, useful information may be obtained from simple testing at bedside. Areas that should be assessed include level of consciousness, orientation, attention and

concentration, memory, calculations, speech and language, spatial orientation and perceptual skills, affect, mood, and behavior.

Level of Consciousness

An altered level of consciousness may occur in the acute stage following traumatic brain injury as a result of diffuse injury to the cerebral hemispheres or damage to the brainstem reticular formation. Other contributing factors include hypoxia, cerebral edema with increased intracranial pressure, and infection. Altered consciousness is often accompanied by confusion, disorientation, and anterograde amnesia, particularly if the limbic structures are affected.

Impairment in the level of consciousness may also be evident in the postacute rehabilitation setting, either because of residual brain injury or secondary factors such as metabolic abnormalities (hypernatremia, hypoglycemia, uremia, etc.), posttraumatic seizures, posttraumatic hydrocephalus, or medication side effects. Deterioration in level of consciousness should always alert the physician to the possibility of one of these complications. From a functional standpoint, an altered or deteriorating level of consciousness will obviously interfere with a patient's ability to actively participate in rehab therapies and will shift the focus of therapy to more passive activities such as muscle stretching and range of motion exercises.

Level of consciousness is easily assessed at bedside by observation and is best described by noting the patient's response to various levels of stimulation. Terms often used to describe altered levels of consciousness include *lethargy* (arousal to voice), *stupor* (arousal to vigorous physical stimulation), or *coma* (unresponsiveness to pain or other external stimuli).[9]

Orientation

Confusion and disorientation are common sequelae of traumatic brain injury and are often associated with an altered level of consciousness. Disorientation most often results from diffuse cerebral injury, particularly that involving limbic structures, but can also be caused by factors such as metabolic abnormalities or even emotional factors. It is generally accepted that the duration of posttraumatic disorientation is related to brain injury severity and outcome, with shorter periods of orientation impairment offering the more favorable prognosis. Beyond this, the methods and meanings of acute orientation deficits, often referred to as *posttraumatic amnesia* (PTA), continue to spark debate.[10]

During the bedside examination, orientation is assessed by asking the patient his name, the date (day of week, month, year), and location (name of hospital, floor number, room number, etc.).

Attention and Concentration

Attention and concentration are often impaired in patients with diffuse head injuries, particularly with insults to the frontal lobes.[3,11] Slowing of cognitive functioning and distractibility are also common findings.[12] These impairments can significantly affect a patient's progress in therapies because of inattention, slowness in performing cognitive tasks, and diminished ability to carry over information from day to day.

Attention and concentration may be informally evaluated during the course of the neurologic examination. Patients may have difficulty attending to the interview and may be easily distracted by external stimuli such as hallway activity or roommates. Speed of cognitive processing may also be grossly assessed by noting the patient's response time to questions or commands. Serial sevens subtraction or backwards spelling tasks are also commonly employed in mental status screening exams.

Memory

Both long- and short-term memory may be affected in the head-injured patient due to direct injury to the mesial temporal lobes and thalamus.[3] In addition, areas that subserve memory, such as the hippocampus, are extremely sensitive to anoxic and hypotensive injury, which often occurs in patients with TBI.[13] There are a number of small series that suggest a possible benefit of hyperbaric oxygen in these individuals.[14–16]

While old (retrograde) memory may be involved, new learning deficits (anterograde memory impairment) are a hallmark feature of moderate to severe TBI. Noting the diffuse nature of TBI (vs. focal stroke or neoplasm), deficits in verbal and visual–spatial memory are common, though the degree varies for each patient. Other cognitive impairments, such as poor concentration and apathy, may also interfere with encoding of new memories such that "forgetting" may actually be secondary to a primary attentional disorder.

The duration of anterograde memory impairment, i.e., posttraumatic amnesia, is an important prognostic factor with regards to recovery.[17] Patients with prolonged posttraumatic amnesia tend to have more residual cognitive impairment and overall poorer functional outcome. Memory impairment may seriously limit patients' progress in the rehabilitation program, especially if the ability to learn new information is affected and the carry-over of information learned in therapies is limited.

At bedside, immediate, recent, and remote memory can be evaluated. Immediate memory is primarily a function of information registration and is most dependent on attention and concentration. It is usually spared following traumatic brain injury, except in the early recovery period or when other factors, such as medication side effects or metabolic encephalopathy, affect patients' ability to attend to task.[11] Immediate memory can be assessed by asking the patient to immediately repeat three objects named. Alternatively, one can use digit span testing. The examiner gives a series of digits at a rate of one per second and asks the patient to repeat these, both forwards and backwards. A normal individual can repeat seven digits forward and six in reverse order. In testing recent memory, the patient can be asked to recall three objects in 3 or 5 minutes. Recent memory can also be assessed by asking the patient simple historical questions such as "What did you have for breakfast this morning?" Remote memory may be assessed by asking the patient about events in the past, his/her address or phone number, names of children, anniversary dates, etc. Again, remote memory is typically preserved, though may be impaired in the acute confusional period.

Calculations

Acutely, problems with calculations reflect attentional deficits. However, focal injury to the dominant parietal lobe may result in more chronic impairment of mathematical skills. Deficits may limit the patient functionally in terms of his ability to manage finances or participate in basic community activities such as shopping.

Calculation skills can easily be assessed at bedside by having patients perform serial subtraction of sevens from one hundred. Other tasks, such as counting change or more complex multiplication or division problems, can be administered. One must take premorbid educational history into account when interpreting the results of these tests.

Speech and Language

Language skills are commonly impaired in traumatic brain injuries that involve the dominant hemisphere. Difficulty with spoken and written languages or problems with language processing may result. Language deficits are usually accompanied by other cognitive impairments.[18] The most common feature of traumatic aphasia is anomia, characterized by difficulty naming, word-finding deficits, and paraphasic errors.[19] Wernicke's

(fluent or receptive) aphasia occurs less commonly following traumatic brain injury. It is caused by focal injury to the dominant temporal lobe and is characterized by fluent paraphasic speech, with impaired comprehension and repetition.[20] Broca's (nonfluent or expressive) aphasia is more common in penetrating type head injuries, due to a lesion of the dominant frontal lobe. Broca's aphasia is characterized by nonfluent speech with disturbed prosody and perseveration. Other language disorders associated with traumatic brain injury include echolalia (repetition of others), and palilalia (repetition of self).[4] Injuries to the medial frontal cortex, caudate nucleus, and globus pallidus, especially those that disrupt dopaminergic pathways connecting frontal lobe and basal ganglia structures, can result in apathy, abulia, and akinetic mutism. This is commonly seen following head injuries in children and in recovery from coma. A number of small series have reported improvement in these conditions with dopaminergic agonists such as bromocriptine, carbidopa/levodopa, and amantadine, or psychostimulants including methylphenidate and amphetamine.[21–23] Stuttering has also been reported following injuries to the right or left internal capsules, frontal white matter, and striatum.[24] Higher level language skills may also be affected, often becoming apparent as the aphasia resolves. Problems include difficulty with complex auditory processing, spelling, sentence construction, synonyms, antonyms, and with abstract language skills such as picture description.[25]

Dysarthria, or impairment in articulation, is also a common sequela of traumatic brain injury, caused by weakness and incoordination of the tongue and pharyngeal muscles. Deficits range from mild inarticulation to unintelligible speech, with the pattern depending on the location of brain injury.[20] Lesions of the hypoglossal nerve cause unilateral tongue weakness and difficulty articulating lingual consonants (t,d,l,r,n). Weakness of the soft palate results in nasal speech characterized by an abnormal resonance to sounds.[26] Patients with pronounced facial weakness often have difficulty with labial and dentilabial consonants (p,b,m,w,f,v). Bilateral involvement of corticobulbar pathways results in "pseudobulbar" speech, characterized by slow, labored speech with imprecise articulation and a harsh, "strained" quality. Cerebellar lesions are associated with dysrhythmic speech, with irregularity of pitch and loudness. Injury to the basal ganglia may result in jerky, dysrhythmic speech with associated choreoathetosis, or slowed, slurred speech lacking inflection and modulation, associated with Parkinsonian features.

Speech and language deficits clearly cause functional impairments, limiting a patient's ability to communicate effectively and to interact verbally with those around him/her. This not only affects the rehabilitation program but has serious implications in terms of a patient's interaction with others and in eventually being able to live independently in the community.

Although a comprehensive evaluation is typically performed by the speech pathologist, or within the comprehensive neuropsychological evaluation, basic aspects of speech and language can be assessed at bedside during the neurologic examination. The physician should observe the patient's spontaneous speech for fluency and syntax. Receptive language skills can be evaluated by having the patient follow one-, two-, and three-step verbal and written commands. Often, patients with receptive language impairments can "hide" their deficits through reliance upon subtle nonverbal cues of the examiner. Families may argue that an aphasic patient is actually understanding more than is true due to this effect. The keen examiner may test for this by employing subtle misdirection. An example would be to ask the patient to "point to the floor" while simultaneously pointing their hand to the ceiling. The receptively-impaired patient will mimic the examiner's movement, having misunderstood the verbal instruction. Similarly, counterintuitive commands such as "touch your right hand to your right elbow" can be used. Finally, asking questions without offering voice inflection or head nods/gestures will often result in a confused nonresponse by such patients with receptive language deficits.

Patients should be asked to name various common objects. Repetition can be assessed by asking the patient to repeat "no ifs, ands, or buts." Patients can be asked to read the newspaper or daily menu aloud, and to write from dictation. Articulation can be grossly assessed by listening to the patient's speech during the interview by having the patient repeat certain test phrases such as "Methodist Episcopal."

Spatial Orientation/Perception

Patients with focal injuries to the nondominant parietal lobe will often have difficulty with spatial orientation and perceptual tasks. This may be manifest as constructional apraxia, characterized by difficulty drawing or copying geometric designs. Disorders of body image may also be evident, manifested by a dressing apraxia, or neglect of the contralateral side of the body. The most serious form of neglect is anosognosia, or the inability of one to recognize one's own deficits.

Perceptual impairments and neglect are a serious hindrance to progress in the rehabilitation program. Patients with poor spatial orientation often wander or get lost. Patients with neglect are a safety risk because they often don't appreciate or pay attention to their deficits. Inattention to the affected side may cause a patient to accidentally roll over on a paretic arm or dangle it in the spokes of a wheelchair. Patients may be unable to safely negotiate their wheelchairs down a hallway or turn into an open doorway without striking a wall.

Constructional praxis may be assessed at bedside by having the patient draw simple geometric figures such as a square or triangle, or more complex forms such as two intersecting pentagons. Patients should be able to bisect a line at the midline and draw an accurate clock face. Neglect can often be identified at bedside by observation; the patient may not attend to his affected side or may ignore his motor or sensory deficits, or miss food or other desired items positioned in the impaired hemi-space.

Affect, Mood, and Behavior

Affect is an external facial expression (smile, frown, tear, laugh), while mood refers to an internal emotional state (happiness, sadness, fear, anger). While affect can be observed, mood can only be revealed by the patient. Inferring the internal mood-state of the patient with neurologic injury through observation only (i.e., relying upon affect in isolation) should be avoided. Neurologic emotional lability ("pseudobulbar") syndromes may remove the correlation of an affective display (tearfulness) with its typically associated mood (sadness). It is recommended that both mood and affect be independently evaluated: affect through direct observation and mood by asking the patient.

Disturbances of affect and mood are common in the early recovery period following traumatic brain injury, especially upon recovery from coma,[3,27] but may be seen even years after injury.[28] Acute patients may experience delirium with disorientation and confusion, distractibility, restlessness, irritability, hallucinations, and delusions. These manifestations are most common in patients who have evidence of frontal or temporal lobe damage.[29] Delirium may also be caused by medication side effects, metabolic abnormalities, or infection.

Later in the recovery period, a change in personality, affect, and mood may be evident as a result of damage to the frontal lobes and limbic structures. Patients may be irritable and aggressive, demonstrate childish behavior, and show exaggeration of their premorbid personality. Other common features of frontal lobe injury include emotional disinhibition, emotional blunting, diminished drive and initiative, egocentricity, perseveration, mental rigidity, affective lability, loss of temper control, and impatience.[3,11] Patients with lesions

of the basiomedial frontal cortices demonstrate impairment in social judgment and in sexual control.[3] Patients with injury to the dorsolateral frontal cortices also demonstrate difficulty with "executive skills," or the inability to plan and execute a complex task.[11]

Both behavioral absences and excesses may be difficult to manage, and left unaddressed, can complicate or even sabotage the rehab process. Patients who are apathetic and lack initiative often do not put forth the maximum effort in therapies. Patients who demonstrate lack of impulse control, aggressiveness, and sexual inappropriateness are often disruptive not only to staff but to other patients participating in the program. Furthermore, family members may have difficulty adjusting to a change in their behavior. It is important for the physician and rehab team to identify these behavioral abnormalities, to develop an optimal behavior modification program to minimize disruptive behavior, and to design the most effective overall rehabilitation strategies to address these problems.

Although not usually assessed formally in the neurologic examination, behavior and affect can be observed during the patient interview. Further information regarding patient behavior can be obtained from nursing staff and from more detailed testing performed by the rehabilitation neuropsychologist. Premorbid behavioral status should be ascertained from family members. Typically, post-TBI behavior is a complex product of premorbid personality, the brain injury itself, and emotional reactions to that injury.

Cranial Nerve Examination

Cranial Nerve I

Modern research has indicated that olfactory dysfunction (anosmia) is a common, though commonly undetected, sequela of traumatic brain injury. It is related to brain injury severity in general, and orbital-frontal cortical injury in particular.[30] While historical estimates of incidence ranged from 4 to 33%,[31–33] it has recently been shown that standardized assessments reveal the incidence to be closer to 50 to 60% following TBI.[34,35] Notably, approximately 40% of these impaired patients were unaware of their olfactory sensory loss. For this reason, reliance upon self- and/or family-report of anosmia is ill-advised.

Impairment in detection and/or recognition of smell occurs due to shearing injury to olfactory pathways which extend from the olfactory epithelium through the cribriform plate to the entorhinal cortex.[36] Notably, occipital blows are five times more likely to lead to such shearing injury than are frontal blows.[37] It has long been recognized that anosmia can lead to functional impairments, including diminished life satisfaction, interference with certain occupations, and potential safety problems due to the inability to detect signs of danger such as smoke or the smell of spoiled food. Evidence now suggests that post-TBI anosmics also have a greater incidence of frontal-lobe mediated executive skill deficits which places them at risk for poor vocational and community integration outcomes.[34–38]

Smell may be assessed at bedside by having the patient identify various common odors such as tobacco or cloves. Noxious stimuli, such as ammonia, should be avoided since these stimulate the trigeminal nerve rather than the olfactory nerve. Standardized "scratch and sniff" measures are now commercially available and offer the advantages of ease of administration and demonstrated validity.[39]

Cranial Nerve II

The optic nerve and anterior visual pathways are affected in approximately 5% of TBI patients,[40] with 3% experiencing persistent visual field defects, impaired visual acuity, or blindness.[41] Loss of vision occurs most commonly following frontal injuries, particularly if there are fractures of the orbital bones. The optic nerve and pathways may be injured

due to shear forces, mechanical stretching, contusion, or vascular insufficiency.[42] Deficits include monocular blindness due to optic nerve injury, bitemporal hemianopsia due to ischemia of the optic chiasm, homonymous hemianopia due to injury to the optic radiations, and cortical blindness due to lesions of the calcarine cortex. The latter is particularly common after head injury in children and is usually transient.[31]

Functionally, visual impairment results in diminished personal pleasure and may limit the patient's mobility due to impaired visual acuity and altered depth perception. In the rehab setting, visual impairments may lead to difficulty with wheelchair propulsion and ambulation and may cause safety concerns. Patients may have difficulty performing daily cares, ultimately leading to a loss of independence. Community reentry skills, such as returning to work or resumption of driving, may also be affected.

Optic nerve function is assessed by pupillary response, fundoscopic examination, visual field testing, and measurement of visual acuity. In comatose patients, optic nerve function is best assessed by the pupillary response. In the case of unilateral optic nerve injury, neither the ipsilateral nor the contralateral pupil constricts when light is shone in the affected eye. Both pupils constrict, however, when light is shone in the unaffected eye. An afferent pupillary defect may also be demonstrated by the swinging flashlight test. When the light is swung back and forth from eye to eye, the pupil on the affected side will dilate as the light is swung to that eye (Marcus Gunn phenomenon). In longstanding optic nerve atrophy, the optic disc may appear pale on fundoscopic examination. The presence of papilledema suggests the possibility of posttraumatic hydrocephalus or increased intracranial pressure of other cause and warrants further investigation.

Visual acuity may be impaired as a result of traumatic injury to the orbit and optic nerve or due to diffuse injuries to the occipital lobe. Acuity may be assessed at bedside by having the patient read a handheld Snellen acuity chart or Rosenbaum near-vision card[42] or by bedside reading materials such as a newspaper or menu. Visual fields are assessed at bedside by confrontation testing. Each eye should be tested separately with comparison of the patient's visual fields to the examiner's.

Cranial Nerves III, IV, and VI

Injury to the oculomotor, trochlear, or abducens nerves occurs in 2 to 8% of patients following head injury. These nerves may be injured in the orbit as the result of orbital wall fractures, or in the cavernous sinus due to basilar skull fractures.[43–45] Delayed injury to these nerves can occur years after TBI due to development of carotid–cavernous sinus fistulas.[46,47] The cranial nerve nuclei or intranuclear pathways may also be injured as a result of brainstem injury.[48] Injury may result in eye deviation, dysconjugate gaze, or abnormal head postures, with subjective complaints of diplopia. Supranuclear or conjugate gaze paresis may result from injury to the gaze centers in the frontal or parietal lobes, horizontal gaze center in the pons, or vertical gaze centers in the midbrain. Diplopia, or gaze paresis, may cause functional impairment by interfering with patients' visual-motor tasks.

Eye movements are evaluated by having the patient track an object in the six cardinal positions of gaze. The inability to move the eye upward, inward, or downward, with preserved lateral movement suggests injury to the oculomotor nerve. This is often accompanied by ptosis and pupillary dilatation. Injury to the trochlear nerve is manifested by the inability to intort the eye or move it downwards, often accompanied by head tilt to the nonaffected side.[49,50] The inability to move the eye laterally, with preservation of other ocular movements, suggests injury to the abducens nerve. In the comatose individual, eye movements can be assessed by oculocephalic or oculovestibular testing (see section on Cranial Nerve VIII).

Cranial Nerve V

A trigeminal nerve lesion occurs in 3.6% of head-injured patients.[51] The injury is most commonly extracranial due to facial fracture and can involve any or all of the branches of the trigeminal nerve. Rarely, the trigeminal nerve may be injured as a result of trauma to the brainstem or due to basilar skull fracture involving the petrous bone.[52] In the latter instance, associated hearing loss and ipsilateral facial weakness are common.

Injury to the sensory branches of the trigeminal nerve results in hemianesthesia of the face. Involvement of the ophthalmic branch leads to corneal anesthesia and potential corneal abrasion. Motor branch involvement results in weakness of the muscles of mastication and impairment of chewing. Loss of sensation in the mouth may cause pocketing of food and increases the risk of aspiration.

In the comatose patient, trigeminal nerve sensory function can be assessed by testing the corneal reflex (sensory limb). In alert, attentive patients, facial sensation can be evaluated with pinprick or cotton swab in the three nerve divisions. Trigeminal motor function can be tested by assessing masseter and pterygoid muscle strength. With trigeminal nerve injury, the jaw will deviate toward the affected side.

Cranial Nerve VII

The facial nerve is injured in approximately 3% of head-injured patients, most commonly due to temporal bone fractures. Associated hearing loss is common. Brainstem trauma may also result in injury to the facial nerve nucleus. Facial nerve injury results in ipsilateral weakness of muscles of the upper and lower face. Injury to the corticobulbar pathways, due to lesion of the frontal lobe, internal capsule, or upper brainstem, also results in facial weakness but spares the upper facial musculature.

Facial nerve injury can cause significant functional impairments. The inability to close the eye fully and an impairment in lacrimation can lead to corneal dryness, abrasion, and pain. Facial weakness may impair swallowing or cause a flaccid dysarthria.

Facial nerve function can be assessed in the comatose patient by the corneal reflex (motor limb). In the attentive patient, facial muscle strength can be assessed by asking patients to smile, purse their lips, whistle, raise their eyebrows or forehead, and close their eyes.

Cranial Nerve VIII

Both the cochlear and vestibular nerves may be injured as a result of head trauma. Hearing loss occurs in 18 to 56% of head-injured patients[53] as a result of injury to the inner ear and related structures. Longitudinal fractures of the temporal bone, most commonly caused by a blow to the temporoparietal area, result in conductive hearing loss due to dislocation and disruption of the ossicles.[54] Transverse fractures of the temporal bone, caused by occipital or frontal blows, cause sensorineural hearing loss, vertigo, and disequilibrium due to direct injury to the acoustic nerve, trauma to the cochlea, or labyrinths.[55,56] Lesions of the auditory or vestibular nuclei occur rarely as a consequence of brainstem contusions. There is not much functional impairment due to hearing loss since the deficit is usually unilateral. Vestibular insults are usually more problematic, leading to dizziness and difficulties with balance and coordination.

Hearing may be evaluated at bedside by whisper or finger rub. Air and bone conduction are assessed by the Rinne and Weber tests. Patients with suspected hearing loss should be referred for more detailed audiometric evaluation.

The presence of direction-fixed horizontal nystagmus usually suggests unilateral vestibular injury. Vertical nystagmus usually results from direct brainstem injury. Nystagmus may also occur as a consequence of medications, particularly anticonvulsants. In the

comatose individual, vestibular function may be assessed by testing the oculocephalic reflexes (Doll's eyes) and oculovestibular reflexes (ice-water calorics). In testing the oculocephalic reflex, rapid turning of the head results in conjugate eye deviation to the opposite side. Injury to the vestibular apparatus or vestibular pathways results in absence of eye deviation. Dysconjugate eye movements suggest injury to the internuclear pathways in the brainstem. In performing oculovestibular testing, the patient's head is tilted to 30°, and the external auditory canal is irrigated with ice water. A normal response is characterized by tonic conjugate deviation of the eyes toward the side of irrigation. In an awake individual, there may be nystagmus, with the fast component directed away from the site of irrigation. Injury to the vestibular pathways results in failure of eye deviation, while injury to the internuclear brainstem pathways results in dysconjugate eye movements. Patients with suspected injury to the vestibular pathways may be more formally assessed with electronystagmography.

Cranial Nerves IX and X

The glossopharyngeal and vagus nerves are only rarely affected in traumatic brain injury, usually the result of basilar skull fracture with extension into the foramen magnum.[51] These nerves are responsible for laryngeal and pharyngeal sensory and motor function, respectively, with injury resulting in impaired phonation and swallowing.

Glossopharyngeal and vagus nerve function are assessed at bedside by the gag reflex. The reflex is diminished or absent on the side of nerve injury. In addition, the palate and uvula may be deviated to the opposite side. The gag reflex may be pathologically brisk when there are lesions of the corticobulbar pathways bilaterally, usually a consequence of extensive injury to the frontal lobes or deep white matter. There is usually an associated "pseudobulbar affect," characterized by emotional lability and spastic tetraparesis.

Cranial Nerve XI

The spinal accessory nerve supplies motor function to the ipsilateral sternocleidomastoid and trapezius muscles. This nerve is affected only rarely in head injury, occasionally seen following basilar skull fractures.

Spinal accessory nerve function is assessed by testing sternocleidomastoid muscle (lateral neck rotation to the opposite side) and trapezius muscle (ipsilateral shoulder shrug) strength. Impairment results in weakness of these muscles.

Cranial Nerve XII

The hypoglossal nerve provides motor function to the ipsilateral tongue. This nerve is also only rarely affected in head-injury patients as a result of basilar skull fractures or injury to the atlanto-occipital region.[57] Injury results in swallowing difficulties due to inability to manipulate the food bolus in the mouth.

The hypoglossal nerve is tested by having the patient stick out the tongue. Injury results in deviation of the tongue to the ipsilateral side.

Motor Examination

Muscle Bulk

In the traumatically brain-injured patient, generalized muscle atrophy may occur as a result of disuse following prolonged coma or immobility. Focal muscle atrophy always suggests lower motor neuron injury and should alert the physician to possible peripheral

nerve, plexus, or nerve root injury. A peroneal neuropathy, for example, may arise secondary to a dislocated knee or as a consequence of an excessively tight lower extremity cast, resulting in foot drop and atrophy of the anterior compartment of the lower leg. The median, ulnar, radial, and sciatic nerves may also be injured as a result of skeletal injury or impingement by heterotopic bone. Brachial plexus or cervical root injuries are common in motorcycle accidents, particularly when the patient lands on his neck and shoulder.

Muscle bulk is generally assessed by observation. Focal atrophy can be discerned by comparing the circumference of the limb in question to the opposite side.

Muscle Tone

Various abnormalities of muscle tone may develop in the head-injured patient. Spasticity is the most common type of tone abnormality seen in brain-injured patients. Spasticity is defined as a velocity-dependant increase in resistance to passive movement, predominantly affecting the flexor groups in the upper extremities and extensor groups in the lower extremities. Tone may also be increased in the truncal muscles. Spasticity results from injury to the corticospinal tracts and is usually associated with muscle weakness, hyperreflexia, and an extensor plantar reflex response (Babinski sign).[58] Rigidity is defined as an increase in resistance to passive movement, independent of velocity, and is most prominent in the flexor muscle groups of the upper and lower limbs. Cogwheel rigidity may result from direct injury to the basal ganglia; however, this is more common as a consequence of anoxia or a side effect of neuroleptic medications. Paratonia, or the inability of a patient to voluntarily relax his muscles during passive movement, is seen as a consequence of bilateral frontal lobe injury. Hypotonia, or diminished muscle tone, is occasionally seen as a consequence of cerebellar injury.

Increased tone may cause pain in the affected limb and may impede rehabilitation by limiting mobility and transfer skills, performance of nursing cares, and activities of daily living. Spasticity in the upper extremity may hamper fine dexterity and limit the ability to perform daily cares. Neck and head control may be impaired, leading to difficulties with grooming and feeding skills. Spasticity of the pharyngeal and laryngeal muscles may impair articulation, phonation, swallowing, and breathing. Increased tone in the trunk musculature leads to problems in positioning in bed, wheelchair seating, standing and ambulation.[58] Treatment of TBI patients with an increase in muscle tone should include daily range-of-motion exercises. Bracing and splinting can be utilized. Medications such as baclofen, tizanidine, diazepam, and dantrolene have been shown to be effective in reducing spasticity.[59] For patients who do not respond to or are unable to tolerate oral medications, placement of an intrathecal baclofen pump may be considered. This has been formally approved for management of spasticity secondary to TBI.[60] Botulinum toxin injections are often of benefit in patients with more focal spasticity, i.e., an increase in muscle tone isolated to a few muscle groups.[61]

If a routine program of passive stretching is not performed, fixed-joint contractures may develop; these occur most commonly at the wrist, elbow, knee, and ankle. Patients with ankle plantar flexion contractures may not have an adequate base of support in order to transfer safely. Contractures of the hip and knee may limit a patient's ability to stand and ambulate. Contractures of the hip adductors may limit access to the perineal area, causing problems with catheter care and skin breakdown. Patients may have difficulty turning in bed or positioning themselves properly in the wheelchair, ultimately leading to pressure ulcerations on contact points (greater trochanters, sacrum, and heels).

Muscle tone is evaluated by passively moving the upper and lower extremities with the patient fully relaxed. Movements that are commonly tested include flexion/extension of

the wrist, pronation/supination of the forearm, flexion/extension of the elbow, and flexion/extension of the knee or hip.

Range of motion of all joints should also be carefully assessed. Limited range of motion is suggestive either of contracture of that joint or heterotopic ossification, particularly if there is evidence of bony overgrowth in the joint region.[62] Heterotopic ossification will be discussed in more detail later in this text.

Muscle Strength

The two most common patterns of muscle weakness following traumatic brain injury are hemiparesis and tetraparesis due to injury to the corticospinal tracts in the cerebral hemispheres or brainstem. Weakness is usually accompanied by spasticity and hyperreflexia. Focal muscle weakness should raise the suspicion of a superimposed nerve root, plexus, or peripheral nerve injury.

Muscle weakness causes obvious functional limitations, depending on its distribution and severity. Patients with severe tetraparesis often are unable even to roll in bed without assistance and may need help with simple daily cares such as feeding and grooming. Although patients with hemiparesis usually require less physical assistance, they are often unable to transfer or ambulate independently and usually require help with daily cares.

Primary movers of the fingers, wrists, elbows, shoulders, neck, ankles, knees, and hips should be assessed. It is important to position the patient properly while conducting muscle strength testing in order to assure that the muscle being tested is appropriately isolated from other muscles with similar function. Strength is most commonly graded on the following scale:[26]

0 = No muscle contraction noted

1 = Flicker of movement (0 to 10% of normal movement)

2 = Movement through partial range of motion with gravity eliminated (11 to 25% of normal movement)

3 = Movement through full range of motion against gravity (26 to 50% of normal movement)

4 = Movement through full range of motion, against gravity, with minimal resistance from the examiner (51 to 75% of normal movement)

5 = Normal muscle power (76 to 100% of normal movement)

Abnormal Movements

Abnormal postures or motor movements may result directly from traumatic brain injury or as a consequence of medication side effects (Table 1.2). Dystonia, defined as inappropriate prolonged contraction of muscles resulting in distortion of the limb,[63] can occur secondary to injury to the basal ganglia or as a side effect of neuroleptic medications.[63–65] Similarly, dyskinesias, characterized by insuppressible, stereotyped, automatic movements of the limbs or orofacial musculature, may also result from basal ganglia injury or from medication side effects. Choreoathetosis, or slow, writhing, spasmodic, involuntary movements of the limbs or facial musculature, is most commonly seen as side effect of anticonvulsants, dopaminergic medications, adrenergic medications, oral contraceptives, or antipsychotic medications, but may also result from traumatic injury to the basal ganglia.[66] Ballismus, characterized by violent flinging of the proximal upper extremity, may occur from direct injury or hemorrhage in the subthalamic region. Tremor has also

TABLE 1.2

Movement Disorders Associated with Traumatic Brain Injury

Dystonia
Dyskinesia
Choreoathetosis
Ballismus
Tremor
Myoclonus
Asterixis
Parkinsonism

been reported as a consequence of head injury. Most frequent is a postural or kinetic tremor which may involve the head or upper or lower extremities.[67]

Myoclonus is defined as sudden, brief, shock-like involuntary muscle contractions. These can be focal, segmental, or generalized, and may be stimulus induced.[68] Myoclonus has also been reported as a direct consequence of head injury, often associated with cerebellar, basal ganglia, or pyramidal signs.[69–71]

Myoclonus may also result from complications including metabolic abnormalities (renal or hepatic failure, hyponatremia, or hypoglycemia), medication side effects (L-Dopa), or hypoxic brain injury.[68] Asterixis is defined as an involuntary lapse of posture occurring at a joint during tonic muscle contraction.[72] This is usually detected as a wrist flap while holding the arms outstretched with the wrists extended. Asterixis has been reported as a consequence of injury to the thalamus, internal capsule, midbrain, or parietal cortex, but is more commonly associated with toxic/metabolic encephalopathy (hepatic or renal failure), or use of anticonvulsant medications.[72] Posttraumatic Parkinsonism has also been described as a result of blunt head injury.[73]

Abnormal movements interfere with both gross and fine motor function by inhibiting normal coordinated movements. These hamper the ability to perform ADLs such as feeding or grooming, and interfere with fine motor activities such as buttoning or pulling zippers. Abnormal postures may interfere with wheelchair positioning, sitting balance, standing, and ambulation.

Sensory Examination

Sensory perception is often affected in patients with traumatic brain injuries, although the sensory deficits are usually overshadowed by motor and cognitive impairments. Injury to the thalamus results in impairment of all sensory modalities on the contralateral face and body. With parietal lobe injuries, there is preservation of pain and temperature sensation, although patients are unable to localize the site of sensory stimulation. In addition, joint position sense, stereognosis (the ability to identify shapes and objects by touch), and graphesthesia (the ability to recognize figures written on the skin) are also impaired. Sensory neglect is often apparent, particularly if the nondominant parietal lobe is involved.

Sensory deficits may lead to serious functional impairments. A patient's inability to detect or localize pain may result in body injury as the result of the patient's lack of awareness and inability to protect the affected extremity. This is even a greater problem in patients who demonstrate neglect. Impaired upper extremity joint position sense may significantly affect a patient's ability to perform daily cares such as feeding or grooming because of the inability to accurately detect and control limb position in space. Lack of feeling in the hands may also impair fine motor movements, making buttoning or fastening

snaps difficult. Lower extremity sensory deficits may lead to difficulties with transfers and ambulation because of difficulties with accurate foot placement and balance. Patients with impaired sensation are at increased risk of developing pressure ulcerations, particularly if there is associated spasticity and impaired mobility.[74]

Patients' responses to sensory testing are highly subjective and dependent on factors which include level of consciousness, attention, and concentration. In a patient with a depressed level of consciousness, only gross sensory testing can be performed. In this case, sensory testing involves evaluation of the patient's grimace or motor response (e.g., withdrawal of limb) to a painful stimulus.

In an alert, cooperative patient, bedside sensory testing should include assessment of the primary sensory modalities, which include pain, light touch, vibration, and joint position sense. Responses should be compared from side to side and between upper and lower extremities. If the primary sensory modalities are intact, higher cortical sensory functions can be assessed. Graphesthesia can be evaluated by asking the patient to identify a letter or number traced in the palm of the hand. Stereognosis is tested by having the patient identify an object or shape placed in the hand. Localization of a sensory stimulus can be evaluated by touching a body part with either a pin or cotton swab and asking the patient to specifically identify the area of stimulation. Sensory neglect can be assessed by double simultaneous stimulation. Patients with neglect will be able to detect a stimulus on either limb when tested individually but will neglect the affected side when the limbs are stimulated at the same time.

Coordination

Coordination is modulated by various central and peripheral nervous system structures, including the corticospinal tracts, basal ganglia, cerebellum, and sensory pathways. Most severe traumatic brain injuries cause diffuse structural injury and can affect any of these systems. Injury to the corticospinal tracts results in muscle weakness and slowing of gross and fine motor tasks. Basal ganglia lesions cause slowed initiation of movement and bradykinesia. Cerebellar injury may result in limb and truncal ataxia, dysmetria (inability to gauge distance, speed, and power of movement, resulting in an overshoot or undershoot of the target), dysdiadochokinesia (impairment in performance of rapid alternating movements), dyssynergia (decomposition of movement, resulting in lack of speed and skill in performing complex motor movements), and intention tremor.[26] Sensory pathway insults, particularly those involving the posterior columns, cause ataxia due to impaired proprioception.

Incoordination can affect a patient's ability to perform either gross or fine hand movements necessary to perform daily cares. Patients may have difficulty bringing food to their mouths and may need assistance with dressing, particularly with buttons, snaps, and shoelaces. Writing may be illegible. Truncal ataxia may impair sitting and standing balance, causing problems with wheelchair seating, standing, and ambulation.

Upper extremity coordination can be assessed by various bedside tests. On finger-to-nose testing, the patient alternates between touching his nose and touching the examiner's finger held at arm's length from the patient. The smoothness and accuracy of the movement are noted, looking for evidence of dysmetria, dyssynergia, or intention tremor. Rapid alternating movements can be evaluated in several ways. Patients can be asked to rapidly flex and extend the fingers, rapidly oppose the tips of the index finger and thumb, alternate hand patting between the palmar and dorsal surface (pronation/supination), or alternate touching the tip of the thumb to the tips of each finger in succession. The speed of movement, rhythm, smoothness of movement, and accuracy should be assessed.

Lower extremity coordination can be evaluated by the heel-to-knee-to-toe test. The patient is asked to touch his heel to his knee and slide his heel up and down his lower leg. Again, the smoothness and accuracy of movement are assessed. Alternatively, the patient can be asked to draw a figure eight or circle in the air with his great toe. Rapid alternating movements can be evaluated by asking the patient to tap his foot rapidly or repeat a pattern of tapping.

Reflexes

Evaluation of muscle stretch reflexes helps localize the sites of brain injury. Hyperactive reflexes suggest injury to the corticospinal tracts and are associated with muscle weakness, spasticity, and an extensor plantar response (Babinski sign). Hypoactive reflexes occur most commonly with diseases or injuries of the lower motor neuron. Focal hyporeflexia, particularly if involving one reflex or reflexes in a single limb, should always raise the suspicion of a spinal root, plexus, or peripheral nerve injury. Diffuse hyporeflexia is most often associated with peripheral neuropathy (e.g., secondary to diabetes, chronic alcohol abuse, or renal disease) but also occurs with cerebellar injury.

The presence or exaggeration of other reflexes also helps localize brain injury. A hyperactive jaw jerk (masseter reflex) suggests bilateral corticospinal tract injury above the level of the mid pons. The presence of primitive reflexes, also called *frontal release signs* (i.e., sucking, grasp, and snout reflexes), suggests bifrontal or diffuse cerebral injury.

The biceps, triceps, brachioradialis, patellar, and Achilles muscle stretch reflexes are most commonly tested. Responses are graded on a 0 to 4 scale:[26]

0 = Absent reflex
1 = Diminished reflex
2 = Normal reflex
3 = Hyperactive reflex, although not necessarily pathologic
4 = Pathologically hyperactive reflex, with clonus or spread to other muscles in the ipsi- or contralateral limb

The plantar response can be elicited in a number of ways. The most common maneuvers are the Babinski technique (performed by stimulating the sole of the foot with a blunt object) and the Chaddock maneuver (performed by stimulating the lateral aspect of the foot). A normal response is plantar flexion of the toes, whereas an abnormal response is characterized by dorsiflexion of the great toe with fanning of the other toes.

Posture and Gait

Traumatic brain injury, because of injury to the motor and sensory systems, commonly results in abnormalities in posture and stance and difficulty walking. Patients with spastic hemiparesis may have difficulty standing because of trunk instability and may be unable to adequately weight-shift in order to ambulate safely. If ambulation is possible, there may be significant gait deviation. Weak hip flexors and ankle dorsiflexors result in impaired swing-through of the limb and inadequate toe clearance during the swing phase of gait. Spasticity and contractures may limit range of motion at the hip, knee, and ankle. Decreased arm swing and circumduction of the lower extremity may be noted. Assistive devices (walker, cane) and lower extremity orthoses may be necessary. Patients with basal

ganglia injury often demonstrate stooped posture and shuffling gait. Patients with marked proprioceptive deficits may have difficulty with foot placement and balance.

The patient should be observed in a sitting and, if possible, standing position for assessment of posture and static balance. Patients can be asked to stand with their feet together and arms outstretched, or to stand on one leg to maintain their balance. Dynamic balance reactions can be tested by pushing the patient off balance, noting whether he is able to maintain his position, and whether he demonstrates protective reflex reactions. If the patient is able to ambulate, gait should be assessed. Attention should be given to position of patient's head and trunk, and whether arm swing is normal and symmetrical. The movement of patient's pelvis and hip, knee, ankle, and foot should also be observed. Balance and coordination can be further assessed by having the patient attempt to walk heel to toe in a straight line (tandem gait).

Change in Status

One of the difficulties in patient assessment is distinguishing deficits that are due directly to the traumatic brain injury from those that are secondary to systemic disease or complications of the head injury. At any point during the patient's recovery, deterioration in neurologic status should always alert the physician to the possibility of such a complication. These include development of posttraumatic epilepsy, hydrocephalus, central nervous system or systemic infections, and toxic/metabolic encephalopathies.

Posttraumatic Epilepsy

Epileptic seizures occur in 2.5 to 5% of patients with traumatic brain injury. These are most commonly secondarily generalized tonic–clonic seizures, although approximately 20% are of complex partial type, manifested by staring, interruption of speech, and automatisms.[75] Early epilepsy (i.e., seizures occurring within the first week following injury) is most common in children under age five and in adults with depressed skull fracture or intracranial hemorrhage. Late epilepsy begins months to years following injury and is felt to be secondary to an epileptogenic scar.

Any alteration in level of consciousness, particularly if intermittent and associated with abnormal motor movements, should raise the suspicion of an epileptic seizure. An EEG is necessary to document seizure activity electrically and to localize the seizure focus. Urgent neuroimaging is warranted to rule out the possibility of an acute structural brain lesion such as hemorrhage or abscess. The possibility of metabolic abnormalities such as hypoglycemia, hyponatremia, hypomagnesemia, or underlying infection (systemic or central nervous system) can lower seizure threshold and should also be considered.

Hydrocephalus

Ventricular dilatation is seen in 29 to 72% of patients following traumatic brain injury.[76] This is most often a consequence of diffuse brain injury with compensatory ventricular enlargement (hydrocephalus ex-vacuo). Hydrocephalus may also develop as a result of impairment in the flow or absorption of cerebrospinal fluid.[77] The true incidence of posttraumatic extraventricular obstructive hydrocephalus, characterized by ventricular enlargement without concomitant enlargement of the sulci, is probably approximately 8%,[78] with the incidence of symptomatic hydrocephalus less than 1%.[79]

Symptoms of hydrocephalus range from loss or alteration of consciousness to the classic triad of normal pressure hydrocephalus, which includes urinary incontinence, gait apraxia, and memory deficits. Any patient with a deteriorating level of consciousness or the clinical features of normal pressure hydrocephalus should be evaluated with a head CT or MRI scan. Additional studies (lumbar puncture, radionuclide cisternography) may also be necessary for diagnosis.

Infection

Intracranial infections, including meningitis, brain abscess, or encephalitis, can occur in patients following traumatic brain injury. Most susceptible are patients with a basilar skull fracture with extension into the paranasal sinuses or middle ear, or those who have had intracranial surgery.[80] Signs and symptoms of intracranial infection include fever, nuchal rigidity, depressed level of consciousness, and focal neurologic signs, including seizures. Workup should include a neuroimaging procedure of the brain. If there is no evidence of a mass lesion, a lumbar puncture should be performed.

Systemic infections (e.g., urinary tract infection or pneumonia) can also cause fever and depressed level of consciousness, especially in patients with underlying brain injury. Seizure threshold is also lowered in these individuals. Any change in patient behavior, deterioration in level of consciousness, or development of breakthrough seizures should raise the possibility of infection. Workup should be guided toward locating the source of infection so that appropriate treatment can be instituted as quickly as possible.

Toxic/Metabolic Encephalopathy

Toxic encephalopathy, due to medication side effects, is common in the head-injured population. Any change in patient's behavior, depressed level of consciousness, or sudden appearance of a movement disorder should raise the suspicion of a medication side effect. The most common offenders include sedative/hypnotics, neuroleptics, and anticonvulsants. Fortunately, these side effects are usually reversible upon cessation of the medication. Other causes for encephalopathy, such as infection or metabolic abnormalities (hyponatremia, hypernatremia, hypocalcemia, hypoglycemia, hyperglycemia, etc.), should be ruled out.

Endocrinologic Dysfunction

Pituitary hormonal insufficiency can occur after TBI. Those at greatest risk include patients with low Glasgow Coma Scale scores, diffuse brain swelling, associated hypoxic or hypotensive events, or concurrent subarachnoid hemorrhage.[81] Laboratory screening of pituitary function, including thyroid, gonadotrophin, cortisol, and growth hormone levels, should be considered in these high-risk individuals.

Depression

The onset of severe mood disorders following TBI can mimic other neurological complications and can impede the rehabilitation process. Persons recovering from severe TBI are at two to five times higher risk of developing depressive illness compared to the general population.[82] Therefore, distinguishing transitory sadness from depression (the former responds to subsequent good news while the latter does not) and knowing when and how

to intervene is critical.[83] The involvement of a rehabilitation neuropsychologist within the interdisciplinary treatment team affords tremendous benefits in this regard, as the careful analysis of premorbid, injury-related, and adjustment-to-injury variables will be needed. Should the presence of a clinical mood disorder be established, the availability of modern serotonin agonist antidepressants (SSRIs), which are often "activating," offer significant advantages over first-generation agents. This is because the older drugs, especially the tricyclic compounds, are often sedating and require extended titration to reach clinically effective dosages. In the TBI population with the near-universal goals of increased attentional clarity and safe mobility, excessive sedation is clearly contraindicated. In addition, the rapid action and relatively benign side-effect profile of the SSRIs generally make them a much better choice for use with patients with TBI. Often, it is a combination of medication and psychotherapy which is most effective in assisting the patient to adapt to the chronic psychosocial changes resulting from TBI.

Summary

The neurologist has a key role to play in the medical and therapeutic management of the TBI patient in the postacute rehabilitation environment. The role extends beyond cursory neurological examination, encompassing occasionally complex neurological diagnosis and management. The neurologist should be comfortable in interfacing with physiatry, otolaryngology, psychiatry, neuropsychology, and all allied health professionals to formulate an optimum approach to comprehensive postacute rehabilitation of the TBI patient.

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2

Posttraumatic Epilepsy and Neurorehabilitation

Theresa D. Hernández, Paul M. Levisohn, and Dean K. Naritoku

CONTENTS

Introduction

Two percent of patients with traumatic brain injury (TBI) experience early seizures, defined as occurring while the patient is still suffering from the direct effects of the head injury, usually within the first 24 hours of injury, though up to 2 weeks later in those with severe head trauma.[1] There is a 3.6-fold increase in late seizures (after the acute effects of head trauma have resolved). The majority of these late-occurring seizures occur in the first year following TBI, though some increased risk continues for 4 years after the trauma. By definition, the occurrence of multiple seizures (two or more) is defined as epilepsy. While epilepsy (i.e., late-occurring seizures) has long been recognized as a common sequel to brain injury, progress in understanding the pathophysiology and treatment of posttraumatic epilepsy has been limited. Consequently, clinicians have little information regarding appropriate therapy of posttraumatic epilepsy, and as a result, therapy of posttraumatic epilepsy has remained empirical and arbitrary. The decision to initiate or withhold antiepileptic drug therapy has far-reaching implications for rehabilitation of the traumatic brain-injured patient. Inappropriate use of anticonvulsants may cause unnecessary cognitive impairment in those persons not requiring medication. At the same time, experimental data suggest that certain types of seizures may retard functional improvement during recovery from brain injury, while other types have no deleterious consequences.

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Thus, it is crucial to differentiate patients who will require and benefit from antiepileptic drug therapy from those who will not.

Evaluation of Episodic Behavioral Changes

Episodes of abnormal behavior occur commonly after severe head injuries and present a diagnostic challenge for the treating physician. There are many potential etiologies for these episodes; therefore, it is crucial to determine the correct diagnosis in order to select the most appropriate and efficacious therapies to avoid iatrogenic complications. Several disease entities result in fluctuations of mental status in the posttraumatic brain-injured state. These include posttraumatic encephalopathy, seizures, postictal state, and numerous encephalopathies of toxic and metabolic etiologies. Episodic dyscontrol and disinhibition from frontal injury may occur. The encephalopathy caused by the posttraumatic state is discussed in detail by Gelber elsewhere in this volume. Mentation and attention tend to fluctuate in the TBI patient and may be mistaken for seizures, especially when there is a superimposed encephalopathy of another etiology. Simple staring spells are rarely due to seizures in the setting of TBI. Nonepileptic spells (psychogenic seizures) and misinterpretation of behaviors by caregivers may be difficult to differentiate from epileptic seizures. Metabolic encephalopathies are characterized by fluctuating mentation and may also be mistaken for seizures. Inappropriate use of antiepileptic drugs in these situations will not only be ineffective but may result in worsening of confusion or agitation.

There are many common etiologies for acute encephalopathies. Medication-induced encephalopathies rank among the most common and easily remedied causes of confusional states. As a result of the brain injury, TBI patients possess a lower tolerance to the central nervous system side effects of psychotropic drugs and other medications. Medications with anticholinergic properties are tolerated especially poorly and should be avoided because of their tendency to cause confusion, hallucinations, and memory loss, especially in older patients.[2,3] Antihistamines and many over-the-counter preparations fall into this category and are often overlooked as causes of transient or prolonged confusion. Several centrally acting sedatives, especially benzodiazepines and barbiturates, have extremely long half-lives. From a pharmacokinetic standpoint, long half-lives result in a greater interval before steady state is achieved; thus, adverse effects on the central nervous system may not be apparent until several days after the start of medications, and cause-and-effect may not be apparent. As a general rule, sedative agents (including benzodiazepines, opioids, and barbiturates) exacerbate encephalopathies; therefore, they frequently aggravate confusion or agitation in TBI patients and should be avoided. Other drugs commonly used in the TBI patient may have profound effects on the central nervous system. The medication list should always be reviewed for histamine antagonists (e.g., cimetidine) and narcotics for the possibility that they are inducing the confusional state.

Several systemic derangements are commonly associated with the posttraumatic state. Head injury may cause the syndrome of inappropriate antidiuretic hormone (SIADH) and result in hyponatremia, which, in turn, may cause confusion. Systemic infections are common in the TBI patient because of reduced mobility and presence of indwelling catheters. Any infection may manifest as an abrupt decline in mental status or agitation. An acute decline or fluctuation in mental status may herald a pulmonary, urinary tract, or wound infection. In patients with open head injuries and skull fractures, the possibility of a central nervous system infection should always be considered when there is an abrupt

decline in mental status. When in doubt, a lumbar puncture must be performed after careful assessment for potential causes of increased intracranial pressure. Hypoxia may also cause agitation and confusion and is commonly caused by pulmonary emboli from deep venous thrombosis or fat emboli. Stroke is usually not a cause of global cognitive dysfunction except in cases of multifocal, brainstem, or diencephalic strokes.

Syncope (fainting) may be confused with seizures, especially if there is associated tonic posturing. As the patient loses consciousness, there is dimming of vision and the patient appears pale and clammy. The patient generally falls limply to the ground or slumps over, if sitting. Occasionally, a brief tonic or tonic-clonic seizure occurs, adding to the confusion regarding the diagnosis. In contrast to epileptic seizures, the patient with a syncopal episode generally regains consciousness and orientation rather quickly. Medications such as tricyclic antidepressants, beta-blockers, and neuroleptics may result in systemic hypotension and lead to syncope.

Panic disorder may mimic epilepsy and is frequently seen in patients after trauma. Panic episodes may be mistaken for complex partial seizures because of altered consciousness that may occur. Panic episodes and other spells of psychogenic etiology are often misdiagnosed as medically intractable seizures, and these diagnoses should be considered in patients who are not responsive to antiepileptic medications. A careful history will help sort out this differential diagnosis. Typically, in the case of a panic attack, the patient complains of feeling dissociated, smothered, and in need of fresh air. The patient may have perioral numbness, tingling of digits, and a feeling of impending doom. Generally, full awareness of surroundings is retained and the patient is able to maintain conversation. Episodes of syncope may occur in patients with panic disorder. They are usually brief and vasovagal in nature. As opposed to patients with complex partial seizures, those with syncope due to panic attacks generally retain full awareness and can maintain a conversation until loss of consciousness. Antiepileptic drugs are ineffective for panic disorder, whereas alprazolam and imipramine are very effective.[4]

Clinical Evaluation of Seizures

Seizures should be considered when episodes of discrete and stereotypic behaviors occur with altered or lost consciousness. While an electroencephalogram (EEG) is often supportive, the diagnosis of epilepsy must be made on clinical grounds. The patient may provide only a vague or incomplete history, and the diagnosis often depends on a careful history taken from observers. Seizures are distinct, stereotyped episodes, with a definite start and end. With the exception of status epilepticus, seizures usually last only a few minutes. Afterwards, mentation will often clear within a few minutes with return to baseline, although postictal somnolence may persist. Prolonged confusion of hours to days is rarely caused by seizures and should alert the clinician to the possibility of other causes outlined above. Directed aggression is not seen during seizures or the postictal state, though confusion and undirected aggressive behaviors may be seen.

Under the International Classification of Seizures,[5] seizures are classified by whether they appear to start from a localized cortical region (partial or localization-related seizures) or from the entire brain at once (primary generalized seizures). Partial seizures are further divided by whether they impair consciousness (complex partial seizures) or not (simple partial seizures). Partial seizures are caused by localized cortical abnormalities and tend to be acquired in nature, whereas primary generalized seizures appear to be caused by

genetic factors. The partial onset seizure category encompasses seizure types that previously went under several terminologies, including Jacksonian, psychomotor, and temporal lobe seizures. Tonic-clonic (*grand mal*) seizures that result from spread of the ictus from a focal onset are described as partial seizures with secondary generalization.

The distinction in seizure onset has important implications for the pathophysiology and therapy of the seizure. Antiepileptic drugs tend to be selective for the seizure type and are analogous to cardiac antiarrhythmic drugs, which are fairly selective for arrhythmia type. Because posttraumatic seizures occur as a result of localized injury to the cerebral cortex, the resulting seizures are usually of partial onset, with or without secondary generalization. The behavioral manifestations of posttraumatic seizures relate to area of onset, usually in the penumbra of injury. Thus, injuries to the convexity of the brain often result in sensory or primary motor manifestations at seizure onset, such as a migrating paresthesias or twitching and jerking of an extremity. Seizures of the temporal lobe may result in psychic phenomena such as a sensation of fear or *deja vu*, followed by automatisms, whereas frontal seizure foci often result in aversive motor or more complex behaviors, described as hypermotor.

During typical complex partial seizures, the patient will often stare and become nonresponsive or poorly responsive to commands. Automatisms frequently occur and take the form of lip smacking and swallowing or chewing (oral–alimentary automatisms) and fidgeting with objects. Although the patient may spontaneously speak or seem to respond to commands, the language is inappropriate to the situation. The patient may affirm or disagree when questioned but, typically, gives little more than simple responses and does not follow complex commands. Generally, combativeness occurs only when the person is restrained. Thus, when directed aggression occurs, such as seeking out and striking a staff member, the episode most likely is a conscious act and not the result of a seizure. After a complex partial seizure, there is often a several-minute period of confusion and disorientation which represents the postictal state. The patient will often feel tired or exhausted and will frequently go to sleep. When present, a history of postictal confusion and lethargy often helps to identify episodes as seizures, as they generally do not occur or are brief with spells of other etiologies. Amnesia for the event is often noted in patients with complex partial seizures. Seizures emanating from the frontal lobes may be confused with nonepileptic events due to the bizarre nature of the seizures (*hypermotor*) reported, occasionally without impaired consciousness and without a period of postictal mental change.

In TBI patients, tonic–clonic (convulsive) seizures result from secondary generalization (i.e., spread of the seizure from the seizure focus at the site of trauma to other parts of the brain, especially the brainstem) which appears to moderate the initial tonic phase of the convulsion.[6] Thus, the tonic–clonic seizure episode often begins as a brief simple or complex partial seizure. The warning or *aura* that patients often describe is actually the beginning of a seizure that is perceived while the person is conscious and is actually a simple partial seizure.

Tonic–clonic seizures consist of two phases: the tonic phase and the clonic phase. These phases are easily identified with a careful history. During the tonic phase, there is a sudden stiffening of all extremities. The epileptic cry may occur during this phase as a result of sudden diaphragmatic contraction. After a brief period, the extremities become tremulous. As the tremor slows in frequency, it evolves into a rhythmic jerking motion — the clonic phase. As the seizure ends, the jerking slows and ceases. After a tonic–clonic seizure, the person is invariably groggy and disoriented for several minutes. Absence of the tonic phase or postictal confusion and somnolence in a person with convulsive behavior should raise the question of nonepileptic episodes, including psychogenic seizures. However, the postictal state may be fleeting or indiscernible after brief complex partial seizures and absent following simple partial seizures. Thus, a minimal or absent postictal state does

not exclude seizures when convulsive activity does not occur. A recent monograph by Lüders and Noachtar[7] is a useful reference for defining the clinical semiology of seizures.

Acute medical management is similar for both partial and tonic–clonic seizures. If semiconscious, the patient should be gently directed away from harm. During a convulsion, the patient should be rolled to one side to avoid aspiration if vomiting occurs. Contrary to common belief, the tongue cannot be swallowed or bitten off and objects should never be forced into the patient's mouth. Insertion of hard objects, such as spoons or "bite sticks," may break teeth and cause serious complications of fragment aspiration and pneumonia. A soft oral airway may be used if it is easily inserted. If available, oxygen via face mask may be provided, as well as suction if needed.

Epilepsy, by definition, consists of recurrent seizures. As with seizures, epilepsies have been classified; in the instance of epilepsy, the classification is into epilepsy syndromes, defined by seizure type, electroencephalographic features, etiology, and natural history.

Primary generalized epilepsies, including absence (*petit mal*), myoclonic, and generalized convulsive epilepsy, commonly begin in childhood or adolescence and are usually idiopathic or genetic in etiology. These epilepsies are diagnosed by their distinctive patterns on the EEG, which consist of bilateral synchronous epileptiform patterns. Their onset in patients following traumatic brain injury is highly unusual and should be considered coincidental. It is important to identify these epilepsy syndromes since primary generalized seizures, especially absence and myoclonic seizures, do not respond to, or may be worsened by, medications used for partial onset seizures, such as phenytoin and carbamazepine.[8] It is important to note that epilepsy itself may result in trauma and TBI; thus, preexisting epilepsy should be considered in patients with TBI and primary generalized epilepsy.[9]

Etiologic Considerations

Risk factors for posttraumatic epilepsy have been examined in several population studies. However, it is difficult to resolve the relative risk of specific characteristics of injury, such as presence of intracranial bleeding and depth of injury, because these markers tend not to be independent variables. For example, although concussion (with loss of consciousness) has been considered a risk factor for posttraumatic epilepsy, patients with mild concussive injury alone have only a 0.6% risk of seizures within 5 years, which is not significantly increased over the incidence of new seizures in the general population.[1]

Data from World War II, the Korean War, and the Vietnam War have provided the risk factors for posttraumatic epilepsy. Overall, the risk for epilepsy following nonmissile head injury was 24% in World War II[10] and 12% during the Korean War.[11] Interestingly, the risk of epilepsy following penetrating missile injury was about 35% for both World War II and the Korean War but was much higher (53%) in the Vietnam War.[12] The differences between studies on Vietnam War veterans and previous war veterans may relate to both improved care of head injury and differences in the nature of injuries. In particular, high-velocity rifles were used in combat and, when combined with improved surgical care, may have resulted in a greater percentage of survivors with epileptogenic lesions.

Risk factors have also been studied in nonmilitary injuries. As outlined above, mild head injuries do not present an increased risk of posttraumatic epilepsy. The incidence of posttraumatic epilepsy after moderate head injuries is 1.6%, and 11.6% after severe injuries.[1] In review of military and nonmilitary injuries, similar risk factors are evident. Early seizures (onset less than 1 week after TBI) also appear to be a risk factor for subsequent

seizures in several series,[13] but the increased risk appears to be dependent on the severity of head injury.[1] In civilian head injuries, early seizures are not predictive of seizure recurrence when the head injury is mild, yet do appear to increase risk in moderate to severe injuries.[1] In children, seizures occurring immediately after minor head trauma are more common, though not necessarily predictive of subsequent epilepsy.[1] The time of seizure onset also appears to be predictive of seizure recurrence. In wartime injuries, early seizures are associated with seizure recurrence and the risk of seizure recurrence increases if the onset is greater than 1 week.[14] More recently, Angeleri and colleagues[15] reported that the risk of posttraumatic epilepsy was 8.58% higher for those individuals with early seizures, and 3.43% greater for individuals with frontal or temporal lesions on CT. The degree of hypoperfusion in the temporal lobes as detected by single-photon computed tomography (SPECT) has also been correlated with posttraumatic epilepsy.[16] Also associated with increased risk of posttraumatic epilepsy (+3.49%) was the presence of an EEG focus at 1 month.

The risk of posttraumatic epilepsy in the presence of an intracerebral hematoma was estimated at 21% in nonmilitary injuries.[1] However, Guidice and Berchou[17] found intracerebral hematomas *not* to be predictive of posttraumatic epilepsy. This may be due to the fact that CT scans were used routinely in all head-injured patients at their center. Earlier studies, which did not utilize CT scanning, would not have detected intracerebral hemorrhage in milder cases that did not require surgery or cerebral angiography. Alternatively, other studies have argued that the most predictive factor for posttraumatic seizures is focal CT abnormalities.[13,18] Brain contusion with subdural hematoma was predictive of posttraumatic epilepsy in a population-based study.[19] In one small series, the development of posttraumatic epilepsy was correlated with the presence of bone fragments on CT scan studies;[20] however, the scope of this study could not establish whether the risk of bone fragments was independent of injury severity. The type of skull fracture also tends to predict the likelihood of posttraumatic epilepsy. Greater risk occurs in patients with depressed skull fractures,[1,13] while linear convexity or basilar fractures carry an intermediate risk. The value of acute magnetic resonance imaging studies in predicting posttraumatic epilepsy is unclear.

Risk factors for posttraumatic epilepsy include duration of coma,[1,17,19] genetic susceptibility to epilepsy,[21,22] and age over 65 years.[19]

When the epidemiologic studies are viewed as a group, it appears that the severity of brain injury best predicts whether posttraumatic epilepsy will occur. While there is debate on the relative risk of any single factor, it is likely that most identified risk factors are indicators of a high degree of brain injury, rather than being specific etiologies. Furthermore, posttraumatic epileptogenesis is probably dependent on several pathophysiologic mechanisms (see text below) which may partially explain the large number of identified risk factors.

Diagnostic Investigations of Posttraumatic Seizures

When faced with the new onset of seizures, laboratory studies should screen for conditions that may have lowered seizure threshold. Serum chemistries should be drawn to exclude electrolyte imbalances and, minimally, should include electrolytes, glucose, calcium, and drug screen. A complete blood count may detect a subclinical infection. Measurement of arterial blood gas in appropriate circumstances will exclude hypoxia. Imaging studies,

consisting of either computerized tomography (CT) or magnetic resonance imaging (MRI), may help identify new lesions contributing to the occurrence of seizures. Prior to initiation of antiepileptic drug therapy, complete blood count and liver function studies should be measured to define any hematologic or hepatic dysfunction and as a baseline in case of idiosyncratic reactions to medication.

The EEG is a useful tool for evaluating patients with episodic behavioral changes. Interictal abnormalities, such as epileptiform spikes or sharp waves, are often present in patients with epilepsy. A difficulty arises in that interictal abnormalities are transient, much like the seizures they attempt to detect. Thus, a normal EEG does not exclude the possibility of epilepsy. Conversely, an abnormal EEG alone does not diagnose epilepsy. As outlined in later sections, there are important consequences of antiepileptic drug therapy; thus, it is crucial that the TBI patient not be treated solely on the basis of EEG findings. The EEG does provide supportive evidence of a seizure disorder when it is clinically suspected, and its greatest utility lies in its ability to help identify whether the seizure onset is partial or generalized. Despite its limitations, the EEG is one of the most important tests in evaluating epilepsy as it provides electrophysiologic information that cannot be obtained from any other laboratory investigation.

For example, a retrospective study of EEG findings in patients with head injury revealed no predictive value of focal or generalized EEG abnormalities.[12,23] However, this study included all abnormalities and did not specifically assess the risk of epileptiform patterns. The EEG is valuable as a prognostic factor in persons who have already experienced a seizure. The interictal hallmark of epilepsy is the epileptiform spike or sharp wave. When well-formed and definite, focal spikes are predictive of seizure recurrence in both brain-injured patients[24] and in patients with seizures of unidentified causes.[25] Focal EEG findings 1 month following TBI was associated with an increased risk of subsequent epilepsy in a prospective study of risk factors following an early seizure.[15]

Prolonged EEG monitoring after traumatic brain injury has been promoted as a means by which to detect subclinical seizures and even predict posttraumatic epilepsy.[26] Postinjury EEG assessment revealed that subclinical seizures occur frequently despite anticonvulsant drug administration.[26] As many as 22% of traumatically brain-injured individuals have postinjury seizures within the first 2 weeks,[26] many of which are subclinical. Postinjury EEG monitoring may help define the impact of seizure activity on patient outcomes, especially as regards the risk for subsequent epilepsy.

The EEG study should follow the technical guidelines of the American EEG Society.[27] To briefly summarize, all studies should utilize at least 16 channels of EEG recording to allow for adequate spatial resolution and localization of EEG abnormalities. Gold disk electrodes should be used and attached to the scalp with either collodion or electrode paste to assure low electrical impedance. Needle electrodes should not be used because of their high impedance and the potential risk of blood-borne pathogens. Standard EEG montages should be used, per recommendations of the American EEG Society. Digital EEG recordings are now routinely obtained which allow for reformatting the montages, if necessary. Drowsiness and sleep-enhanced expression of epileptiform abnormalities and recording during these stages of consciousness must be performed. The patient should be partially sleep deprived during the night prior to the EEG study as this will increase the probability of recording epileptiform abnormalities and avoid the need for sedation.

There has been much debate over the advantages of special EEG electrodes used to improve the detection of interictal abnormalities. Nasopharyngeal electrodes are now rarely used. Standard scalp electrodes with high-distance electrode montages are as effective as nasopharyngeal electrodes at detecting epileptiform abnormalities and are considerably more comfortable.[28,29] Other scalp electrodes, such as T1 and T2 electrodes, are often used to increase sensitivity to temporal spikes.[30]

Prolonged EEG recording may be extremely useful in cases where the cause of altered mental status episodes cannot be ascertained by conventional means and the spells occur with enough frequency to be detected within the designated recording period. Twenty-four-hour ambulatory EEG monitoring is usually available at larger medical centers. These devices continuously record EEG and EKG activity for 1 to 2 days and may be performed on an outpatient basis. Newer digital equipment allows for higher quality recordings than was possible with analog recordings which were often limited to eight channels. Nevertheless, there are several limitations to ambulatory recording. Artifact makes interpretation of ambulatory EEGs difficult and technologists must review large amounts of data. As EEG technicians or other health care staff are not present to observe the recording, it may be difficult to later sort artifact from true abnormalities during playback. Moreover, if a diary is not carefully maintained during the recording period or the patient is unable to trigger the alarm on the recording unit reliably, it may not be possible to correlate the episodes in question with the EEG or EKG, or the episode may even be missed entirely.

Intensive neurodiagnostic monitoring involves continuous 16- to 64-channel recording of electroencephalographic, electrocardiographic, and other electrophysiologic data with simultaneous video recording of behavior. It is available at most epilepsy centers and many tertiary care facilities. These studies allow precise correlation of behavioral changes with electrophysiologic data to determine the exact etiologies of the behavioral episodes. Intensive neurodiagnostic monitoring is costly and requires hospital admission. However, it may provide the only means to obtain definitive and conclusive information. As such, it should be reserved for situations where the diagnosis cannot be determined by usual means or when nonepileptic spells are suspected. Intensive neurodiagnostic monitoring is essential for localization of epileptic foci when epilepsy surgery is contemplated.

Potential Epileptogenesis Associated with Psychotropic Medications

Behavioral and affective disorders are common after traumatic brain injury, and it is often necessary to treat the brain-injured patient with psychotropic medications. Of concern is whether these agents lower seizure threshold. In high doses, tricyclic antidepressants induce seizures, but it is less clear to what extent they are proconvulsant at clinically effective doses. Many reports of tricyclic-induced seizures are retrospective and do not take into account the normal incidence of new onset seizures. When drug monitoring has been instituted to avoid high levels, the risk has been estimated at only 0.4%.[31] Although a 0.2% risk of seizures has been estimated for fluoxetine therapy on the basis of preclinical trials, fluoxetine is anticonvulsant in experiments using epileptic rodents with convulsive seizures.[32] In a retrospective study of persons with depression and established epilepsy, antidepressant therapy actually improved seizure frequency in the majority (56%) of patients.[33] This raises the question of whether this positive effect on seizure control occurs indirectly (i.e., through improvement of depression) or, instead, by directly raising seizure threshold. Interestingly, a double-blind placebo study has demonstrated imipramine to be effective adjunctive antiepileptic therapy in intractable atonic, myoclonic-astatic epilepsy, and absence epilepsy in subjects without affective problems.[34,35] Thus, at nontoxic levels, tricyclic antidepressants may possess anticonvulsant properties for certain seizure types, despite being proconvulsant at toxic levels. This bimodal response is frequently seen in other drugs with anticonvulsant properties, such as phenytoin and lidocaine.

The ability of tricyclic antidepressants to increase seizure frequency may be selective for seizure type. For example, a selective increase of tonic–clonic seizures may occur with use of imipramine or maprotiline in patients with mixed seizure types.[35] Neuroleptics are frequently utilized in the posttraumatic state for agitated behavior and there are several reports of their proconvulsant effect. Unfortunately, little data exist on the actual risks of antidepressants and neuroleptics in the setting of traumatic brain injury. However, from existing information on these agents, it appears that the actual clinical risk of seizure exacerbation by psychotropic medications is small and is usually far outweighed by the need to effectively manage a severe affective or disruptive state in the TBI patient. Thus, these medications should be used when necessary for psychiatric and behavioral problems. As a caveat, though the neuroleptics may not pose a risk for seizures after TBI, there are data showing that the administration of these drugs is detrimental to neurobehavioral recovery in this population.[36]

Therapy for Posttraumatic Epilepsy

It is common practice to initiate antiepileptic drugs (AED) following acute TBI as prophylaxis against seizures. Such treatment decreases the risk of early seizures but does not appear to prevent late-occurring seizures, that is, posttraumatic epilepsy. However, studies on prophylaxis regarding the use of newer AED is lacking.[37,38] Nevertheless, it is appropriate to treat those with late occurring seizures, e.g., posttraumatic epilepsy. Initiation of antiepileptic drug therapy should begin only after careful evaluation of the patient and seizures have been clearly identified. Almost all clinicians will begin therapy once two seizures have occurred, but there is debate on whether therapy should be initiated after the first seizure. Many clinicians will not treat a single seizure without recurrence; others will treat, depending on the situation. As outlined in later sections and based on recent meta-analysis of anticonvulsant prophylaxis trials,[39] as well as a Practice Parameter published by the American Academy of Neurology, there are clearly no firm data to justify long-term prophylactic AED therapy in TBI patients who have not experienced a seizure.[38]

Selection of AED therapy must be based on several factors, including efficacy for seizure type and side effects. A specific AED may be quite selective for seizure type, thus necessitating seizure classification. Posttraumatic epilepsy is caused by focal or multifocal injury and consists of partial onset seizures and secondarily generalized tonic–clonic seizures. Accordingly, appropriate AED for posttraumatic epilepsy are those used for partial onset seizures. The most commonly used antiepileptic drugs are listed in Table 2.1.

The effectiveness of AED in the treatment of epilepsy of all etiologies has been extensively examined. A multicenter, double-blind, randomized study compared the efficacy of phenytoin, carbamazepine, primidone, and phenobarbital against partial onset seizures. All of the drugs were equally efficacious in terms of seizure control.[40] However, barbiturates were tolerated poorly, resulting in a high dropout rate in these treatment groups.

Similar results were obtained in a British study involving patients with newly diagnosed partial onset epilepsy which compared the efficacy of carbamazepine, phenytoin, and valproic acid.[41] Valproic acid exhibited the same efficacy as phenytoin and carbamazepine against partial onset seizures and convulsion, suggesting its usefulness for these seizure types. A Veterans' Administration study compared the efficacy of carbamazepine to valproic acid for partial onset seizures and indicated a modest, but significantly lower, efficacy of valproic acid against complex partial seizures.[42] Nevertheless, valproic acid appeared

Table 2.1

Guide to AED Dosing and Adverse Effects

Medication/ Target Dose mg/d [Pediatric Dose mg/kg/d]	Target Serum Levels	Idiosyncratic	Dose Related	Age Specific/Other
Carbamazepine **800–1000** [10–30] mg/kg/day	4–12 μg/ml	Dermatologic, hematologic, hepatic (fatal 1/ 50–200,000)	Vertigo, visual disturbance (diplopia), leukopenia	Hyponatremia in adults, leukopenia, liver induction, myoclonus in pts. with general S/W
Ethosuximide [15–40] mg/kg/day	40–100 g/ml	Leukopenia, SLE, nephrotic sx, rash	Sedation, GI upset	Behavioral
Felbamate **2400–3600** [45–60] mg/kg/day	30–100 g/ml	Aplastic anemia, hepatic failure, rash (rare)	Anorexia, insomnia, headache, irritability	Aplastic anemia, drug interactions
Gabapentin **1800–3600** [30–100] mg/kg/day	4–20 g/ml	Rash (rare)	Somnolence, irritability, wt. gain	Renal excretion, no drug interactions
Lamotrigine **300–500** [1–15] mg/kg/day (with vs. w/o inducer) (dose depends on presence of hepatic enzyme inhibitors)	3–20 g/ml	Rash, hypersensitivity reaction	Ataxia, diplopia, GI, headache	Rash (1–5% in children), Stevens-Johnson
Levitiracetam **1200–2400** [20–60] mg/kg/day	5–50 g/ml	None reported to date	Somnolence, ataxia	Agitation, aggression
Oxcarbazepine **1200–2400** [15–45] mg/kg/day	MHD — 10–55 g/ml	Rash (25% cross-reactivity with CBZ)	CNS diplopia	Hyponatremia (3% of adults)
Phenytoin **200–600** [4–8] mg/kg/day	10–20 g/ml	Rash (5–10%), hematologic, hepatic, lymphadeonpathy, others	Cosmetic, CNS, ataxia, nystagmus	Elevated LFTs, induction, reduced vitamin D, possible cerebellar degeneration
Phenobarbital **60–120** [2–6] mg/kg/day	15–40 g/ml	Rash, Stevens-Johnson, SLE	Somnolence, irritability	Possible irreversible cognitive effects, liver induction
Primidone **750–1500** [5-20] mg/kg/day	4–12 g/ml	Rash	Sedation, irritability, GI upset	Similar to PB
Tiagabine **32–56** [.25–1.25] mg/kg/day	5–70 g/ml	Psychiatric	CNS, tremor, weakness, GE reflux, gait difficulty	
Topiramate 100–400 [5–25] mg/kg/day	3–25 g/ml	Rash (rare), elevated LFTs	Somnolence, memory disturbance, anorexia, renal stones, parasthesiae, dysgeusia	Language disturbance when used in polypharmacy, avoid ketogenic diet

Table 2.1 (Continued)

Guide to AED Dosing and Adverse Effects

Medication/ Target Dose mg/d [Pediatric Dose mg/kg/d]	Target Serum Levels	Idiosyncratic	Dose Related	Age Specific/Other
Valproic acid 1000–3000 [20–60] mg/kg/day	50–150 g/ml	Hepatic failure, pancreatitis	Tremor, weight gain, alopecia, sedation and cognitive changes, thrombocytopenia, prolonged bleeding time	Hepatic failure (1/500 under age 2 on polypharmacy), elevated LFTs, GI upset with syrup, incidence of PCOS unknown, liver enzyme inhibition
Vigabatrin [40–100] mg/kg/day	—	Visual field constriction, sedation, CNS	Psychiatric symptoms (rare), visual field constriction	Especially effective of Infantile Spasms and Tuberous Sclerosis
Zonisamide 200–600 [4–10] mg/kg/day	10–30 g/ml	Rash, hematologic, hepatic	Renal stones, anorexia, somnolence	Oligohydrosis in children, avoid in sulfa drug sensitivity

Disclaimer: Doses, therapeutic levels, and adverse effects are based on reported clinical experience and not on adequate scientific information from clinical trials. Not all drugs are approved for use in children.

to be equally effective to carbamazepine against secondarily generalized tonic-clonic seizures. Because valproic acid is generally well tolerated, it should be considered for patients who are unresponsive or intolerant to carbamazepine. Kwan and Brodie[43] likewise have found that all carbamazepine, valproate, and lamotrigine had equal efficacy in newly diagnosed patients with epilepsy, though tolerability differed. More patients on carbamazepine changed medication due to adverse events than those on the other two drugs.[43]

All antiepileptic drugs may cause significant problems with adverse effects, especially neurotoxicity, and pose problems for the TBI patient. Indeed, several antiepileptic drugs commonly cause ataxia at high levels and may also exacerbate gait abnormalities at lower levels, in some patients. This may present a problem to the patient who is returning to ambulation. There is a significant incidence of hyponatremia in carbamazepine-treated patients over the age of 25,[44] as well as those on oxcarbazepine.[45] Postural tremor is a common side effect of valproic acid that may pose a problem to the TBI patient and can be particularly troublesome in patients who are prone to postural tremor. The tremor is reversible, dose dependent, and responds to a dose reduction or other medications that block essential tremor (propranolol, primidone). Because the barbiturates, including phenobarbital and primidone, are poorly tolerated and result in a high incidence of cognitive impairment, they should not be used as first line drugs, but rather used in patients refractory to other antiepileptic medications.

Eight new AED (felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, and zonisamide) have been approved by the FDA since 1993, predominantly for use as adjunctive therapy in partial onset seizures. In general, they appear to have high therapeutic indices, that is, a wide window between efficacy and toxicity, and have demonstrated to be effective and safe in controlled studies.[46–49] Improved pharmacokinetics provide an additional advantage of some of these newer AED, including renal clearance, the lack of significant protein binding, and the absence of CyP450 induction.[49] However, serious idiosyncratic adverse effects can occur. The use of felbamate has

been restricted by the FDA for use in severe intractable epilepsy because of a significant risk of aplastic anemia estimated by the FDA to be 1:2000. Lamotrigine is associated with a risk of serious rash in approximately 1:1000 patients, usually at onset of therapy. Vigabatrin has not been approved for use in the United States, in part, because of potential retinal toxicity. Additionally, treatment-emergent side effects can be troublesome. For example, topiramate is associated with word-finding difficulties in some patients, particularly at higher doses or when the drug is used in polypharmacy. Gabapentin may cause weight gain and somnolence. Levetiracetam may cause behavioral side effects. While monitoring of serum drug levels, complete blood counts, and liver function are not required with most of the new AED (with the notable exception of felbamate); the difficulty in assessing clinical status of patients with significant traumatic encephalopathy may make such monitoring advisable. Practitioners should take advantage of published reviews of these drugs in textbooks and journals to familiarize themselves with their use.

In a systematic review of efficacy and tolerability of the newer AED, Marson and Chadwick[50] found no statistical differences between gabapentin, lamotrigine, tiagabine, topiramate, vigabatrin, and zonisamide. Nevertheless, the addition of these new drugs will provide alternatives for patients who do not tolerate or respond to current antiepileptic drugs. Undoubtedly, they will be tested in posttraumatic epilepsy and may provide a better armamentarium for this problem.

In general, all AED should be introduced slowly to avoid problems with neurotoxicity, including somnolence and altered mental status. If introduced too quickly, carbamazepine may cause severe dizziness; lamotrigine may precipitate a serious rash. However, when multiple seizures or status epilepticus occurs, loading with phenytoin is often effective in controlling seizures. For intravenous use, fosphenytoin is better tolerated than phenytoin. Valproic acid is also available for intravenous use and can be used in relatively high doses acutely, if necessary. The intravenous preparations of both of these drugs may be useful for patients who are unable to take oral medications, for instance, after surgical procedures. With all AED, clinical efficacy and tolerability determine appropriate dosing. Most of the newer AED do not have well established therapeutic plasma level measurements, but the presence of significant traumatic encephalopathy may make determination of AED plasma levels appropriate. Drug plasma levels may be utilized to provide a rough guideline for therapy but should not be used as the sole indicator of therapy or toxicity.[51] It should be noted that a plasma steady state is not achieved for up to seven half-lives of a medication so that levels are rarely useful acutely after dosing changes.

Phenytoin is unique among the commonly used AED in that it saturates its metabolic enzymes at therapeutic levels which results in zero-order kinetic elimination. As a result, the effective half-life is variable and becomes longer with higher levels of phenytoin. As a result of nonlinear kinetics, there is a proportionate increase of serum level at low doses of phenytoin, but at therapeutic levels, small increments result in marked elevations of levels.[52] This phenomenon is responsible for what is mistakenly identified as wild fluctuations in phenytoin levels. In addition, phenytoin and valproic acid compete for protein binding, making routine measurements of phenytoin levels inappropriate when used in combination with valproate. Rather, unbound phenytoin levels should be obtained through reference laboratories as they are not routinely available in most hospital laboratories. Also of note are the kinetics of Dilantin Kapseals which allow once a day dosing, not true for phenytoin suspension or chewable 50 mg tablets.

The use of phenytoin, carbamazepine, and oxcarbazepine suspensions may be useful in patients who cannot swallow tablets or capsules. However, care must be taken to adequately shake the bottle before administering a dose to allow for even distribution of drug in the solution. Lamotrigine, levetiracetam, and zonisamide can be dissolved and given as a solution. Both valproic acid and topiramate are available as sprinkle capsules, but

they cannot be given through gastric tubes due to the tendency of the sprinkles to adhere to the tubing.

Several AED are being evaluated for their potential neuroprotective effects, including antiepileptogenicity, in both experimental and clinical studies. Temkin performed a meta-analysis of 47 studies of the effectiveness of anticonvulsant drug administration for seizure prevention and antiepileptogenicity.[39] Of these, 13 were conducted after traumatic brain injury. There was no good evidence to support that anticonvulsant drug administration after traumatic brain injury is antiepileptogenic in the long term, though acutely (within the first week), there was seizure reduction associated with phenytoin[53] and carbamazepine.[54] Temkin emphasizes the need for "rigorous clinical trials" to determine the drug's antiepileptogenic effects as well as any neurobehavioral costs. She goes further to state that "Clinical use of any drug to prevent epileptogenesis should be avoided until clinical trials have proven the drug to be effective for that purpose."[53, pg 522]

It is likely that there are individual differences in response to and tolerance of any given antiepileptic drug. Therefore, additional medications should be tried in patients who have failed to respond to or who are unable to tolerate initial treatment. In all cases, the therapeutic plan should strive for a single antiepileptic drug regimen. Monotherapy has been shown to be more efficacious than polytherapy and minimizes toxicity, drug interactions, and cost.[55]

Mechanisms and Models of Posttraumatic Epilepsy

When considering the appropriate treatment of posttraumatic epilepsy, it is worthwhile to understand the mechanisms whereby trauma leads to the epileptogenic state. Studies of posttraumatic epileptogenesis implicate several potential pathologic etiologies that may result in a seizure focus. These etiologies can be broadly separated into those related to the acute or primary insult (i.e., penetration of parenchyma, shearing forces, and disruption of blood-brain barrier) and those caused by late or secondary sequelae (i.e., vascular disruption, cicatricial pulling, and synaptic reorganization). Given the wide variations of brain injury and complications, it is unlikely that any single mechanism is responsible for posttraumatic epileptogenesis. Thus, posttraumatic epileptogenesis probably utilizes combinations of several mechanisms, many of which are supported by scientific studies and concur with clinical aspects of this type of epilepsy.

In 1930, Foerster and Penfield[56] induced seizure activity by electrical stimulation of areas surrounding a gunshot lesion of cerebral cortex. These findings suggested the presence of an epileptic zone or penumbra surrounding the site of injury. Furthermore, retraction of dura that had become adherent to the damaged cortex also triggered seizures. They concluded that posttraumatic seizures are most likely to occur after dural penetration, which induces formation of scar tissue between brain and dura, and subsequent pulling of the ipsilateral and, sometimes, contralateral hemispheres toward the lesion, as a result of contraction brought about by normal maturation of the scar (cicatricial contraction). This hypothesis is supported by clinical findings that head injuries associated with dural penetration are associated with the highest incidence of posttraumatic epilepsy (27 to 43%).[22]

Additional putative mechanisms include glial cell proliferation and damage to blood vessels, axon collaterals, and blood-brain barrier, each of which is known to precipitate brain injury.[57] Jasper[57] hypothesized that the toxicity of extravasated blood increases neuronal activity abnormally in some brain regions and disrupts blood flow in others. These pathophysiologic changes could result in the alternating periods of seizure activity and

functional neuronal depression that characterize acute status epilepticus induced by brain contusion.[57] Alternatively, damage to inhibitory axon collaterals by shearing forces may result in reduction of inhibitory tone and excessive depolarization that ultimately produce seizure discharges.[57] Overt penetration of dura and disruption of brain parenchyma may not be absolute requisites for posttraumatic epilepsy.

Lowenstein and colleagues[58] reported that extradural fluid percussion induces profound decreases in hippocampal hilar neurons and hyperexcitability of dentate granule cells in rodents. Postinjury hyperexcitability in the granule cell and molecular layer of the dentate gyrus has been shown to be persistent (observable at 15 weeks) and pervasive (e.g., bilateral).[59] Measures taken at earlier time points throughout the hippocampus revealed dramatic physiological and receptor-mediated disruptions in excitatory/inhibitory balance, with the changes being time dependent and only observable ipsilateral to the site of traumatic brain injury.[60,61] Thus, even nonpenetrating brain injury can cause pathologic changes in distal structures, possibly tipping the balance in favor of posttraumatic seizures. These findings could help explain the emergence of posttraumatic epilepsy in persons with milder, low velocity head injuries who do not appear to have frank penetration of dura or intracerebral bleeding.

Because penetrating brain injuries carry the greatest risk for posttraumatic epilepsy, alterations in blood flow may play a role. Not only does brain injury disrupt vascularization at the site of damage, it also affects areas "downstream" from the insult. Disruption in blood flow could bring about both ischemic and hypoxic conditions which produce significant increases in synaptic glutamate release and decreased inactivation of glutamate. Overactivation of glutamate receptors, including NMDA receptor activation, results in excessive Ca^{++} influx,[62] which promotes phosphorylation of the $GABA_A$ receptor to its nonfunctional, desensitized state.[63] Trauma has also been associated with GABA-mediated Ca^{++} influx,[64,65] which would not only lead to depolarization, but also, potentially, to cell death. Loss of inhibitory neurons, coupled with other trauma-induced disruptions in normal brain function, could result in a state that both primes the brain for acute seizures and provides the foundation for long-term epileptogenic changes.

A related hypothesis implicates blood breakdown products, particularly hemosiderin, in the cellular events that lead to epileptogenesis. An important role for iron deposition has been supported by experimental studies in animals. Subpial iontophoresis of ferrous or ferric chloride into sensorimotor cortex of cat or rat induces a chronic epileptic focus with many striking similarities to lesions in human posttraumatic epilepsy.[66,67] Electrocorticographic seizure activity is observed within 48 hours after injection and behavioral convulsions occur between 48 hours and 57 days. These abnormalities recur spontaneously and persist for more than 12 weeks after injection.[67] Examination of the iron-induced focus reveals many histopathologic changes found in posttraumatic epileptic foci from humans:[66,67] meningocerebral cicatrix, consisting of fibroblasts and iron-laden macrophages, surrounds the iron injection cavity with neuronal loss and gliosis occurring next to the injection site. Hypertrophied astrocytes encompass the entire iron focus. It has been hypothesized that a cascade of events is initiated by the iron focus, resulting in the genesis of a posttraumatic epileptic focus. Breakdown of blood from brain injury-induced extravasation creates iron deposits that may induce free-radical oxidant formation and subsequent lipid peroxidation.[68] In support of this hypothesis is the finding that antioxidant administration reduces the incidence of iron-induced seizure activity.[68]

The possibility of hemosiderin deposition leading to posttraumatic epilepsy has also been studied in humans.[15] Following traumatic brain injury, MRI scans were utilized to detect the presence of hemosiderin, gliosis, or both. Evidence of hemosiderin deposits was found in 81% of patients. Although there was no correlation between the presence of

hemosiderin, alone, and posttraumatic epilepsy, the presence of cortical hemosiderin surrounded by a "gliotic wall" was significantly correlated with the development of posttraumatic epilepsy.

The mechanisms discussed so far largely address seizure activity that occurs acutely following brain injury. However, the onset of posttraumatic seizures is bimodal — the highest incidence occurs during the first week (early onset seizures) with a secondary peak occurring at about 6 months.[69] This latency suggests there is a maturation process resulting in the genesis of an epileptic focus. Because the latent period can last months to years after the insult in humans, most of what we know about the mechanisms underlying posttraumatic epileptogenesis comes from animal models.

Modeling posttraumatic epilepsy in animals poses quite a challenge. First, not only is it difficult to evoke spontaneous seizures secondary to traumatic brain injury, chronically monitoring animals to determine when, and if, subconvulsive vs. convulsive seizures occur is an enormous task. Second, because the goals of animal models vary, it may not be possible to test all aspects of interest in every model. For example, a model of posttraumatic epilepsy that attempts to mimic the postinsult latent period, may not allow for neurobehavioral assessment of acute postinsult seizures or anticonvulsant drug administration. As well, such a model may not use trauma as the precipitating event. Alternatively, a model designed to assess postinjury neurobehavioral change may not allow for the assessment of the spontaneous epileptogenic process. With these limitations in mind, discussion of some of the animal models is worthwhile.

Status epilepticus, induced by excitotoxins (e.g., kainic acid or pilocarpine)[70,71] or electrical stimulation[72–74] has been proposed to share commonalities with posttraumatic epileptogenesis.[75] The initial precipitating insult of prolonged seizures is followed by a latent period, after which spontaneous seizures occur. Like experimentally-induced traumatic brain injury, status epilepticus results in dramatic and significant morphological, physiological, and neurochemical alterations. Indeed, the insult-associated plasticity and neuronal reorganization seen after experimentally-induced insult via seizures or frank trauma appears to share similarities.[75,76] Likewise, another useful model involves the cortical "undercut method" in which the initial brain insult is followed by a dormant period after which cortical epilepsy is evident.[77]

Lastly, the kindling model refers to a phenomenon whereby a brain region can be rendered permanently epileptic when subjected to brief, repeated electrical stimulations that, alone, would not induce behavioral seizures.[78] Clinical evidence that "seizures beget seizures" is supported by a prospective study of unselected patients with new onset of seizures which demonstrated that the probability of seizure control was inversely related to the number of seizures experienced prior to initiation of antiepileptic drug therapy.[79,80] Furthermore, the time interval between seizures appears to decrease with subsequent episodes in untreated patients.[81]

The kindling paradigm in which the brain "learns" to seize has been used to study epileptogenesis and neuronal plasticity. Typically, electrical stimulation is administered by an implanted depth electrode and, initially, results only in a brief localized epileptiform discharge on EEG, without a behavioral response. With continued daily stimulation, there are progressive increases in duration of both EEG epileptiform discharges and motor seizure activity.

The resulting convulsive behavior evolves through stages that are highly reproducible from animal to animal and may be graded by levels of behavioral severity.[82] Stage 0 is no behavioral response; Stage 1 consists of chewing motion; and Stage 2 consists of head nodding. At Stage 3, the animal displays clonus (jerking) of forelimbs, and at Stage 4, there is forelimb clonus with rearing onto hind limbs. The fifth, and most severe, stage consists of forelimb clonus with rearing and falling.

Electrical kindling of seizure activity induces neuronal changes within the brain that result in more severe generalized seizures from a stimulus that initially produced only focal seizure activity. Numerous transient and long-term changes occur during, and as a result of, electrical kindling, with the most dramatic being seen within the excitatory and inhibitory amino acid transmitter systems.[83–88] For example, kindling significantly reduces neuronal sensitivity to GABA; the changes are long lasting and may be seen at 4 and 12 weeks after the last fully kindled (Stage 5) seizure.[89–92] Loss of sensitivity to GABA evolves during the course of kindling, and correlates with seizure severity.[89] These changes are believed to result from a compensatory desensitization of the receptor in response to increased GABA release during the electrical kindling process.[93,94] Thus, the very mechanisms utilized by the brain to suppress kindling appear to be counterproductive and ultimately facilitate the kindling process.

Because sequelae of brain injury also elicit aberrations in the excitatory and inhibitory tone,[60] using the kindling model to produce postinjury epileptogenesis is a useful tool, particularly in combination with focal cortical damage. In this model,[95,96] injury severity is controlled using a reproducible focal cortical lesion[97,98] that induces behavioral deficits in animals similar to those seen in humans with brain injury.[99] This focal cortical lesion in animals does not routinely produce spontaneous convulsions, yet it does lower the seizure threshold in the amygdala. In our laboratory, we observed a 37% decrease in Stage 5 seizure threshold following cortical lesion in comparison to fully kindled animals without lesions. Electrical kindling of the amygdala after focal cortical lesion is a useful and unique model as it allows for the study of the neurobehavioral impact of epileptogenesis (with and without anticonvulsant drug administration), while still controlling seizure severity, timing, and number.

Posttraumatic Seizures, Epilepsy, and Anticonvulsant Prophylaxis: Implications for Neurobehavioral Recovery

Brain damage resulting from traumatic brain injury can significantly impair physical, cognitive, and social function. Recovery from such deficits can be variable, and permanent neurological disability occurs in as many as 90,000 survivors of brain injury in the United States each year.[100] These disabilities are further compounded by posttraumatic epilepsy, which results not only in spontaneous and unpredictable seizure recurrence but also in toxicities associated with antiepileptic drug therapies. Individuals with posttraumatic epilepsy pose a special case in that they are neither patients with only a brain injury nor patients having only epilepsy. Thus, the treatment requirements for posttraumatic epilepsy extend beyond those available for either the epilepsy or brain injury alone. This makes it difficult to generalize from the anticonvulsant drug toxicity and efficacy profiles obtained from epileptic subjects without brain injury, and few anticonvulsant drugs have been systematically investigated in traumatic brain injury patients alone.[36,38,101–103] Treatment strategies that acknowledge these complexities will improve patient quality of life.

The controversy surrounding whether or not anticonvulsants should be administered prophylactically requires assessing the potential neurobehavioral impact of seizures vs. the risk of AED administration.[101,104,105] Anticonvulsants are often administered after brain injury even though they have not been found to be effective in preventing later development of posttraumatic epilepsy.[38,39] Several early studies suggested a beneficial effect of prophylactic anticonvulsant therapy,[106,107] but later controlled studies failed to support these findings. For example, when studied in a double-blind, placebo-controlled, random-

ized manner, phenytoin administered following TBI had no impact on the later development of epilepsy, though it did reduce the incidence of early seizures (i.e., those occurring within the first week after injury).[37,53]

The lack of effectiveness of anticonvulsant drugs in preventing posttraumatic epilepsy is also paralleled in experimental kindling studies. Although many antiepileptic drugs may block fully kindled convulsions in animals, they do not prevent the kindling process and do not prevent the increases in seizure severity. Specifically, phenytoin and carbamazepine may block seizures but do not consistently prevent epileptogenesis from occurring.[85,108] In contrast, phenobarbital and benzodiazepines do appear to be antiepileptogenic in that they are effective in slowing the progression of amygdala-kindled seizures.[109–111] Valproic acid has also been found to retard the rate of amygdala kindling but only when used at high doses with significant toxicities.[112,113] Antagonists that directly compete for the NMDA receptor inhibit the progression of electrically-kindled seizures but have relatively less effect on seizures once kindling has been achieved.[114] This suggests a potential antiepileptogenic role of NMDA receptor antagonists that is independent of its ability to block acute seizures. A full scale trial is underway in which magnesium, which blocks the *N*-methyl-*D*-aspartate (NMDA) channel, is being administered after traumatic brain injury.[39] Other transmitters have been targeted to determine their antiepileptogenicity in the kindling model as well. Administration of the alpha adrenergic receptor agonist clonidine can significantly retard the rate of evolution of kindled seizure stage but, by itself, does not block the fully established kindled seizure.[115,116] Thus, a key role of noradrenergic neurotransmission in the regulation of epileptogenesis has been proposed.[117,118]

The search for effective *antiepileptogenic* drugs may necessitate a change in current experimental drug development paradigms so that potential prophylactic drugs may be screened. Use of models of epilepsy, rather than acute seizures, holds great promise for future development of antiepileptogenic drugs. These models include the electrical kindling paradigm, studies in genetically seizure-prone animals, and models in which the focal insult (e.g., status epilepticus, cortical "undercut") is followed by a dormant period and epilepsy.[75,77] Ultimately, however, the effectiveness of a drug as an antiepileptogenic agent will require prospective, placebo-controlled trials in TBI and other high-risk patients.

Currently available antiepileptic drugs do not appear to affect the pathophysiologic processes resulting in spontaneous seizure recurrence and may be merely masking the outward manifestations of seizure activity. The question is, does this come at a cost to the traumatically brain-injured patient? The neurobehavioral effects of anticonvulsant drug therapy is known. Indeed, it has been argued that, since brain injury carries only an approximate 5% risk for posttraumatic epilepsy, the remaining 95% needlessly receive anticonvulsant medication.[119] This group of patients is exposed to the toxicities of anticonvulsant administration without any potential benefit. Even in normal volunteers, antiepileptic drugs cause significant cognitive impairment, albeit minor in many cases.[120] Barbiturates commonly cause cognitive impairment, even at low doses.[121] For many drugs, however, toxic levels can account for some of their untoward effects. For example, it was initially suggested that carbamazepine induced less cognitive impairment than phenytoin.[122] When the data were reexamined so that patients with toxic phenytoin levels were removed from the study, no significant differences in cognitive impairment could be found between treatments.[123] A subsequent study, which maintained levels in therapeutic ranges, verified these findings.[121] Although valproic acid is thought to cause minimal problems with cognition, withdrawal of this medication improved psychometric scores.[124] In a study that included completely randomized assignment of drug vs. placebo, phenytoin administration after traumatic brain injury was associated with impaired function on several neuropsychological measures of cognition, which are among the most common and dis-

TABLE 2.2

Postinjury Factors and Their Impact on Neurobehavioral Function

Seizure Type	Effect	Reference
Animal studies		
Kindled (early Stage 0/subclinical; ipsilateral or contralateral focus)	0	(Hernández and Warner, 1995; Kline et al., 2000)
Kindled (early Stage 1/clinically evident; ipsilateral focus only)	⇓	(Hernández and Warner, 1995; Kline et al., 2000)
Kindled (late Stage 1/clinically evident; ipsilateral or contralateral focus)	0	(Hernández and Warner, 1995; Kline et al., 2000)
Pentylenetetrazol (clinically evident)	⇑	(Hamm et al., 1995; Hernández and Schallert, 1988)
Electroconvulsive shock (generalized)	⇑	(Feeney et al., 1987)
Human studies		
Early posttraumatic seizures (subclinical)	0	(Vespa et al., 1999)
Late posttraumatic seizures	0	(Haltiner et al., 1996)
Posttraumatic epilepsy	⇓	(Armstrong et al., 1990; Dikmen and Reitan, 1978)
Posttraumatic epilepsy (controlling for injury severity)	0	(Haltiner et al., 1996)
Anticonvulsant Drug	**Effect**	**Reference**
Animal studies		
Diazepam	⇓	(Hernández et al., 1989a; Schallert et al., 1986)
Phenytoin	⇓	(Brailowsky et al., 1986)
Carbamazepine	0	(Schallert et al., 1992)
Phenobarbital	⇓	(Hernández and Holling, 1994; Watson and Kennard, 1945)
Vigabatrin	0	(Wallace et al., 1999)
Human Studies		
Phenytoin	⇓	(Dikmen et al., 1991; Smith et al., 1994)
Carbamazepine	⇓	(Smith et al., 1994)
Benzodiazepines	⇓	(Goldstein, 1995)
Anticonvulsant Drug + Seizures	**Effect**	**Reference**
Animal studies		
Phenobarbital + Kindled (early Stage 0)	⇓	(Montañez et al., 2000)
Vigabatrin + Kindled (early Stage 0)	⇓	(Montañez et al., 2001)

Note: 0 = no effect; ⇓ = hindered; ⇑ = improved; "early" = occurring within the first week postinjury; "late" = occurring after the first week postinjury.

abling problems faced by individuals with brain injury.[101] Phenytoin and carbamazepine have each been shown to adversely affect psychomotor function following brain injury, though this is reversible upon drug discontinuation.[103] The newer AED have not been studied for their effects on cognitive function in patients with TBI. These negative consequences of treatment with AED on cognitive functioning are not surprising when one considers anticonvulsant drugs can adversely affect cognitive function in *nonbrain-injured individuals*[120,125,126] and that drug sensitivity is greater after brain injury.

Animal studies addressing these issues paint a similarly negative picture (Table 2.2). For example, if diazepam is administered during the first 3 weeks after unilateral anteromedial cortex damage, recovery from somatosensory deficits is delayed indefinitely.[98] Even if diazepam is administered only for the first 7 days after brain damage, recovery is significantly delayed.[127,128] Phenobarbital also appears to interfere with somatosensory and motor recovery following brain damage in rats and nonhuman primates.[129,130] Not all anticonvulsant drugs have been found to be detrimental after brain damage in animals: carbamazepine[131] and vigabatrin[132] had no impact on recovery from somatosensory deficits. As a caveat, however, when an anticonvulsant dose of vigabatrin was coadmin-

istered against subconvulsive kindled seizures, recovery was impeded.[133] Similarly detrimental to functional recovery was phenobarbital administration prior to evoked subconvulsive seizures.[134] These data suggest that the interaction between anticonvulsant drugs and subclinical seizures after brain insult are detrimental to functional recovery and the net effect is greater than either factor alone. This further supports the value of EEG monitoring after traumatic brain injury,[15,26] however, not only as a means of detecting subclinical seizures, but also to influence treatment strategies that optimize neurobehavioral outcome.

There are several potential mechanisms by which anticonvulsants may adversely affect the recovering brain. First, these drugs suppress repetitive firing, which is important for long-term potentiation (LTP), a phenomenon associated with learning. LTP is discussed in the chapter by Lehr in this volume. Second, barbiturates and benzodiazepines directly modulate the $GABA_A$ receptor and increase neuronal inhibition. That there is a link between enhanced postsynaptic GABA-mediated inhibition and impaired functional recovery is well established.[98,127–130,135–137] Likely mechanisms include toxicity of excessive intracellular Cl–[138,139] and Ca++[64,65] associated with GABA postinjury, GABA receptor-dependent excitotoxicity,[140] and decreases in growth factor production attributed to GABA augmentation.[141] Finally, suppression of repetitive firing or general CNS depression could be counterproductive following brain injury, especially since neuronal depression already occurs as a consequence of brain injury. This condition of postinjury neuronal depression has been referred to as *diaschisis*,[142] which is the temporary disruption of neuronal activity in undamaged areas functionally related to injured areas.

Evidence that diaschisis occurs after brain injury has been well established with measures of blood flow, metabolism, electrical activity, and neurotransmitter levels.[143–146] Moreover, this depression of neuronal activity after brain injury has been correlated with behavioral deficits, and restoration of normal neuronal activity correlates with behavioral recovery.[147–149] The use of positron emission tomography (PET) has made it possible to measure posttraumatic neural depression after brain injury in humans. Measures of cerebral glucose metabolism clearly show a state of metabolic depression postinjury, though there is not a clear relationship between this and functional level (e.g., consciousness).[150]

Based on the brain's functionally-depressed state after trauma, it has been hypothesized[98] that posttraumatic seizures may be the result of adaptive mechanisms initiated by the injured brain in its attempt to restore normal neuronal activity. For this to be the case, the neurobehavioral consequences of seizures would need to be associated with improved recovery or no deleterious effect (e.g., neutral). Experimental data in animal studies suggest the effects of seizures are not uniform, and greatly depend on seizure type, severity, and frequency (Table 2.2). For example, mild or infrequent seizures have been found to improve the recovery process.[151–153]

At first blush, these data may seem counterintuitive. However, when the entire array of neural and functional consequences of seizures are considered, a complex yet fairly clear picture emerges that is dependent on the timing, type, and severity of postinjury seizures. For example, using an animal model of posttraumatic epilepsy (described above), it appears that the impact of seizures is bimodal; convulsive seizures (Stage 1) during the 6-day postlesion, critical period are detrimental to the recovery process, whereas subconvulsive seizures have no functional impact.[95,154] This effect is time dependent and hemisphere specific in that Stage 1 kindled seizures occurring on postlesion Day 7 or later have no impact on the recovery process. Moreover, contralaterally kindled seizures exert no impact on recovery regardless of when they occur. Potential mechanisms for these effects stem from the fact that Stage 0 seizures exert no impact on peak basic fibroblast growth factor (bFGF) expression, whereas Stage 1 seizures block this important neurotrophic contributor to functional recovery.[155] Interestingly, kindled seizures in nonbrain-injured

animals have been associated with neurogenesis,[156,157] which may contribute, in a positive or negative way, to the recovery process, depending upon whether these new cells replace lost ones, make functionally relevant connections, or contribute to aberrant plasticity (e.g., excitability that might contribute to epileptogenesis). It would be interesting to assess the impact of postinjury seizures, with or without anticonvulsant drug administration, on neurogenesis in traumatically brain-injured animals.

There is other evidence that seizure effects vary. Clinical studies have shown that simple abnormal EEG activity is associated with impaired cognition[158] and that response time is impaired even during single focal interictal spikes in humans.[159] Learning is also impaired in young rodents undergoing repetitive and frequent audiogenic seizures.[160] In contrast, repetitive kindled seizures do not appear to affect most aspects of learning and memory,[161,162] though some (e.g., acquisition) are impacted by the transition from partial to generalized seizures.[161] Taken together, these data suggest that, at least in some situations, seizures may inhibit learning. Finally, brief seizures do not necessarily cause brain damage,[88] yet prolonged seizures cause neuronal death via excitotoxicity.[75,163] This latter type of seizure activity following trauma would likely contribute to further cell death or interfere with the plasticity underlying recovery processes.

While seizures, *per se,* may not be detrimental to functional outcome, there is significant evidence suggesting that *posttraumatic epilepsy* poses significant problems for rehabilitation of the TBI patient. The uncertainty caused by randomly occurring loss of consciousness places yet an additional barrier to independence. At the most, uncontrolled epilepsy may necessitate placement in specialized care facilities and, at the least, may prohibit driving privileges. Uncontrolled seizures are also associated with a significant risk of trauma and unexpected death (SUDEP).[164] Some data suggest the impact of posttraumatic epilepsy on neurorehabilitation may extend beyond these social aspects and could actually impede brain recovery. World War II veterans with head injury who developed posttraumatic epilepsy had a lower survival rate than veterans without epilepsy.[165] The incidence and severity of cognitive deficit in hemiplegic children is highly correlated with the presence of seizure activity, independent of the amount of cerebral damage.[166] A retrospective study on head-injured patients demonstrated that functional measures were lower in patients that developed posttraumatic epilepsy upon entry into rehabilitation than those who did not. Although both groups improved significantly, functional outcome remained lower in the epileptic group.[167] Importantly, these studies could not address the question of whether the results were due to seizures, injury severity, or anticonvulsant drug administration. Haltiner and colleagues[168] were able to tease apart some of these issues: when injury severity is controlled, neither late posttraumatic seizures nor posttraumatic epilepsy had an influence on neuropsychological outcome measures.

To effectively delineate the neurobehavioral impact of seizures vs. epilepsy following traumatic brain injury in humans, it is necessary to know when, and if, the patient is having seizures. To this end, Vespa and colleagues[26] continuously monitored patients after TBI for up to 14 days. Of these individuals, 22% had clinically-evident or nonclinically evident seizures. When comparing outcome between these individuals and those in the nonseizure group, it appears that seizures are not necessarily detrimental. For example, both groups exhibited increased intracranial pressure (ICP) after brain injury, but the overall ICP was actually greatest in the nonseizure group. Cerebral perfusion pressure (CPP) was slightly, though significantly, lower in the nonseizure group. There was no difference between the groups in terms of length of stay, nor in outcome (Glasgow Outcome Score [GOS]); both good and poor outcomes were equally likely regardless of whether there had been seizures or not. A caveat, however, is that there was a greater mortality rate within the seizure group, which could be fully accounted for by those individuals with status epilepticus. If these individuals were removed from the analysis,

it appeared that the seizure group had a lower mortality rate than the nonseizure group. It is also worth noting that Vespa and colleagues[169] have shown postinjury seizures can be correlated with elevated glutamate levels as assessed by intracerebral microdialysis. Such an elevation could contribute to further seizures and/or damage, though it remains unclear in this type of study as to the exact level of glutamate that would be toxic.

In summary, experimental data suggest the effect of seizures on functional recovery of the injured brain is not uniform and depends on seizure type, timing, and severity. Specifically, recurrent and/or severe seizures may have a negative impact on recovery, while mild, infrequent seizures may be associated with improved behavioral recovery or be without neurobehavioral consequence. Thus, it is only when the seizures are severe enough to cause further brain damage, or frequent enough to develop into epilepsy, that they appear to be detrimental to the behavioral recovery and quality of life.

Conclusions

The accurate diagnosis of episodic behaviors is crucial to providing the most appropriate therapy for TBI patients. Although posttraumatic epilepsy is a common entity, it may be difficult to recognize. Posttraumatic epilepsy must be carefully distinguished from other types of behavioral spells because either unnecessary antiepileptic drug therapy or uncontrolled seizures may potentially impair neurologic recovery. At present, there is little evidence to support prophylactic use of anticonvulsants in TBI patients. Their use in this way does not prevent epileptogenesis clinically and much data implicates negative effects on cognition and recovery of brain function. Thus, antiepileptic drug therapy should be withheld until there is a *bona fide* diagnosis of epilepsy — that is, at least two separate seizure events that are not due to transient metabolic derangements. Once the diagnosis of epilepsy is secure, effective therapy should be initiated promptly to prevent the deleterious effects of uncontrolled seizures on brain recovery. Future research will need to address whether control of posttraumatic epilepsy improves functional outcome and if these gains outweigh the adverse effects of antiepileptic drug therapy. In addition, the mechanisms of posttraumatic seizures will need to be better understood so that therapies that prevent epileptogenesis may be achieved.

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3

Neurotransmitters and Pharmacology

Ronald A. Browning

CONTENTS

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Editor's Note

Pharmacological treatment of traumatic brain injury (TBI) is complex and still in its infancy as a field of clinical investigation. Patients with TBI have a wide variety of central nervous system (CNS) problems, as well as numerous peripheral disorders (e.g., hypertension, reduced bowel function) that can be addressed pharmacologically. One of the major difficulties in identifying useful medications for TBI patients is the diversity of brain injury encountered in this population. The non-CNS medical problems in TBI patients often require the use of drugs to control hypertension or increase bowel function and drugs that affect the autonomic nervous system are commonly used for such disorders. While this chapter focuses on the medications that are used to alter neurological or behavioral functions (i.e., those that act on the CNS), neurotransmission in the autonomic nervous system and the drugs that modify it are also described.

Introduction

Most drugs that are used for an action on the central nervous system (CNS), such as those employed in neurology and psychiatry, exert their action by acting at the site where neurons communicate with one another, namely, the synapse. These drugs, therefore, exert their effect by modifying the process of neurotransmission. The exceptions to this rule are those classes of drugs known as: (1) the *local anesthetics,* which prevent nerve conduction by blocking sodium channels and, thereby, alleviating pain, (2) *general anesthetics,* which produce a reversible loss of consciousness by unknown means, although recent evidence suggests these agents can also modify neurotransmission, and (3) some *antiepileptic agents,* which prevent seizures by acting directly on voltage-gated ion channels to alter nerve conduction. It should be noted that some antiepileptic drugs do produce their beneficial effects by altering neurotransmission (e.g., tiagabine).

Drug classes whose mechanism of action involves a modification of synaptic neurotransmission include narcotic analgesics (used to alleviate pain), antipsychotic agents (used to treat schizophrenia), antidepressants, antianxiety agents (e.g., **diazepam** or Valium®), some antiepileptic drugs, antispasmodics, and muscle relaxants. In addition, due to the ubiquitous role of the peripheral autonomic nervous system in the regulation of organ-system function such as cardiovascular, respiratory, gastrointestinal, nasal congestion, and the like, it is not surprising to find that drugs altering peripheral neurotransmission are used to treat a wide variety of disorders such as hypertension, heart disease, gastrointestinal disorders, hiccups, asthma, hay fever, etc.

The question of whether or not a substance functions as a neurotransmitter is not an easy one to answer and requires extensive experimental testing by neuroscientists. Neurobiologists have set specific criteria that must be fulfilled before a substance is accepted as a neurotransmitter. These criteria were established in the mid-1960s by Werman[1] and, while the original criteria were extremely useful for over 25 years, they may not be entirely adequate because knowledge of how neurons communicate with one another and with target organs in the periphery has expanded. Indeed, some of the recently discovered signaling molecules, such as the gases nitric oxide and carbon monoxide, do not fulfill the previously established criteria, yet clearly function as important neural messengers.[2–4]

Nevertheless, there are about seven chemicals that have been well-established as neurotransmitters and another 20 to 30 substances that are highly suspected as neurotransmitters or neuromodulators in the nervous system. The seven well-established or classical neurotransmitters include:

1. Acetylcholine
2. Norepinephrine
3. Dopamine
4. 5-Hydroxytryptamine (5-HT, serotonin)
5. Gamma-aminobutyric acid (GABA)
6. Glycine
7. Glutamate/aspartate

All of these have been associated with the action of drugs that exert an effect on the nervous system. In addition, there are several neuropeptides which serve as neurotransmitters or neuromodulators (i.e., modify the action of the classical neurotransmitters) that have been associated with the action of drugs and these will be discussed.

In order to appreciate the physiological and/or biochemical mechanisms by which drugs alter neurotransmission, one must have an understanding of the events involved in synaptic neurotransmission. Thus, we will begin with a description of the physiology of chemical neurotransmission and, then, proceed to discuss the individual neurotransmitters and the drugs that mediate their effects through such neurotransmitters. It should be kept in mind that synaptic transmission is not only important for understanding the action of drugs, but it is vital for all functions of the nervous system, and it appears to be the site at which learning and memory take place in the CNS (see Chapter 10).

Chemical Neurotransmission

In the mammalian nervous system (both central and peripheral), the predominant form of communication between two nerves and between nerve and muscle (or nerves and glands) is chemical. Electrical transmission between nerve cells can also occur, but is not easily modified by drugs and will not be considered here. The site at which this chemical transmission occurs is called the *synapse*. From Figure 3.1, it can be seen that the synapse consists of several cellular and subcellular structures. Although synapses can occur at several locations on a neuron which is receiving information from another neuron, the more typical arrangement is that described in Figure 3.1. Thus, the axon terminal of one neuron generally synapses on the cell body (soma or perikaryon called *axosomatic synapses*) or dendrites of another neuron (called *axodendritic synapses*). Axons may also synapse on other axons, especially at the nerve terminals (called *axo-axonic synapses*) and, under unusual circumstances, dendrites may synapse with other dendrites (*dendrodendritic synapses*) or cell bodies may synapse with one another (*soma-somatic synapses*). At the prototypical synapse, the neurotransmitter, which is usually a small water soluble organic amine, is synthesized from precursors within the axon terminal, taken up into and stored in a small round or ovoid vesicle, and released from the nerve terminal in a calcium-dependent process when an action potential or nerve impulse reaches the nerve terminal. Indeed, the steps associated with neurotransmission at a chemical synapse are as follows:

Step 1: The first step is the release of the neurotransmitter from its storage site in a vesicle due to the arrival of an action potential which, in turn, opens voltage-dependent calcium channels and allows the influx of calcium from the extracellular fluid. The calcium then triggers a release process called *exocytosis*. Exocytosis involves fusion of the vesicle membrane with the nerve membrane and the opening of the vesicle into the synaptic cleft (Figure 3.1). Thus, the vesicle extrudes its contents into the synaptic cleft. The release process can be regulated by receptors found on the nerve terminal (called *presynaptic receptors* or *autoreceptors*). Exocytosis is described in more detail below.

Step 2: The next step in neurotransmission involves binding of the neurotransmitter to *receptors* in the postsynaptic membrane and the initiation of postsynaptic events, i.e., a depolarization or a hyperpolarization. Receptors give both neurotransmitters and drugs their selectivity and specificity. The receptors, which are typically membrane proteins or glycoproteins, only recognize and bind chemicals of the "correct" chemical structure. Thus, just as only one key opens a lock, only one chemical structure can initiate postsynaptic events via the receptor. The receptors for neurotransmitters come in two varieties: (1) those that actually form an ion channel in the membrane (such as the nicotinic cholinergic receptor) and mediate rapid events when the transmitter binds and are called *ligand-gated ion channels*, or (2) those that are connected to ion channels indirectly via "second messenger" molecules that become activated inside the cell when the transmitter binds to the

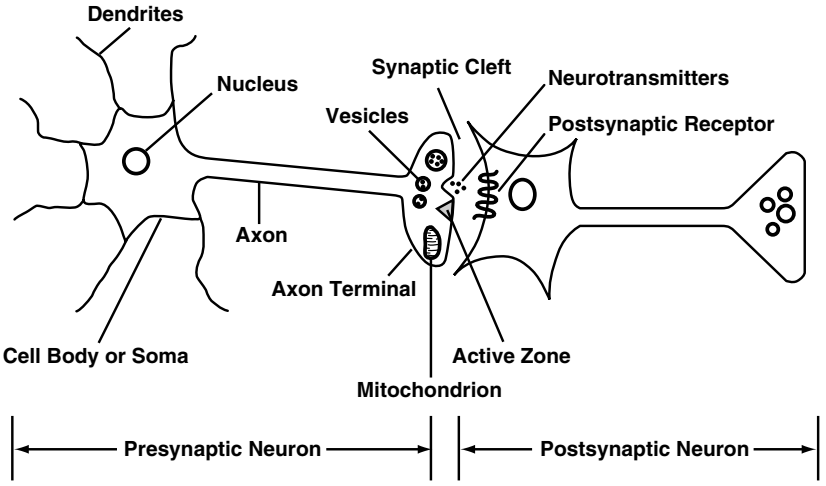

FIGURE 3.1
Drawing of an axosomatic (typical) synapse between two neurons. The neuron synapsing on another neuron is referred to as the *presynaptic neuron,* while the neuron receiving the input is called the *postsynaptic neuron*. Various subcellular structures associated with the synapse are labeled. The active zone is the site at which vesicles attach to the docking sites just prior to release.

receptor. In the latter case, the receptor is linked to a guanine nucleotide binding protein (called a *G-protein*) which functions as the link between the receptor protein and the enzyme(s) that synthesize the "second messenger." This class of receptors is referred to as *G-protein linked receptors* or *metabotropic receptors.*

The potentials that develop in the postsynaptic cell either move the membrane potential further from the threshold for triggering an action potential (hyperpolarization) or move it closer to the threshold (depolarization). Hyperpolarization (inhibitory postsynaptic potentials or IPSPs) results from the opening of chloride or potassium channels in the membrane, allowing chloride to flow in or potassium to flow out. Hyperpolarization, then, inhibits postsynaptic firing. Depolarization (excitatory postsynaptic potentials or EPSPs) results from the opening of channels that allow both sodium and potassium to flow down their concentration gradients through the same channel. This is different from the sodium-selective channel that is involved in the propagation of the action potential down the axon. If the depolarization is great enough, the threshold for an action potential is reached and an action potential (regenerative, sodium current) is propagated down the axon to initiate more synaptic transmission.

In the central nervous system, a neuron can only respond in one of two ways: (1) it either reaches threshold and fires an action potential, which, in turn, propagates information to the next neuron via synaptic transmission or (2) it is inhibited and does not fire an action potential.

Step 3: The third step of the neurotransmission process consists of the postsynaptic response. The postsynaptic response can consist of an action potential in the neuron, the contraction of muscle or the secretion of a gland.

Step 4: This step consists of inactivation of the neurotransmitter in the synaptic cleft. The transmitter must be removed from the synaptic cleft in order for the postsynaptic cell to repolarize, which is necessary for the synapse to remain responsive to incoming information. The two most important mechanisms for removing the neurotransmitter from the cleft are: (1) reuptake into the neuron from which it was released, and (2) enzymatic degradation. In addition, other mechanisms include diffusion away from the cleft and uptake (transport) into other cells (e.g., glial cells, muscle cells in the periphery, or other

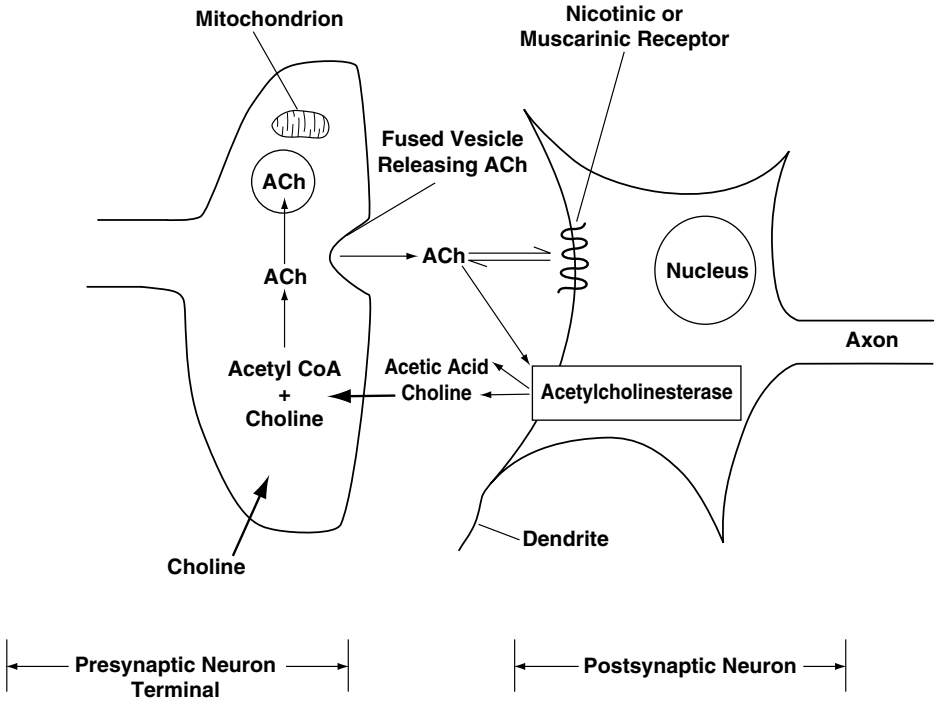

FIGURE 3.2
Drawing of a cholinergic synapse showing the fate of ACh after release into the synaptic cleft. Note that the neuron utilizes choline from two sources: (1) the blood and (2) that which is recycled from the breakdown of released ACh in the synaptic cleft. Acetylcholinesterase associated with the postsynaptic membrane terminates the action of released ACh.

neurons). Just as the neurotransmitter can be taken up and reused by the cell that released it, the vesicle membrane can be retrieved from the nerve terminal where it fused. Thus, vesicles are also recycled.

Sites Where Drugs Act

Drugs may either facilitate (enhance) or inhibit neurotransmission. Some of the mechanisms by which drugs can facilitate neurotransmission include:

- Stimulation of the release of the neurotransmitter into the cleft
- Increased synthesis of the neurotransmitter in the presynaptic terminal
- Prevention of inactivation of the transmitter following release (e.g., blocking reuptake or blocking enzymes of degradation)
- Stimulation of the postsynaptic receptors directly to produce a response. A drug that does this is called an *agonist*

Some of the mechanisms by which drugs inhibit neurotransmission include:

- Inhibition of the synthesis of the transmitter
- Prevention of transmitter release
- Interference with neurotransmitter storage in the vesicle
- Blocking the neurotransmitter receptor

A drug which binds to a receptor, blocking the neurotransmitter action but producing no effect, is called an *antagonist*.

In the sections that follow, we will consider the individual neurotransmitters and the drugs that produce clinical effects by altering chemical neurotransmission.

Acetylcholine (ACh)

Acetylcholine is one of the most widely studied neurotransmitters and one of the oldest, phylogenetically. It was, in fact, the neurotransmitter for which chemical neurotransmission was originally demonstrated, when it was found to be released from nerves innervating the frog heart by Loewi in 1921.[5] It has been most thoroughly studied in the peripheral nervous system where it functions as a neurotransmitter of the motoneurons innervating skeletal muscle (involved in the voluntary control of movement). ACh is also the neurotransmitter of the preganglionic sympathetic and parasympathetic fibers as well as the postganglionic parasympathetic fibers.[5] The response to stimulating parasympathetic nerves innervating various organs in the body is shown in Table 3.1. As you can see, these nerves affect every organ in the body. Drugs which alter neurotransmission at these synapses can have very profound effects.

ACh is also a neurotransmitter in the central nervous system where specific pathways have been identified in the brains of primates and other species. Basically, there are two groups of ACh pathways:[6] (1) those innervating the forebrain (cell bodies in the basal forebrain around the medial septum and nucleus basalis of Meynert), as well as the interneurons in the striatum (basal ganglia) and (2) those innervating the brainstem and diencephalon (cell bodies in the laterodorsal tegmental nucleus and the pedunculopontine tegmental nucleus). Some of the proposed functions of ACh in these CNS pathways are given in Table 3.2, but it is clear that there is much to learn about the intricate details of how ACh regulates such things as learning and memory, sleep, seizures, and emotional states.

Synthesis, Storage, Release, and Inactivation of ACh

Neurons that utilize ACh as a neurotransmitter are referred to as *cholinergic* neurons and a schematic diagram of such a neuron is shown in Figure 3.2. Acetylcholine is synthesized within cholinergic neurons from the precursor, *choline*, which comes from the diet, and/or the breakdown of phospholipids, primarily in the liver.[7] Some of the choline that is taken up into cholinergic neurons for synthesis of ACh comes from the enzymatic degradation of released ACh (Figure 3.2). In fact, about 50% of the choline released as ACh is recaptured by the neuron for the synthesis of more ACh.[8]

Choline is transported into the nerve by a transporter or "carrier" protein in the membrane. This transporter or carrier has a high affinity for choline, which means that it avidly picks up choline from the surrounding area. It has, however, a limited number of transport

TABLE 3.1

Organ Response to Parasympathetic Nerve Stimulation

Organ Receiving Innervation	Response to Stimulation	Receptor Type
Eye		
Iris, sphincter	Pupillary constriction (miosis)	Muscarinic
Ciliary muscle	Contraction — near vision	Muscarinic
Heart		
SA node	Decrease in heart rate	Muscarinic
Atrium	Shortens refractory period	Muscarinic
AV node	Slows conduction	Muscarinic
Ventricles	No response — poor innervation	
Vasculature	No parasympathetic innervation (has muscarinic receptors which can respond with vasodilation)	Muscarinic
Trachea and bronchioles	Constriction	Muscarinic
Stomach and intestine	Increase in motility, tone, and secretions; relaxation of sphincters	Muscarinic
Urinary bladder		
Detrusor muscle	Contraction, bladder emptying	Muscarinic
Trigone and sphincter	Relaxation	Muscarinic
Sex organs, male	Erection	Muscarinic
Sweat glands	Secretion	Muscarinic
Lacrimal glands	Secretion	Muscarinic
Nasopharyngeal glands	Secretion	Muscarinic

Source: Hoffman, B. B. and Taylor, P., Neurotransmission: The autonomic and somatic motor nervous systems, in *The Pharmacological Basis of Therapeutics*, Hardman, J. G., Limbird, L. E., and Gilman, A. G., Eds., McGraw-Hill Medical Publishing, New York, 2001, 115.

TABLE 3.2

Some Proposed Functions of ACh in the CNS

Learning and memory (cholinergic neurons lost in Alzheimer's disease)
Sleep and arousal states
Body temperature
Susceptibility to seizures
Affective states (mood)
Cardiovascular function via hypothalamus
Motor disorders (Parkinson's disease)

sites, meaning that it can get filled up or saturated. Increasing the concentration of choline up to the point at which the sites become filled results in a proportional increase in the rate of choline transport. However, once all the transporters are occupied, the rate of transport becomes constant.

Theoretically, one should be able to increase the synthesis of ACh by increasing the availability of choline, especially since the enzyme that converts choline to ACh, choline acetyltransferase, is not saturated with substrate (choline).

A cosubstrate to choline is utilized in the synthesis of ACh. This cosubstrate is called *acetylcoenzyme A* (acetylCoA). AcetylCoA derives from pyruvate via the breakdown of glucose and is, therefore, plentiful inside the neuron.

Experimental studies have established that the rate-limiting factor in the overall ACh synthesis is the uptake of choline by the neuron.[8,9] Since ACh neurons are lost in Alzheimer's disease, it has been of interest to attempt to increase ACh synthesis in brains of Alzheimer's patients. Although some studies have suggested that this is possible,

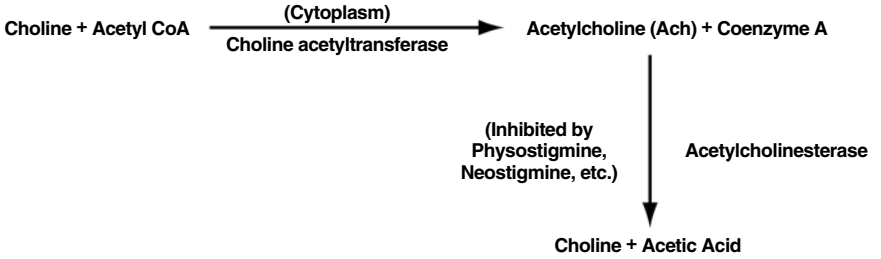

FIGURE 3.3
Synthesis and enzymatic degradation of acetylcholine (ACh). ACh is synthesized in the cytoplasm of the nerve terminal where choline acetyltransferase (synthetic enzyme) is found. Acetylcholinesterase (degradative enzyme) is associated with the postsynaptic membrane.

choline has not been found terribly useful for improving memory in this or other populations.[10] The reason for this may be that the choline uptake transporter saturates and that the intracellular or cytoplasmic choline concentration can only be increased to a limited extent. There are no known drugs to increase the uptake of choline, though there are experimental drugs which inhibit the uptake of choline and interfere with the synthesis of ACh, such as hemicholinium and triethylcholine, both of which are competitive inhibitors of choline uptake.

Choline can also get into neurons by another mechanism, called *"low-affinity" uptake,* which may account for the increase in synthesis of ACh that is seen in some peripheral organs following the administration of high doses of choline. Much higher concentrations of choline are required to saturate the transport proteins involved in low-affinity transport.

It has recently been hypothesized that the selective vulnerability of cholinergic neurons in Alzheimer's disease may be due to the double role of choline in forming membrane phospholipids and ACh in these neurons and the selective breakdown of cell membrane to shunt choline into the neurotransmitter leading to cell membrane damage.[11] If the latter hypothesis is true, treatment with choline may be beneficial. There is evidence that giving choline to rats can increase the release of ACh in the striatum[12] and this effect can apparently be enhanced by caffeine.[13]

The enzyme that catalyzes the synthesis of ACh is choline acetyltransferase (ChAT), which is a soluble enzyme (nonmembrane bound) found in the cytoplasm of cholinergic neurons. The gene responsible for forming ChAT is expressed only in cholinergic neurons and this enzyme, therefore, serves as a phenotypic marker for cholinergic neurons. The overall synthetic scheme is given in Figure 3.3.

Once ACh is synthesized, it is stored in small spherical (synaptic) vesicles along with several other constituents, including adenosine triphosphate (ATP) and a protein called *vesiculin*. The sequestration of the ACh within these tiny vesicles serves to protect it from destruction by the enzyme, acetylcholinesterase. Although there appears to be some ACh in the cytoplasm of the neuron, the vast majority is found within the vesicles from which it is released directly into the synaptic cleft. This is accomplished by the complex process called *exocytosis*.

Exocytosis requires that the vesicle membrane fuse with the neuron membrane and "dump" its contents into the cleft in an all-or-none process. Some of the ACh that is free within the cytoplasm of the neuron may have just been synthesized en route to being taken up by the vesicle membrane transporters for storage within the vesicle. ACh is believed to be transported into the vesicle by an ATPase that pumps protons (hydrogen ions) into the vesicle so the inside does not become charged and also maintains an isotonic state, in spite of the high concentration of ACh in the vesicle.[14] The only drug currently

known to interfere with the storage of ACh is **vesamicol**, which blocks the uptake of ACh into the vesicle and prevents the release of newly synthesized ACh.[14,15]

The latter findings greatly strengthened the hypothesis that ACh is released from the neuron by exocytosis. Exocytosis is a calcium-dependent process and calcium is necessary for fusion to occur between the vesicle membrane and the cell membrane. The voltage change that occurs in the nerve terminal with the arrival of the action potential opens calcium ion channels, allowing calcium to enter the nerve terminal and initiate the exocytotic process. Considerable electrophysiological and morphological evidence indicates that ACh is released from neurons by exocytosis.[8,14] Although no clinically used drugs inhibit ACh release, some toxins are known to inhibit its release, including botulinum toxin A.[5] Botulinum toxin A (Botox®) is commercially available and can be injected directly into muscles to block ACh release and relax the muscle. It is approved for the treatment of blepharospasm and facial wrinkles.[16]

Once ACh has been released from the neuron, it can diffuse to the postsynaptic receptor to mediate a response in the postsynaptic neuron. However, it must then be inactivated if the synapse is to remain functional. In the case of ACh, inactivation occurs by enzymatic destruction of the neurotransmitter. Almost all other neurotransmitters (except for the peptides) are inactivated by reuptake into a neuron. Thus, ACh is unique among neurotransmitters in terms of the mechanism of inactivation following release into the synaptic cleft.

The enzyme that degrades ACh is called *acetylcholinesterase*. However, several cholinesterases have been found in the body. One of them circulates in plasma and is known as *pseudocholinesterase* or *butyrylcholinesterase*, which hydrolyzes butyrylcholine faster than ACh.[8] Acetylcholinesterase is associated with the synaptic cleft and is attached both to the presynaptic and postsynaptic membranes. This enzyme has been shown to exist in several molecular forms that differ in their lipid solubility and in the way they attach to membranes. Several inhibitors of acetylcholinesterase are available and these produce a dramatic increase in the concentration of ACh in the body. Such drugs are widely used in medicine and are discussed below.

Acetylcholine Receptors

Like other neurotransmitters, ACh produces its effects and obtains its selectivity by binding to specific receptors in the postsynaptic cell membrane. These receptors chemically recognize ACh and allow it to interact with specific functional groups in the receptor. Based on the studies of Dale,[17] it has long been known that there are two major types of ACh receptors, which were first identified in the peripheral nervous system: (1) ACh receptors at which nicotine can mimic the action of ACh that were termed *nicotinic* by Dale and (2) ACh receptors that are activated by the alkaloid muscarine (from mushrooms) and were called *muscarinic* receptors. The nicotinic receptors were found to be localized at the neuromuscular junction (voluntary nerves to skeletal muscle), the autonomic ganglia, and the adrenal medulla, while muscarinic receptors were found at the effector organs innervated by the postganglionic parasympathetic fibers. Both types of ACh receptors have been found in the brain.

Nicotinic Receptors

Nicotinic receptors have been widely studied, and most of our knowledge about nicotinic receptors comes from work on electric fish such as the Torpedo, which uses its electric organs to kill prey. It turns out that the high voltage in these fish is generated by ACh

receptors, which are highly concentrated in the electric organ. Thus, the electric fish has served as a rich source of nicotinic receptor protein for the biochemists to study.

The nicotinic receptor was found to be a ligand-gated ion channel composed of four subunits (termed *alpha, beta, gamma,* and *delta*). However, it takes five subunits to form the ion channel, so the channel is formed by two alphas, one beta, one gamma, and one delta subunit.[18] The ACh binds to the alpha subunit of the receptor and, since there are two alpha subunits, it takes two molecules of ACh to open the channel. The techniques of molecular biology (genetic engineering) have contributed greatly to our knowledge of the nicotinic receptor, as well as to our knowledge of the molecular structure of other receptors. These studies have led to a widely accepted model of the nicotinic receptor at the neuromuscular junction of mammals.

However, the nicotinic receptor associated with neurons (e.g., the autonomic ganglia and in the brain) appear to be slightly different. For example, it has long been known that they are not blocked by the classical neuromuscular nicotinic antagonist, *d*-tubocurarine, but are blocked by hexamethonium, another nicotinic antagonist. Research on neuronal nicotinic receptors is still quite active and has important bearing on nicotine addiction and Alzheimer's disease since nicotine has been shown to increase the release of ACh in the cerebral cortex.[19,20] A greater understanding of the different subtypes of neuronal nicotinic receptors (which is now unfolding) is certain to have a big impact on the future treatment of CNS disorders. There is now some evidence that nicotinic receptor agonists may be beneficial in restoring memory that has been impaired due to Alzheimer's disease.

Muscarinic Receptors

Muscarinic receptors are thought to make up the majority of the ACh receptors in the mammalian brain. Unlike nicotinic receptors, the muscarinic receptors are linked to G-proteins and second messengers that carry the signal to ultimately produce a response or change in the cell. Based on molecular cloning technology, five subtypes of muscarinic receptor have been identified. The basic chemical structure (i.e., the amino acid sequence) of these muscarinic receptors has been determined.[21] The best described of the muscarinic receptors are the so-called M1, M2, and M3 which correspond to the m1, m2, and m3 cloned receptors.[22] Inasmuch as the muscarinic receptors are G-protein linked, they mediate their effects through second messengers. Muscarinic receptors may be involved in mediating either excitation or inhibition in the brain, which is usually produced by the opening (inhibition) or closing (excitation) of K^+ channels (i.e., potassium channels).

All G-protein coupled receptors consist of a polypeptide chain (protein) with seven hydrophobic regions (i.e., areas containing amino acids that are more lipid than water soluble). It has been found that these hydrophobic regions of the molecule correspond to positions where the protein loops (crosses) through the cell membrane. So, these receptors loop back and forth through the membrane seven times and are said to contain *seven membrane-spanning regions.* Other G-protein coupled receptors (GCPRs) with seven membrane-spanning regions include the adrenergic, dopaminergic, and serotonergic receptors (see the following text).

The M2 receptor found in the heart is the one most often involved in inhibition. The M1, M3, and cloned m5 subtypes increase phospholipase C activity via a G protein called Gq. The activation of phospholipase C by the latter muscarinic receptors and Gq leads to the hydrolysis of phosphatidyl inositol and the formation of diacylglycerol (DAG) or inositol triphosphate (IP_3), which, in turn, function as second messengers to activate protein kinase C and increase intracellular calcium levels, respectively. M2 and M4 receptors result in the inhibition of adenylate cyclase by acting through a *Gi* protein and, in

addition, may activate (open) K^+ channels directly. These effects can lead to a slowing of the heart as shown in Table 3.1.[23]

Atropine is a nonselective antagonist for all muscarinic receptors while **pirenzepine** is selective for the M1 receptor and **AFDX 116** and **methoctramine** are antagonists for the M2 receptor. The release of ACh and other neurotransmitters may be partially regulated by the activation of M2 receptors located on presynaptic nerve terminals.[24]

Clinically Useful Drugs That Alter Cholinergic Neurotransmission

Facilitators of Cholinergic Neurotransmission

Cholinergic Agonists

There are a number of cholinergic agonists (drugs which bind to the receptor and produce a response or mimic the action of ACh), but only the muscarinic agonists find significant clinical usefulness. These drugs are primarily used in ophthalmology to treat glaucoma or to treat bowel and bladder retention postoperatively.

Muscarinic agonists include **acetylcholine**, which is not used because it is rapidly destroyed by acetylcholinesterase or butyrylcholinesterase; **methacholine**, which is only partially sensitive to the action of acetylcholinesterase and is available as a diagnostic tool; **bethanechol** (Urecholine®), which is used for bowel and bladder retention; **carbachol**, which is used to treat glaucoma and has some nicotinic agonist activity as well; and **pilocarpine**, a naturally occurring alkaloid found in plants, which is a potent muscarinic agonist used to treat glaucoma. Pilocarpine is generally given in eye drops applied topically to the eye.

All of these drugs are used for their effect on the peripheral autonomic nervous system rather than the CNS. Presumably, some of these agonists have some difficulty crossing the blood–brain barrier. However, when given in high doses, pilocarpine gets into the brain and causes seizures in experimental animals.[25] Another muscarinic agonist, **oxotremorine**, seems to produce marked effects on the brain at low doses in that it produces many of the symptoms of Parkinson's disease. Based on the apparent role of the ascending cholinergic neurons in the brain in regulating states of consciousness, it seems possible that cholinergic agonists that enter the brain produce arousal and insomnia. Indeed, even small doses of pilocarpine, given intravenously in cats, have been shown to produce arousal.[23]

There are no therapeutically useful nicotinic agonists except nicotine, itself, which is used in patches or gum to treat smokers' dependence. However, clinical trials are being conducted to test the efficacy of nicotine in the treatment of Alzheimer's disease. Given the fact that the neuronal nicotinic receptor is different from the muscle receptor and that there are several subtypes of neuronal nicotinic receptors, it is likely that we will soon see some new nicotinic drugs that are useful in various neurological disorders.

Cholinesterase Inhibitors

Other than agonists, the only drugs used clinically to facilitate cholinergic neurotransmission are the inhibitors of acetylcholinesterase. These include the reversible cholinesterase inhibitors such as **physostigmine** (Antilirium®), **neostigmine** (Prostigmin®), **pyridostigmine** (Mestinon®), and **edrophonium** (Tensilon®) that are used to treat myasthenia gravis. Physostigmine crosses the blood–brain barrier while others do not, due to the fact that they are highly charged molecules. **Tacrine** (Cognex®), **donepezil** (Aricept®), **rivastigmine** (Exelon®), and **galantamine** (Reminyl®) are lipid soluble reversible cholinesterase inhibitors that easily reach the brain. These drugs are approved for the treatment of memory and cognitive impairment associated with Alzheimer's disease. There are also several

irreversible inhibitors of cholinesterase, such as the **organophosphates** (e.g., diisopropylfluorophosphate or DFP), which irreversibly inhibit the enzyme and are used, primarily, as insecticides. However, some of these are present in eye drops for the treatment of glaucoma. Obviously, the irreversible cholinesterase inhibitors are extremely toxic and are of interest because of their toxicological effects. They are too dangerous for systemic use.

Inhibitors of Cholinergic Neurotransmission

Muscarinic Antagonist

Alkaloids present in the belladonna plant have long been used as muscarinic antagonists. These include atropine and **scopolamine** (hyoscine), both of which are nonselective muscarinic antagonists. These drugs readily enter the brain after systemic administration and some antimuscarinic agents, like **benztropine** (Cogentin®), are used exclusively for their effect on the brain. The latter compound has been used to prevent the Parkinsonian-like side effects associated with antipsychotic drugs like Haldol®. In the days before H_2 histamine receptor antagonists (e.g., cimetidine), which are among the most commonly used ulcer drugs, atropine and other belladonna alkaloids were used to treat gastric ulcers and other conditions associated with increased gastrointestinal (GI) activity. However, **pirenzepine**, the M1 selective antagonist, has been found to be better at reducing gastric secretion. A new muscarinic antagonist, **ipratropium** (Atrovent®), is delivered in an aerosol in the treatment of bronchial asthma. Anticholinergic drugs reduce bronchial secretions and cause bronchodilatation, while decreasing GI activity and dilating the pupils. Hence, they are also used by ophthalmologists to dilate the pupils for examination of the retina. When there is hypersecretion of saliva or bronchiolar secretions, as there is during general anesthesia, atropine or other antimuscarinic drugs are also used to reduce secretions and to dilate bronchiolar passages.

Nicotinic Antagonists

Nicotinic antagonists, at the present time, may be divided into two general categories: (1) those that are muscle nicotinic receptor antagonists or, so-called *neuromuscular blockers,* such as **d-tubocurarine** (curare, the South American arrow poison), and (2) the neuronal nicotinic antagonists, or so-called ganglionic blockers, such as **hexamethonium** or **mecamylamine** (Inversine®). Neuromuscular and *ganglionic blockers* interfere with neurotransmission by acting on the postsynaptic nicotinic receptor (ion channel) and binding to it, in a competitive or noncompetitive manner, to prevent the binding of ACh to the receptor. The drugs that act at the neuromuscular junction to produce muscle paralysis bind directly to the nicotinic receptor, preventing access of ACh. This is also how some of the ganglionic blocking agents work (e.g., mecamylamine, **trimethaphan**). However, some of the ganglionic blockers (e.g., hexamethonium) enter the ion channel and form a plug, which also effectively interferes with neurotransmission by preventing influx of sodium ions.[26]

The neuromuscular blocking agents are also classified into two types: (1) depolarizing blockers and (2) nondepolarizing blockers. **Succinylcholine** (Anectine®) is the most commonly used and best-known depolarizing blocker. It binds to the nicotinic receptor at the neuromuscular junction and produces a depolarization of the membrane, which remains in persistent depolarization for a long time, rendering the synapse nonfunctional. After a period of time, the neuromuscular block actually converts to a competitive-type block, which is called *Phase II.* Giving a cholinesterase inhibitor will not antagonize the action of a depolarizing blocker, and, in fact, may make the block worse. On the other hand, *d*-tubocurarine, **gallamine**, **vecuronium**, and **pancuronium** are competitive neuromuscular blockers which compete with ACh for the receptor. Thus, administering a cholinesterase

inhibitor (e.g., physostigmine or neostigmine) can reverse the block produced by competitive antagonists such as *d*-tubocurarine. All neuromuscular blockers and most ganglionic blockers have a charged nitrogen atom and, therefore, do not get into the brain when injected systemically. In fact, if they are injected into the cerebrospinal fluid, they typically cause seizures. Mecamylamine, on the other hand, is a secondary amine which can enter the brain. Ganglionic blockers are used to lower blood pressure during removal of tumors of the adrenal gland and neuromuscular blockers are used to relax muscles during endoscopic examinations, surgery, and electroconvulsive shock therapy.

Cholinergic Drugs in the TBI Patient

There is evidence of changes in ACh neurotransmission following TBI. Immediately following injury, there appears to be a hyperfunction of the cholinergic system, which lasts 15 minutes to 4 hours. During this time, administration of antimuscarinic drugs has been shown in animal studies to enhance the recovery of function.[27] This is followed by a period of cholinergic hypofunction where administration of cholinergic agonists can reduce cognitive deficits. Thus, cholinesterase inhibitors such as those used in Alzheimer's disease (e.g., tacrine, donepezil, rivastigmine, or galantamine) may be beneficial for improving memory in TBI patients. Indeed, donepezil was found to improve memory in two TBI patients.[28] Clearly, more extensive clinical trials are warranted and should be undertaken.

Norepinephrine

Norepinephrine (NE) is one of three endogenous chemicals known as *catecholamines* that function as neurotransmitters in the mammalian nervous system. The other two are epinephrine, which is a neurotransmitter in brain but a hormone in the periphery, and dopamine, which is a neurotransmitter in brain. NE is the neurotransmitter of the sympathetic postganglionic fibers of the autonomic nervous system where it is involved in such things as increasing heart rate, constricting blood vessels or raising blood pressure, reducing gastrointestinal motility, and dilating pupils (see Table 3.3 for the response of various organs to sympathetic nerve stimulation). There are some exceptions to the rule that all postganglionic sympathetic nerves are "adrenergic" (i.e., use NE as a transmitter), namely, those postganglionic fibers going to sweat glands and those going to certain blood vessels in lower mammals. These both use ACh as a transmitter.

The finding that catecholamines form fluorescent compounds in tissue exposed to formaldehyde gas greatly facilitated the mapping of such neurons in the brain. The technique known as *fluorescence histochemistry* was developed by Falk and Hillarp in Sweden in the early 1960s.[29]

The noradrenergic neurons in the brain are found in one of two systems: (1) the locus coeruleus system and (2) the lateral tegmental system. A description of these two systems is beyond the scope of this chapter, but can be found in an excellent review by Moore and Bloom.[30] Histochemical studies showed that the noradrenergic axons have a very widespread distribution, reaching essentially all levels of the neuraxis. For example, neurons in the nucleus locus coeruleus of the pons innervate everything from the cerebral cortex to the spinal cord. The diffuse nature of the noradrenergic innervation allows this system to have global influences on brain function. The NE system in the brain has been implicated

TABLE 3.3

Organ Response to Sympathetic Nerve Stimulation

Organ Receiving Innervation	Response to Stimulation	Receptor Type
Eye		
Iris, radial muscle	Dilation (mydriasis)	$Alpha_1$
Iris, ciliary muscle	Relaxation of far vision	$Beta_2$
Heart		
SA node	Increase in heart rate	$Beta_1$
Atrium	Increase in contractility	$Beta_1$
AV node	Increased conduction velocity	$Beta_1$
Ventricle	Increased contractility	$Beta_1$
Vasculature		
Skin and mucosa	Constriction	$Alpha_1$
Skeletal muscle	Constriction, dilatation	$Alpha_1$, $Beta_2$
Cerebral	Constriction	$Alpha_1$
Abdominal viscera	Mostly constriction, some dilation	$Alpha_1$, $Beta_2$ for dilation
Trachea and bronchioles	Relaxation	$Beta_2$
Stomach and intestine	Decrease in motility and tone and secretion; contraction of sphincters	$Alpha_1$, $Alpha_2$ $Beta_2$
Urinary bladder		
Detrusor muscle	Relaxation	$Beta_2$
Trigone and sphincter	Contraction	$Alpha_1$
Sex organ, male	Ejaculation	$Alpha_1$
Sweat glands	Localized secretion (palms of hands)	$Alpha_1$
Lacrimal glands	Slight secretion	$Alpha_1$
Nasopharyngeal glands	No direct innervation	—

Source: Hoffman, B. B. and Taylor, P., Neurotransmission: The autonomic and somatic motor nervous systems, in *The Pharmacological Basis of Therapeutics*, Hardman, J. G., Limbird, L. E., and Gilman, A. G., Eds., McGraw-Hill Medical Publishing, New York, 2001, 115.

in a wide variety of functions including anxiety, affective states (mood), arousal, REM sleep, aggression, pain perception, pleasure experience, seizures, and endocrine function.

Synthesis, Storage, Release, and Inactivation of NE

Neurons which synthesize and use NE as a neurotransmitter are referred to as *adrenergic* neurons or *noradrenergic* neurons. NE is synthesized in postganglionic sympathetic neurons and in neurons of the brain from tyrosine, an amino acid which is formed from phenylalanine in the liver. Phenylalanine is referred to as an essential amino acid because it must be supplied in the diet. Tyrosine is transported into adrenergic neurons by a high-affinity uptake transporter.[31] Once inside the neuron, tyrosine is converted to NE by the reactions shown in Figure 3.4.

The rate-limiting enzyme in the overall synthesis of catecholamines (both NE and dopamine) is tyrosine hydroxylase, which is found in the cytoplasm of the neuron. This enzyme utilizes molecular oxygen and tyrosine as substrates and requires iron and tetrahydrobiopterin as cofactors. Under most conditions, the concentration of tyrosine in the neuron saturates the enzyme. Thus, increasing the tyrosine concentration will not enhance the rate of NE synthesis.[32] However, under conditions of increased utilization (e.g., stress), it may be possible to increase the rate of NE synthesis by administering tyrosine.[32]

The second step in the pathway, the conversion of DOPA (dihydroxyphenylalanine) to dopamine requires aromatic-L-amino acid decarboxylase, which uses pyridoxal phosphate (vitamin B_6) as a cofactor (Figure 3.4).

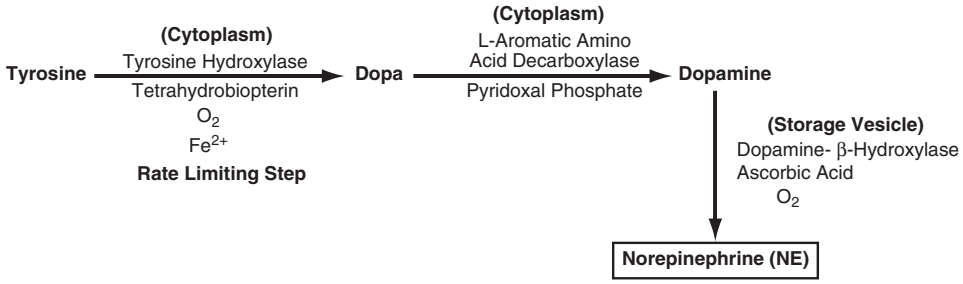

FIGURE 3.4
Synthesis of norepinephrine (NE) in the adrenergic nerve terminal. Shows the enzymes and cofactors required for synthesis, as well as their location (see parentheses) within the neuron.

The third step in the pathway utilizes dopamine-β-hydroxylase (DBH) to convert dopamine to NE. DBH is a copper-containing enzyme which uses ascorbic acid as a cofactor and is located in the membrane of the storage vesicle. Thus, as dopamine is actively transported into the vesicle, it gets converted to NE.[8] Apparently, there is some soluble DBH inside the vesicle which is coreleased with NE. Inhibition of DBH should reduce the levels of NE without affecting the levels of dopamine. In the adrenal medulla and in some neurons of the brain, NE is converted to epinephrine by the enzyme phenylethanolamine-*N*-methyltransferase (PNMT), which is found in the cytoplasm of cells.[5] Synthesis of NE within a neuron is regulated by a wide variety of factors, including the intracellular concentration of NE and the firing rate of the neuron.

Once synthesized, the catecholamines (NE, dopamine, and epinephrine in the brain) are stored in both small (200 to 300 Å) or large (500 to 1200 Å) membrane-bound vesicles. Inside the vesicle, NE is stored in a complex with ATP (adenosine triphosphate), as shown in Figure 3.5. NE is actively transported into the vesicle from the surrounding cytoplasm by an ATP-Mg^{++} dependent process.[33] Uptake of NE into the vesicle, as well as the storage inside the vesicle, is inhibited by the drug **reserpine**, which ultimately leads to the depletion of the tissue content of NE.

The release of NE from nerve terminals occurs when the terminal is depolarized by the incoming action potential. This results in the opening of voltage-dependent Ca^{2+} channels and triggers the process of exocytosis, similar to the release of ACh described above. The sites at which drugs can act to alter neurotransmission at a noradrenergic synapse are shown in Figure 3.5.

Many drugs can facilitate the release of NE from nerve endings to increase the concentration in the synaptic cleft and the postsynaptic receptors. These include the **amphetamines** (Adderall®) and **methylphenidate** (Ritalin®), which stimulate the release of NE and dopamine by a Ca^{2+}-independent mechanism that does not involve exocytosis.

Following release of NE into the synaptic cleft and interaction with the postsynaptic receptors, the neurotransmitter action is terminated primarily by reuptake into the presynaptic terminal from which it was released.[8,32] The reuptake process for NE involves a sodium-dependent process which is inhibited by **antidepressants** and **cocaine**, but not by drugs like reserpine, which inhibit the vesicular uptake. The molecular characteristics of the uptake transporter protein have been studied in great detail and the chemical structure of this protein has been determined from cloning experiments.[34] Although reuptake has been shown to be the major process responsible for terminating the action of NE, enzymatic degradation also takes place via the enzymes monoamine oxidase (MAO) and catechol-*O*-methyltransferase (COMT).

MAO, which is present in the outer membrane of the mitochondrion, is involved in the intraneuronal degradation of free NE that is present in the cytoplasm of neurons. The

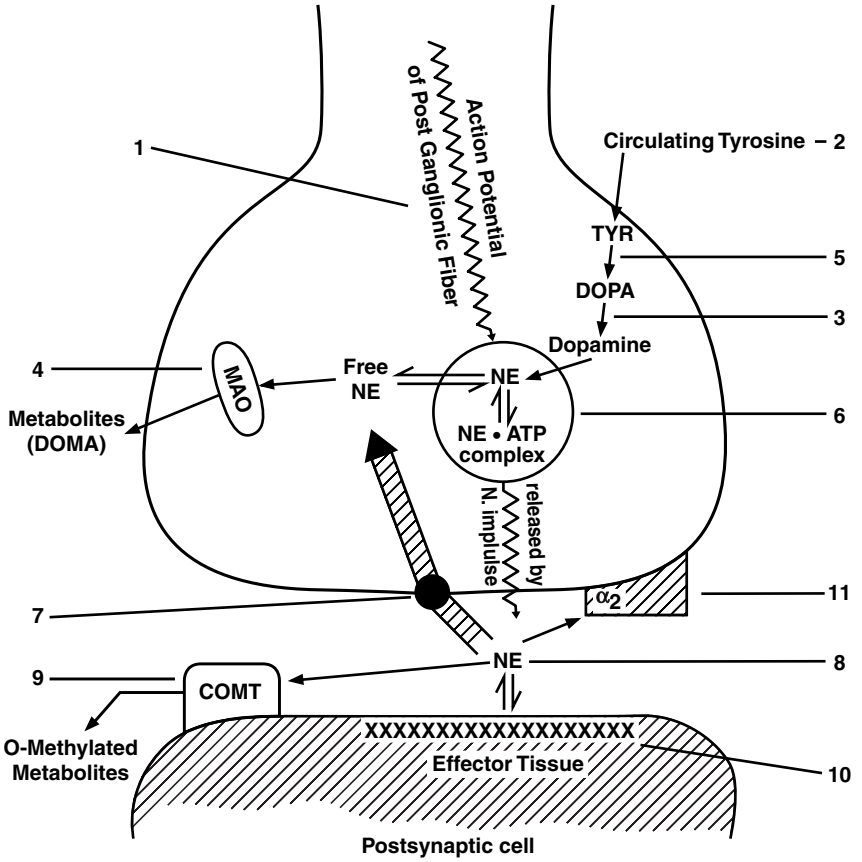

FIGURE 3.5
Drawing of an adrenergic (sympathetic) neuron terminal synapsing on an effector organ in the peripheral autonomic nervous system. This also serves as a model for adrenergic synapses in the central nervous system (CNS). The numbers shown indicate the sites where drugs are known to act to modify neurotransmission. These are as follows: (1) some drugs (e.g., guanethidine and bretylium) inhibit release by blocking the propagation of the action potential (essential for release) into the nerve terminal; (2) under conditions of stress, it may be possible to increase NE synthesis by increasing the concentration of circulating tyrosine (i.e., by administering tyrosine); (3) a more effective way to increase dopamine and NE synthesis is to administer L-DOPA because it bypasses the rate-limiting step involving tyrosine hydroxylase; (4) inhibitors of monoamine oxidase (MAO) (e.g., tranylcypromine) act at Site 4 to prevent the degradation of NE; (5) inhibitors of tyrosine hydroxylase (e.g., alpha-methyltyrosine) act here to block synthesis of NE; (6) drugs which interfere with the storage of NE (e.g., reserpine) act on the vesicle and eventually deplete the neuron of NE; (7) drugs which block reuptake (e.g., cocaine and tricyclic antidepressants) act to increase the concentration of NE in the synapse; (8) NE in the synaptic cleft can act as an agonist on the postsynaptic receptors, as can other agonists for alpha or beta receptors; (9) inhibitors of COMT can increase the availability of NE for agonist action; (10) NE, as well as other directly acting agonists, initiate a response; however, antagonists can also act here to block the response; (11) presynaptic alpha$_2$ receptors decrease the release of NE when these receptors are activated by NE or drugs such as clonidine.

MAO that is found in human and rat brain is present in two forms that are referred to as *Type A* and *Type B*, based on the fact that they have different substrate specificity and different sensitivity to specific inhibitors. For further discussion of the different types of MAO, the reader is referred to Cooper et al.[8] COMT is present in most cells of the body and takes care of the extraneuronal metabolism of catecholamines (NE and dopamine) before they reach the urine.[8,32]

Drugs which act as inhibitors of MAO cause elevations in the intraneuronal content of catecholamines (NE and dopamine) and eventually enhance the concentration of

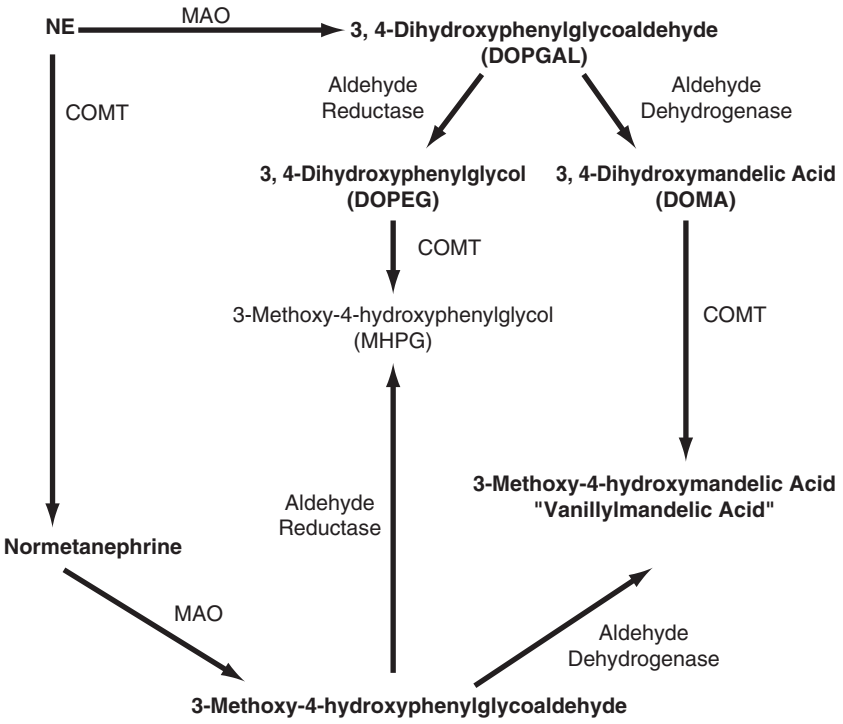

FIGURE 3.6
Enzymatic degradation of NE by monoamine oxidase (MAO) and catecholamine-*O*-methyltransferase (COMT).

neurotransmitter reaching the receptors. MAO inhibitors are employed as antidepressant drugs. COMT inhibitors are used in the treatment of Parkinson's disease to reduce the metabolism of levodopa and enhance its action. The metabolic products resulting from the action of COMT and MAO on NE and dopamine are shown in Figure 3.6. These products represent clinically important metabolites that can be measured in cerebrospinal fluid (CSF) or urine to provide an index of how the catecholamine systems have been altered by disease or drug treatment.[32]

Norepinephrine Receptors

Norepinephrine receptors (adrenoceptors) mediate the effects of NE. Adrenoceptor subtypes that respond to NE include alpha$_1$, alpha$_2$, and beta$_1$. Beta$_2$ receptors have a lower affinity for NE, but have a high affinity for epinephrine and are involved in mediating some of the effects of the latter neurotransmitter or hormone. Specific agonists and antagonists exist for each receptor and some of these are described later in this chapter.

In recent years, a great deal of information has been gained about the molecular nature of the adrenoceptors, both in terms of their coupling to second messenger systems (so-called *signal transduction mechanisms*) and their chemical structure. Each receptor is known to be an integral membrane protein with seven trans-membrane-spanning regions and a molecular weight of 64,000 to 80,000 Da.[35]

Unlike the nicotinic cholinergic receptor, which is intimately associated with an ion channel and produces ultra-rapid effects, the adrenoceptors mediate their effects through G-protein coupled receptors (GPCRs) like the muscarinic ACh receptor.[5,32] Both beta$_1$ and beta$_2$ adrenoceptors are linked to adenylate cyclase in the membrane by a G_s (stimulatory

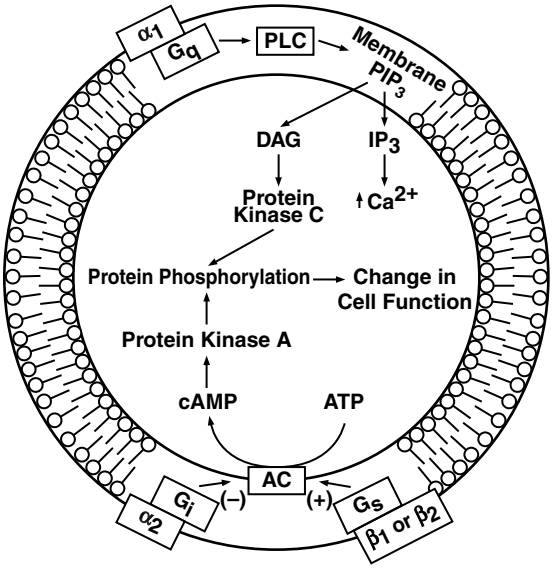

FIGURE 3.7
Diagram of second messenger (signaling) system linked to alpha- and beta-adrenergic receptors in a cell (neuron or effector cell) containing such receptors. The α_1 receptor is linked by a G-protein (G_q) to phospholipase C (PLC) which, when activated (by agonist binding to the α_1 receptor), leads to the breakdown of phosphatidylinositol 4,5-bisphosphate (PIP_2) to form two second messengers (diacylglycerol, or DAG, and inositol triphosphate, or IP3). The DAG activates protein kinase C which can, in turn, phosphorylate proteins including those in ion channels, while IP3 causes an increase in intracellular calcium by releasing it from various stores. The calcium can activate calcium/calmodulin-dependent protein kinase which can phosphorylate other proteins. $Beta_1$ and $beta_2$ receptors act through a G_s protein to stimulate adenylyl cyclase (AC), leading to an increase in the formation of cyclic adenosine monophosphate (cAMP) which can activate protein kinase A to increase the phosphorylation of various proteins. Note that the α_2 receptor acts through a G_i protein (inhibitory G-protein) which leads to inhibition of adenylyl cyclase and a decrease in the intracellular concentration of cAMP. As can be seen here, protein phosphorylation is the major mechanism by which receptors act through signal transduction to alter cell function.

G) protein which is activated by a combination between the receptor protein and an adrenergic agonist. The alpha subunit of the G_s protein with GTP bound to it can then interact with adenylate cyclase and activate it, leading to the conversion of ATP to cyclic AMP. The latter can, in turn, activate various protein kinases which are involved the phosphorylation (i.e., the addition of a phosphate group or PO_4^-) of various proteins that regulate membrane ion transport to alter membrane potentials (Figure 3.7).

The $alpha_2$ adrenoceptors, which are usually located presynaptically (Figure 3.5), also mediate their effect on membrane potential through a G-protein and adenylate cyclase activity, but unlike the beta receptors, the $alpha_2$ receptor is linked to a G_i protein which causes an inhibition of adenylate cyclase and a reduction in the amount of cyclic AMP (and, presumably, a reduction in protein phosphorylation) in the neuron.

The $alpha_1$ adrenergic receptor mediates its action through another second messenger system which is linked to the receptor by a G_q protein. The second messengers produced when an agonist binds to the $alpha_1$ receptor are actually metabolites of phosphoinositide breakdown mediated by phospholipase C and include inositoltriphosphate (IP3) and diacylglycerol (DAG), as was the case for certain muscarinic receptors described above. IP3 causes the release of Ca^{2+} from intracellular storage sites and the Ca^{2+} can then activate protein kinases to produce phosphorylation of membrane proteins (Figure 3.7). The DAG activates protein kinase C which, in turn, phosphorylates various proteins to mediate various cellular responses of $alpha_1$ agonists.[8,36]

Three subtypes of alpha$_1$ receptors (e.g., α_{1a}, α_{1b}, α_{1d}) and three subtypes of alpha$_2$ receptors (α_{2a}, α_{2b}, and α_{2c}) have been identified.[37] There are also three subtypes of beta receptor (β_1, β_2, and β_3). Selective agonists and antagonists are available for alpha$_1$, alpha$_2$, beta$_1$, and beta$_2$ receptors, and these drugs are primarily used for their effects on the peripheral autonomic nervous system, especially in the area of cardiovascular disease. Chronic treatment with agonists or antagonists can result in compensatory changes in the sensitivity and/or receptor number of adrenergic receptors. Such changes appear to be carried out by enzymes that phosphorylate the receptor (i.e., receptor kinases).[37]

Clinically Useful Drugs That Alter Noradrenergic Neurotransmission

Facilitators of Noradrenergic Neurotransmission

Adrenergic Agonists

These are also referred to as direct-acting sympathomimetic amines and they are classified as either alpha or beta agonists. There are both alpha$_1$ and alpha$_2$ agonists available, but many are nonselective. **Norepinephrine** (Levophed®), itself, is available and is an agonist for alpha$_1$, alpha$_2$, and beta$_1$ receptors, while epinephrine is an agonist for all adrenergic receptors. **Phenylephrine** is an alpha$_1$ agonist that is used in nose drops (Neo-Synephrine®) as a nasal decongestant where it acts to vasoconstrict the mucosal blood vessels and reduce congestion. Other alpha agonists that are predominantly alpha$_1$ selective include **methoxamine** and **metaraminol**. **Clonidine** (Catapres®) is an alpha$_2$ agonist used as an antihypertensive agent because of its action on the brain where stimulation of alpha$_2$ receptors presumably decrease the activity of the peripheral sympathetic nervous system. Other alpha$_2$ agonists include **guanfacine** and **guanabenz**.

Isoproterenol (Isuprel®) is a beta agonist that stimulates both beta$_1$ and beta$_2$ receptors and has been used as a bronchodilator because of the beta$_2$ receptors in the bronchioles that mediate bronchiolar relaxation (Table 3.3). Indeed, most of the beta agonists are used for the treatment of diseases that are associated with bronchoconstriction such as asthma. Selective beta$_2$ agonists are also available and have the advantage of not causing cardiac stimulation when used in asthma. These include **metaproterenol** (Metaprel®), **terbutaline** (Brethine®), and **albuterol** (Proventil®). There are no highly selective beta$_1$ agonists available. However, dopamine and **dobutamine** (Dobutrex®) are used for their ability to stimulate beta$_1$ receptors in the heart to increase cardiac output in states of shock or heart failure.

Drugs Which Block NE Reuptake

Inasmuch as reuptake is the major mechanism for inactivating released NE, drugs which block this process have a marked ability to facilitate noradrenergic neurotransmission. The classical example of a drug that does this is **cocaine**. Cocaine, however, also blocks dopamine and serotonin reuptake. Many of the antidepressant drugs (so-called *tricyclic antidepressants*) are potent and selective inhibitors of NE uptake and, presumably, mediate some of their beneficial effects in depression via this mechanism.[38] Selective NE uptake inhibitors include **desipramine** (Norpramin®), **protriptyline** (Vivactil®), **nortriptyline** (Aventyl®), and **maprotiline** (Ludiomil®). All of these are used to treat depression. Side effects of these drugs include their ability to increase heart rate and blood pressure due to peripheral effects on the cardiovascular system. At plasma concentrations that exceed the recommended level, these drugs can also lower the seizure threshold and may precipitate seizures. However, therapeutic plasma levels have been shown to exert anticonvulsant effects in experimental animals.

Drugs Which Increase NE Release

Several drugs are available to increase the release of NE (as well as dopamine in CNS) from nerve endings. The mechanism by which this is accomplished is not entirely clear. However, it appears to involve the release of NE from a nonvesicular pool which does not require calcium and does not involve exocytosis. The current hypothesis is that these drugs are taken up by the uptake transporter for NE, bringing the carrier to the inside of the neuron where NE can bind to it for exchange transport. Such drugs also interfere with the uptake of NE by vesicles, increasing the cytoplasmic concentration of NE and making more available for reverse transport.[5] Drugs that facilitate the release of NE include **amphetamine**, **dextroamphetamine** (Dexedrine®), **methamphetamine** (Desoxyn®), and **methylphenidate** (Ritalin®). These drugs also increase the release of dopamine from nerve terminals, which is believed to be responsible for many of their effects and will be discussed later.

Amphetamine is the racemic mixture of D- and L-amphetamine. Dextroamphetamine is three to four times more potent in stimulating the CNS than is L-amphetamine. One commercial product contains a mixture of amphetamine and dextroamphetamine (Adderall®). All amphetamine analogues have powerful cardiovascular stimulating effects leading to an increase in blood pressure and the work of the heart. The CNS stimulating effects of amphetamine on arousal and locomotor activity are dependent on newly synthesized NE or dopamine since these effects are blocked by alpha methyltyrosine, a tyrosine hydroxylase inhibitor used to block NE synthesis.[26]

The amphetamines, as a group, are used to suppress appetite in the treatment of obesity and to treat narcolepsy (a sleep disorder) and attention deficit hyperactivity disorder (ADHD). These drugs are regulated as controlled substances because of their abuse potential. High doses can produce a psychosis that is indistinguishable from an acute paranoid schizophrenic syndrome. Moreover, it has been shown, in both rats and nonhuman primates, that repeated injections of methamphetamine can produce neurotoxicity leading to the loss of both dopamine and serotonin containing neurons in the brain.[39–42] The mechanism responsible for this neurotoxicity remains unknown, although several hypotheses have been proposed.

Drugs That Decrease the Enzymatic Degradation of NE

NE is degraded intraneuronally by the enzyme monoamine oxidase (MAO) as indicated above. Inhibiting this enzyme should eventually increase the concentration of NE in the synaptic cleft. Several MAO inhibitors are used clinically as antidepressants. These include **tranylcypromine** (Parnate®), **phenelzine** (Nardil®), and **isocarboxazid** (Marplan®). Some MAO inhibitors are being used to prevent further deterioration of Parkinson's disease. One drug in the latter category is **selegiline** (deprenyl, Eldepryl®), which is selective for MAO-B. Patients on MAO-inhibitors cannot eat foods containing tyramine (a potent NE releaser). Normally, tyramine is metabolized by MAO in the intestine, but this enzyme is inactive in patients on an MAO inhibitor. Tyramine reaching the circulation causes a hypertensive crisis with very dangerous consequences. Thus, individuals taking MAO inhibitors must avoid foods containing tyramine, such as wine, beer, cheese, and other fermented products.

Inhibitors of Noradrenergic Neurotransmission

Adrenoceptor Antagonists

There have long been available drugs that are selective antagonists of either alpha or beta adrenergic receptors. Now, we have drugs that are even selective for a specific subtype

of alpha or beta receptor. The main advantage of a subtype selective antagonist is that it will have fewer side effects. Nonselective alpha antagonists include **phenoxybenzamine** and **phentolamine**, while nonselective beta-antagonists include **propranolol** (Inderal®), **sotalol**, and **pindolol**. Of interest for the treatment of hypertension are the $alpha_1$ selective antagonists, **prazosin** (Minipress®) and **terazosin** (Hytrin®). $Beta_1$ selective antagonists are useful because they can be used to reduce blood pressure, stop cardiac arrhythmias, or prevent subsequent heart attacks with minimal effects on bronchiolar smooth muscle. **Metoprolol** (Lopressor®), **atenolol** (Tenormin®), **acebutolol** (Sectral®), and **esmolol** (Brevibloc®) are all currently marketed $beta_1$ selective antagonists used to treat cardiovascular disorders.

Inhibitors of NE Release

Some drugs are selectively taken up into noradrenergic nerve terminals and then prevent the release of NE, apparently by blocking the invasion of the action potential into the terminal (i.e., a local anesthetic-like effect). Drugs in this category are referred to as *adrenergic neuronal blocking agents* and include **guanethidine** (Ismelin®), **guanadrel** (Hylorel®), and **bretylium**. Initially, these drugs cause a transient release of NE, prior to the inhibition of release. When used chronically, guanethidine also has a reserpine-like effect (see below) by interfering with NE storage and depleting the neurons of NE. Such drugs are primarily used as antihypertensive agents. However, bretylium is now used exclusively to treat cardiac arrhythmias.

Inhibitors of Storage

Reserpine is the classical drug for inhibiting the storage of catecholamines (NE, epinephrine, and dopamine) and serotonin (see the following text). Reserpine binds to the vesicle membrane and interferes with the uptake of monoamines into the vesicle, rendering the vesicle nonfunctional. When NE cannot be stored in the vesicle, it leaks out into the cytoplasm and is degraded by MAO. Thus, reserpine leads to a depletion of the NE from the nerve terminals. It is primarily used in combination with other drugs as an antihypertensive agent.[43]

Inhibitors of NE Synthesis

There are two sites within the NE synthetic pathway where drugs can be used to block synthesis: (1) the tyrosine hydroxylase step (which is the rate-limiting enzyme) and (2) the dopamine β hydroxylase step. The latter is more selective and can be accomplished with the drug **disulfiram** (Antabuse®) or its active metabolite diethyldithiocarbamate (DDTC). Unfortunately, these drugs inhibit many other enzymes and have many side effects. The most common way to interfere with synthesis of NE is to inhibit tyrosine hydroxylase with **α-methyltyrosine** (metyrosine, Demser®). However, this drug also blocks the synthesis of epinephrine and dopamine and is, therefore, not very selective.

Noradrenergic Drugs in the TBI Patient

There is considerable evidence that enhancing noradrenergic neurotransmission in the CNS has beneficial effects on recovery of function after TBI in animal studies.[44–48] Moreover, interference with noradrenergic neurotransmission (e.g., using alpha adrenoceptor antagonists) was found to retard the recovery of motor function in rats after head injury.[49] Because of these findings, Feeney and coworkers[49] have put forth the NE hypothesis of recovery. Consistent with this hypothesis is the finding that amphetamines, when paired with physical therapy, have been shown to enhance recovery following stroke.[50,51]

The above findings indicate that drugs which enhance NE neurotransmission (e.g., *d*-amphetamine, tricyclic antidepressants) facilitate recovery following TBI. However, more clinical studies are needed since most of the data has been obtained in animals.

Dopamine

Although dopamine can be found in the peripheral nervous system in such places as the carotid body and sympathetic ganglia, it is of interest primarily for its neurotransmitter role in the CNS where it is involved in a wide variety of functions from regulating motor function (basal ganglia) to inhibiting the release of prolactin from the pituitary gland. Most of the dopamine neurons in the brain have their cell bodies either in the midbrain (e.g., substantia nigra) where they are involved in the regulation of emotional states or motor activity (e.g., substantia nigra dopamine is lost in Parkinson's disease) or the hypothalamus where it is involved in regulating endocrine function.[8] Thus, there are three major dopaminergic pathways in the CNS: (1) the nigrostriatal pathway (which projects from substantia nigra to the striatum and is important in Parkinson's disease), (2) the mesocortical/mesolimbic system (which projects from the ventromedial aspects of the midbrain to the limbic system and the cerebral cortex, playing a role in psychiatric disorders), and (3) the tuberoinfundibular pathway (which projects from the arcuate nucleus of the hypothalamus to the median eminence of the pituitary stalk and regulates endocrine function).

Synthesis, Storage, Release, and Inactivation of Dopamine

Dopamine is an intermediate compound in the synthesis of NE and is, in fact, the immediate precursor of NE (see Figure 3.4 and Figure 3.8). Thus, the synthesis is identical to that of NE up through the formation of dopamine, but does not proceed to NE because dopaminergic neurons lack the enzyme dopamine-β-hydroxylase. As was the case with NE synthesis, tyrosine hydroxylase is the rate-limiting enzyme in the synthetic pathway and, if one wants to block synthesis, this is the enzyme to block.

Dopamine synthesis is regulated somewhat differently than is NE synthesis. This is largely because dopaminergic neurons have autoreceptors on the dopamine nerve terminal that regulate both synthesis and release, whereas NE neurons have autoreceptors (which are α_2) that regulate release only.[8] However, like NE, the intracellular concentration of dopamine can regulate synthesis through end-product inhibition. Again, tyrosine hydroxylase is normally saturated with tyrosine, so that administering tyrosine is not an effective way to enhance the synthesis of dopamine. However, DOPA decarboxylase is not saturated with substrate and synthesis of dopamine can be increased by the administration of DOPA, given as *levodopa,* which is now the drug of choice in the treatment of Parkinson's disease. In Parkinson's disease, the nigrostriatal dopaminergic pathway degenerates and the administration of levodopa helps replace the dopamine in the striatum.

Dopamine is stored in vesicles in a manner similar to that of NE in a complex with ATP. Several soluble proteins called *chromogranins* are also present in the dopamine storage vesicle. The release of dopamine from nerve terminals, like that of NE, is triggered by the arrival of an action potential. Release occurs by a process of exocytosis and, therefore, is calcium-dependent. The release of dopamine is apparently reduced by a negative feedback mechanism when excess dopamine in the synaptic cleft interacts with presynaptic

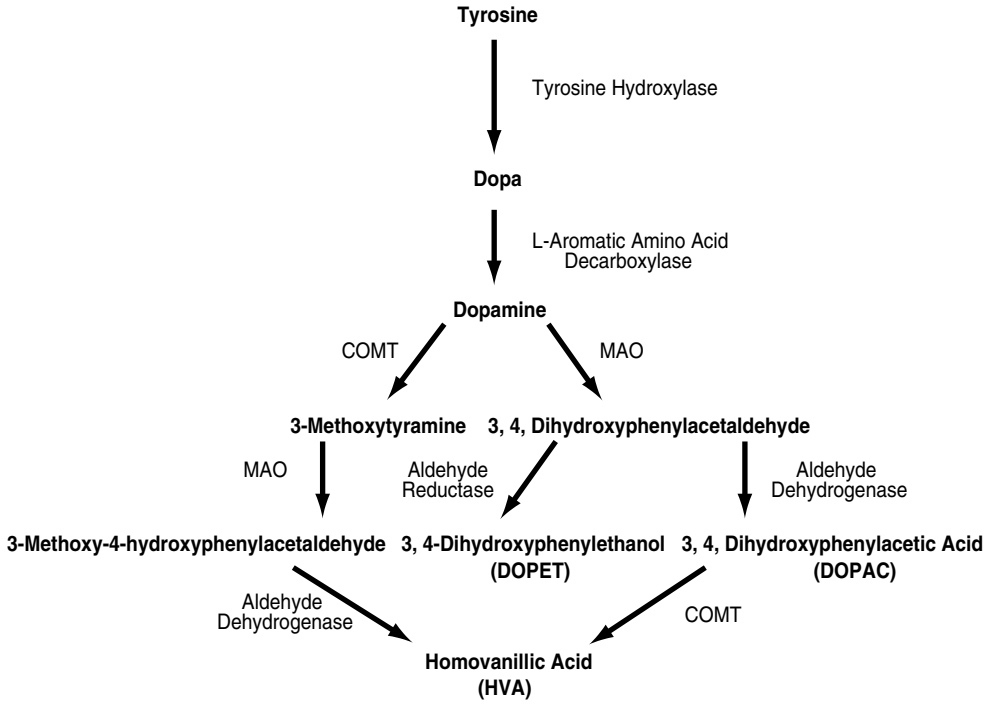

FIGURE 3.8
Synthesis and degradation of dopamine. Note that HVA is the major metabolite. COMT: catechol-*O*-methyltransferase; DOPA: dihydroxyphenylalanine; MAO: monoamine oxidase.

receptors (autoreceptors). Activation of autoreceptors on the cell body reduces the firing rates of dopaminergic neurons.[8] All dopaminergic autoreceptors are believed to be of the D_2 or D_3 subtype (see Dopamine Receptors section).

Dopamine is inactivated following release by a high-affinity uptake transporter (reuptake), which transports it back into the neuron from which it was released. This is an energy requiring process that is dependent on sodium and is similar to the NE reuptake. As is the case with NE and most other neurotransmitters, the dopamine transporter has been cloned and found to be a member of a large family of transporter proteins that have 12 membrane-spanning regions. Indeed, much is known about the molecular characteristics of the dopamine transporter.[52]

Although reuptake into the neuron from which it was released is the primary mechanism for terminating the physiological effects of released dopamine, it may also undergo enzymatic metabolism similar to NE. Thus, both MAO and COMT can convert dopamine to inactive compounds according to the schema shown in Figure 3.8. Moreover, the resulting metabolites DOPAC and HVA (Figure 3.8) are often used as indices of the rate of dopamine turnover in the CNS. Antipsychotic drugs (neuroleptics) which block dopamine receptors increase the concentration of dopamine metabolites in cerebrospinal fluid (CSF) and in brain.[8]

Dopamine Receptors

Two subtypes of dopamine receptors (D-1 and D-2) have been identified and described in great detail using receptor binding techniques.[53] However, using molecular cloning techniques, five dopamine receptors have been identified and all of them, including the

new ones (D-3, D-4, and D-5), are now classified as either D-1-like or D-2-like receptors.[54–57] The D-1-like include the D-1 and D-5 receptors, while the D-2-like include D-2, D-3, and D-4 receptors. The D-1-like receptors appear to mediate their effects through a G_s protein which activates adenylate cyclase and increases cyclic AMP, while the D-2-like receptors appear to be negatively coupled to adenylate cyclase, producing an inhibition of the latter through a G_i protein. All of the dopamine receptors (D-1, D-2, D-3, D-4, and D-5) have seven hydrophobic regions corresponding to the predicted seven membrane-spanning regions of the other G-protein linked receptors in this family.

There is considerable sequence homology (similar sequence of amino acids in the protein) between the various dopamine receptors as well as between these receptors and other members of this family such as the $beta_1$ and muscarinic receptors.[54] The D-3 receptor appears to represent both an autoreceptor and postsynaptic receptor and is found in limbic areas of brain.[54] The D-4 receptor is of great interest because it has been implicated in the effects of **clozapine** (an atypical antipsychotic agent) and may account for the atypical effects of clozapine (Clozaril®). For most antipsychotic drugs, there is a high correlation between their clinical potency and their D-2 receptor blocking action. However, clozapine is much more potent at blocking D-4 receptors and has fewer motor side effects than the other antipsychotic drugs. Moreover, clozapine is effective at alleviating the symptoms of schizophrenia in some patients who are refractory to other antipsychotic drugs. Because of these differences, clozapine and newer antipsychotic drugs are referred to as *atypical antipsychotics*. The D-4 receptor is largely found in the limbic system and there is some evidence that the D-4 receptor is markedly increased in the brains of schizophrenic patients.[57] In general, the functions of most subtypes of dopamine receptor are unknown; D-1 receptors have only been found postsynaptically, but D-2 receptors occur either pre- or postsynaptically and autoreceptors are usually of the D-2 subtype. The use of D-1 and D-2 agonists has shown that activation of both receptors may be necessary for expression of certain dopamine functions.

The dopamine neurons have been implicated in the abuse of stimulants such as cocaine and amphetamine. Mesolimbic dopaminergic neurons have also been implicated in addiction to alcohol, opioids, and nicotine. It has been proposed that variations in the gene for the D-2 receptor may contribute to inter-individual differences in vulnerability to alcoholism and polysubstance abuse.[58]

Clinically Useful Drugs That Alter Dopamine Neurotransmission

Facilitators of Dopaminergic Neurotransmission

Dopamine Agonists

Dopamine, itself, does not cross the blood–brain barrier and, therefore, cannot be used for effects on the CNS. However, dopamine is used intravenously for its effects on the cardiovascular system where it acts on $beta_1$ receptors in the heart to increase contractility and on dopamine receptors in the renal vasculature to cause vasodilation. Because of the latter two actions, dopamine is used to treat various forms of shock. **Apomorphine** is a nonselective dopamine agonist that does get into the brain and has been used to treat such things as Parkinson's disease. However, it is poorly absorbed from the gut and must be administered parenterally. Apomorphine achieves high concentrations in the chemoreceptor trigger zone (CTZ) in the area postrema of the medulla oblongata, which regulates vomiting. Because of its effects here, apomorphine produces nausea and vomiting, limiting its usefulness in the treatment of dopamine deficiency syndromes. Other nonselective dopamine agonists include **bromocriptine** (Parlodel®) which has long been used to treat endocrine disorders, such as hyperprolactinemia, where it acts in the anterior pituitary

gland to inhibit the release of prolactin. Bromocriptine is also now recommended for the treatment of Parkinson's disease. **Lisuride** and **pergolide** (Permax®) are two other dopamine agonists that, along with bromocriptine, have been used in Parkinson's disease.

Several new selective D-1 or D-2 agonists are now being examined experimentally. For example, **SKF 38393** is a D-1 agonist while **LY 17155** is a D-2 agonist. These are being used as tools to learn more about the function of D-1 an D-2 receptors, but they could become clinically useful in the future. Drugs selective for the D-3, D-4, or D-5 receptor have not yet been developed.

Drugs That Increase the Synaptic Concentration of Dopamine by Acting Indirectly

These include the indirectly acting agents, such as **amphetamine** and **methylphenidate** (Ritalin®), which increase the release of dopamine into the synaptic cleft, the dopamine reuptake inhibitors (**GBR 12909**, amphetamine, **nomifensine**, benztropine, amantadine), and the drugs which increase dopamine synthesis (**levodopa**, amantadine). The reader will note that some drugs have more than one action. For example, amphetamine and amantadine increase the release of dopamine from nerve endings as well as prevent the inactivation by reuptake.

Drugs That Block Enzymatic Degradation of Dopamine

Like other catecholamines, dopamine is degraded by MAO and COMT (see Figure 3.8). Therefore, MAO inhibitors can increase the synaptic concentration of dopamine. Selegiline (Eldepryl®) (described previously) is now being used to treat Parkinson's disease because it may prevent the formation of neurotoxins that destroy dopaminergic neurons and arrest the progression of the disease. All of the MAO inhibitors described above under NE will also prevent the enzymatic degradation of dopamine. Two COMT inhibitors have recently become available for the treatment of Parkinson's disease. These include **tolcapone** (Tasmar®) and **entacapone** (Comtan®), which block the conversion of levodopa to 3-*O*-methyldopa and increase the amount of levodopa that gets converted to dopamine in the brain.[59]

The COMT inhibitors can reduce the "wearing off" symptoms in patients treated with levodopa/carbidopa. However, caution should be exercised in the use of tolcapone because of potential liver toxicity.

Inhibitors of Dopaminergic Neurotransmission

Drugs That Interfere with Dopaminergic Neurotransmission

In this category, we have just two groups of drugs: (1) the receptor antagonists or blockers and (2) the drugs which interfere with storage (e.g., reserpine). As would be expected, the only ones that provide selective effects on dopaminergic neurotransmission are the receptor blockers, since reserpine-like drugs interfere with the storage of all monoamines. We will, therefore, consider only the dopamine antagonists here.

Antagonists of dopamine receptors are primarily used as antipsychotic drugs (also called *neuroleptics*) to treat schizophrenia. The fact that essentially all of the drugs effective in schizophrenia are dopaminergic antagonists has led to the hypothesis that schizophrenia is caused by too much dopamine at certain synapses — a hypothesis that has been difficult to prove. Essentially, all of the dopamine antagonists block D-2 receptors, but D-1 and D-4 receptors may be affected by certain drugs. The atypical antipsychotic drugs, unlike the older (typical) drugs, appear to have a low affinity for the D-2 receptor and have a higher affinity for the D-3 or D-4 receptor. The latter drugs are also effective antagonists at the 5-HT_{2A} receptor.[60] A list of the dopamine antagonists is given in Table 3.4.

Dopamine antagonists have many side effects because they block dopamine receptors not only in the limbic system, which regulates emotion, but also in the basal ganglia,

TABLE 3.4

Dopamine Receptor Antagonists (Blockers)

Chemical Class	Examples of Drugs	Receptor Type
Phenothiazines	Chlorpromazine	D-1 and D-2
	Thioridazine	
	Perphenazine	
Thioxanthenes	Chlorprothixene	D-2
Butyrophenones	Haloperidol (Haldol®)	Some selectivity for D-2
Dihydroindoles	Molindone	D-2
Dibenzodiazepines	Clozapine (Clozaril®)	D-4(?)
Substituted benzamides	Metoclopramide (Reglan®)	D-2
	SCH23390	Selective for D-1
Atypical Antipsychotics	Clozapine (Clozaril®)	D-2, D-4, 5-HT_{2A}
	Risperidone (Risperdal®)	D-2, D-4, 5-HT_{2A}
	Olanzapine (Zyprexa®)	D-2, D-4, 5-HT_{2A}
	Quetiapine (Seroquel®)	D-2, D-4, 5-HT_{2A}
	Ziprasidone (Geodon®)	D-2, D-4, 5-HT_{2A}

Source: Baldessarini, R. J. and Tarazi, F. I., Drugs and the treatment of psychiatric disorders: Psychosis and mania, in *The Pharmacological Basis of Therapeutics*, Hardman, J. G., Limbird, L. E., and Gilman, A. G., Eds., McGraw-Hill, New York, 2001, 485.

where loss of dopamine function causes Parkinsonian-like symptoms, and in the pituitary where they cause endocrine-related side effects. **Metoclopramide** (Reglan®) is a dopamine antagonist used for its peripheral effects and its effects on the chemoreceptor trigger zone (which is outside the blood–brain barrier) to prevent nausea and vomiting. Although it penetrates the brain poorly, some does reach the basal ganglia which can cause some Parkinsonian-like side effects. All of the D-2 dopamine receptor antagonists have antiemetic properties, but only some (e.g., metoclopramide and **prochlorperazine** [Compazine®]) are approved for such use.

Dopaminergic Drugs in the TBI Patient

Several reports in recent years suggest that enhancing dopaminergic neurotransmission may be beneficial to patients with traumatic brain injury. Improving dopaminergic function appears to be useful for two types of deficits in these patients. First, some TBI patients display Parkinsonian-like symptoms; and second, dopaminergic agents may improve arousal and the ability to focus attention on the task at hand, including rehabilitation therapy. Just as L-DOPA (levodopa) is effective in Parkinson's disease, it may help similar symptoms in patients with TBI. The combination of L-DOPA with a peripheral decarboxylase inhibitor will reduce the metabolism of L-DOPA in the periphery and increase the amount that actually reaches the brain. Thus, the combination of levodopa and carbidopa (a decarboxylase inhibitor) is often used. Sinemet® (a mixture of L-DOPA and Carbidopa) has, in fact, been used successfully in some patients with TBI.[61,62] There is also some evidence from animal studies that treatment with dopamine agonists (e.g., ropinirole) can either reduce or reverse the motor and cognitive deficits produced by brain injury.[63]

Dopamine agonists are also available and may have an advantage because they do not depend on intact dopaminergic neurons. The dopaminergic agonists include such things as the ergot derivatives (e.g., bromocriptine, **pergolide**, and **lisuride**), nonergot agonists such as **ropinirole** (Requip®) and **pramipexole** (Mirapex®), and the antiviral drug with dopaminergic agonist activity, **amantadine**. There is some evidence that these drugs can reduce fatigue, distractibility, and bradykinesia, and improve attention, concentration, and purposeful movement in TBI patients.[64,65]

The use of dopamine antagonists can be advantageous in controlling the symptoms of psychosis, but could impair motivation. The role of dopamine neurons in motivation and reward, as well as in addiction, is well established.[6] Thus, blocking dopamine receptors could reduce motivation. Perhaps it would be possible to enhance motivation with a dopamine reuptake inhibitor like **bupropion** (Wellbutrin®, Zyban®). There is one report showing that bupropion improved restlessness in a TBI patient.[66]

5-Hydroxytryptamine (Serotonin)

5-Hydroxytryptamine or serotonin (5-HT) is an indolamine that is found both in the periphery and in the CNS. About 90% of the 5-HT in the body is found in the gastrointestinal tract (in enterochromaffin cells and neurons of the myenteric plexus), while 8% of the 5-HT of the body is found in platelets, and only 2% is found in the brain.[8] It is, however, the 2% in the brain that receives most of the attention and this is the fraction we will focus on.

Within the brain, 5-HT is localized in neurons that express the gene for tryptophan hydroxylase (Trp-OH). Extensive mapping of serotonergic neurons in the CNS of the rat has been performed using fluorescence histochemistry and immunocytochemistry. In general, the cell bodies of the serotonergic neurons are located along the midline of the brainstem in what are called *raphe nuclei*. Originally, nine separate groups of 5-HT cell bodies were described by Dahlstrom and Fuxe,[67] but more recently, other cell groups have been detected in the area postrema (vomiting area) and in the caudal locus coeruleus, as well as in the interpeduncular nucleus.[8] Like the noradrenergic neurons, the serotonergic neurons have a widespread distribution innervating essentially all areas of the CNS from the cerebral cortex to the spinal cord. The more caudal cell groups (B-1 to B-3) primarily innervate the brainstem and spinal cord, while the rostral cell groups (B-6 to B-9) innervate the forebrain. A detailed description of the neuroanatomy of serotonergic neurons has been provided by Molliver.[68]

Synthesis, Storage, Release, and Inactivation of Serotonin

The amino acid precursor for 5-HT synthesis is tryptophan, which is an essential amino acid supplied in the diet. Tryptophan, like tyrosine, is a neutral amino acid that also gains entry into the brain by the large neutral amino acid transporter. Thus, plasma tryptophan will compete with other neutral amino acids, such as tyrosine and phenylalanine, for transport into the brain, which means that the concentration of brain tryptophan will be determined not only by the concentration of tryptophan in plasma but also by the plasma concentration of other neutral amino acids.[8,69] Once in the extracellular fluid of the brain, tryptophan is transported into the serotonergic neurons by a high-affinity and a low-affinity transport system where it can then be converted to 5-HT by a two-step reaction (Figure 3.9) with each step being catalyzed by a different enzyme.[70]

The rate-limiting step in the overall conversion of tryptophan to serotonin is the first step which is catalyzed by tryptophan hydroxylase (Figure 3.9) and results in the conversion of tryptophan to 5-hydroxytryptophan (5-HTP). Like tyrosine hydroxylase, tryptophan hydroxylase is a cytoplasmic mixed-function oxidase which requires molecular oxygen and a reduced pteridine as cofactors. It should also be noted that a membrane-associated form of tryptophan hydroxylase has been found, indicating that some of the enzyme may be membrane bound. Various inhibitors of tryptophan hydroxylase have

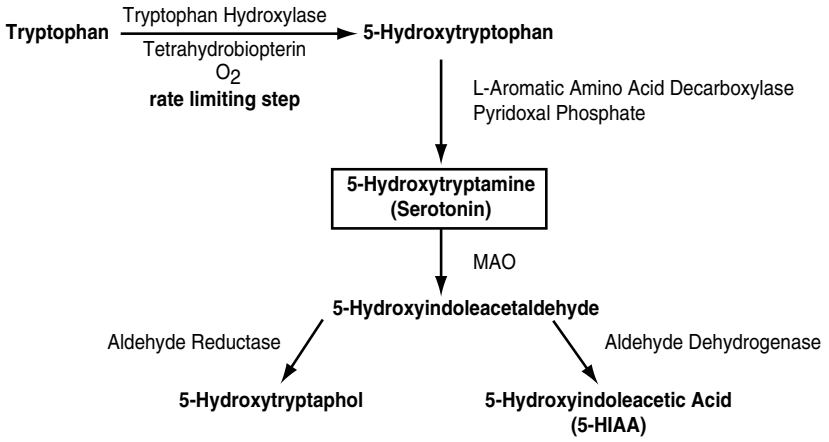

FIGURE 3.9
Synthesis and degradation of 5-hydroxytryptamine (serotonin) in the CNS. Note that 5-HIAA is the major metabolite. MAO: monoamine oxidase.

been identified, the best known of which is parachlorophenylalanine (PCPA), which has been used experimentally to study the function of 5-HT.

Inasmuch as the K_m of tryptophan hydroxylase (50 to 120 μM) is higher than the concentration of brain tryptophan (30 μM), the enzyme is not saturated with tryptophan, which means that increasing the concentration of brain tryptophan can increase the synthesis of 5-HT and lead to higher brain levels of serotonin.[70,71] Thus, it has been found that dietary manipulations of tryptophan can change the brain concentration of serotonin. The 5-HTP formed by the action of tryptophan hydroxylase on tryptophan is immediately converted to 5-HT (serotonin) by the action of L-aromatic amino acid decarboxylase, the same enzyme that converts DOPA to dopamine in catecholaminergic neurons. The decarboxylation of 5-HTP, like that of DOPA, requires pyridoxal phosphate as a cofactor. Inasmuch as the decarboxylation takes place in the cytoplasm, the resulting 5-HT must then be transported into vesicles for storage (see text below).

The rate of 5-HT synthesis appears to be regulated by the rate of neuronal firing. The latter control over 5-HT synthesis appears to be exerted on tryptophan hydroxylase by a Ca^{2+}-dependent phosphorylation of the rate limiting enzyme.[71]

The available evidence suggests that serotonin, like the catecholamines, is stored in membrane-bound synaptic vesicles inside nerve terminals.[72] A substantial portion of the serotonin in brain is found in isolated vesicles and these vesicles have been shown to take up serotonin.[73,74] Release of 5-HT, like that of other neurotransmitters, appears to occur by exocytosis in a calcium-dependent manner.[72] However, certain drugs such as ***p*-chloroamphetamine** are believed to release serotonin from the cytoplasmic pool rather than the vesicular pool[75] and there is some evidence that the depolarization mediated release by neurons can involve either vesicular or cytoplasmic pools.[76] The available evidence suggests that 5-HT is stored in the vesicles in a complex with ATP and perhaps a serotonin-binding protein.[72]

The release of 5-HT from nerve endings is also believed to be regulated via a negative feedback mechanism through serotonin autoreceptors located on the presynaptic (serotonergic) nerve terminals. The evidence indicates that these 5-HT autoreceptors are of the 5-HT_{1B} subtype (see following text).[71] Most of the postsynaptic effects of 5-HT are believed to be inhibitory, although it has been shown to facilitate excitatory neurotransmitters at some sites in the brain.[71]

Mechanisms similar to those of catecholamine inactivation (see above) have been shown to occur for serotonin inactivation. Thus, both reuptake into the neuron from which it was

released and monoamine oxidase may be involved in the inactivation of 5-HT following its action in the synaptic cleft. A high-affinity, sodium-dependent, energy-dependent (requires ATP) uptake of 5-HT has been demonstrated in experimental studies,[69] and reuptake into serotonergic terminals appears to function as the primary inactivation mechanism for removing released serotonin from the synaptic cleft. This concept is supported by studies showing that inhibitors of serotonin uptake such as **fluoxetine** (Prozac®), **sertraline** (Zoloft®), or **paroxetine** (Paxil®) enhance the action of serotonin. However, others[77] believe that the primary fate of released 5-HT is uptake by nonserotonergic cells, followed by degradation by monoamine oxidase to form 5-hydroxyindoleacetic acid (5-HIAA). The latter investigators have suggested that brain or CSF levels of 5-HIAA can be used as an index of serotonin turnover and utilization.[77] From Figure 3.8, it can be seen that 5-hydroxytryptophol can also be formed by the action of monoamine oxidase on serotonin in brain, although the major metabolite is 5-HIAA.[71]

Serotonin Receptors

In the last 10 years, there has been an explosion of information about the 5-HT receptor. The 5-HT receptor family has become very large with at least 14 distinct receptors, all of which have been cloned. These include the 5-HT_1 subfamily (including 5-HT_{1A}, 5-HT_{1B}, 5-HT_{1D}, 5-ht_{1E}, 5-ht_{1F}), the 5-HT_2 subfamily (including 5-HT_{2A}, 5-HT_{2B}, and 5-HT_{2C}), the 5-HT_3 subfamily, as well as the individual 5-HT_4,5-ht_5, 5-HT_6, and 5-HT_7 receptors. The lower-case designation (e.g., 5-ht) is used for receptors in which no known function has yet been established.[78]

The 5-HT_1 subfamily is negatively coupled to adenylate cyclase through a G_i protein similar to the $alpha_2$ adrenergic receptor and, when activated, produces a decrease in the adenylate cyclase activity. The 5-HT_2 subfamily, consisting of 5-HT_{2A}, $_{2B}$, and $_{2C}$, is linked to phospholipase C and the phosphoinositide second messenger system through a G_q protein similar to the $alpha_1$ adrenergic receptor. The 5-HT_4, 5-HT_6, and 5-HT_7 are positively coupled with adenylate cyclase through a G_s protein similar to the beta adrenergic receptors.[78] The intracellular signaling system for the 5-ht_5 (5-ht_{5A}, 5-ht_{5B}) receptors has not been determined. There are no clinically used drugs that act on the 5-HT_5, 5-HT_6 or 5-HT_7 receptors. However, we are likely to see such drugs in the future.

The 5-HT_3 family was originally identified in the periphery.[79] These receptors are unique among the monoamine receptors in that, instead of being G-protein linked receptors, they are ligand-gated ion channels similar to the nicotinic ACh receptor. The 5-HT_3 receptor is a nonselective cation channel that allows Na^+ and K^+ to enter the cell when 5-HT is bound to it. Thus, the 5-HT_3 receptors result in excitation. Originally, the 5-HT_3 receptors were identified primarily by their affinity for specific agonists and antagonists,[79,80] but they have now been cloned.[81] The 5-HT_3 receptors appear to be present in the area postrema where they play a role in regulating vomiting. Indeed, the 5-HT_3 antagonists **ondansetron** (Zofran®) and **granisetron** (Kytril®) are widely used to treat the nausea and vomiting associated with cancer chemotherapy.

Clinically Useful Drugs That Alter Serotonergic Neurotransmission

Facilitators of Serotonergic Neurotransmission

Drugs That Increase the Synthesis and/or Release of 5-HT

Since the rate-limiting enzyme, Trp-OH, is not saturated with tryptophan, it is possible to increase the synthesis of 5-HT by administering tryptophan. However, a number of factors affect the amount of tryptophan that actually gets into the brain, such as the ratio

of tryptophan to other neutral amino acids in the plasma that compete with tryptophan for transport into the brain, and the concentration of free fatty acids in the plasma which compete with tryptophan for binding to plasma proteins.

Tryptophan administration has apparently been used in the treatment of depression, but its effectiveness has been questioned. It is also possible to increase the release of 5-HT from nerve terminals with **fenfluramine**, a drug that was marketed as an appetite suppressant (anorexiant) to treat obesity. Fenfluramine is no longer on the market in the United States because of toxicities associated with pulmonary hypertension and damaged heart valves. It was one of the ingredients in Fen-Phen used to treat obesity.

Drugs That Are 5-HT Agonists

The availability of agonists highly selective for specific subtypes of 5-HT receptors is low. Serotonin, itself, does not cross the blood–brain barrier and many of the other agonists are hallucinogenic. However, there are three partial agonists for 5-HT_{1A} receptors (**ipsapirone**, **gepirone**, and **buspirone**) that are being used for the treatment of anxiety. Of these, buspirone (Buspar®) is the only one approved for use in the United States in the treatment of anxiety. **Sumatriptan** (Imitrex®), **zolmitriptan** (Zomig®), **naratriptan** (Amerge®), and **rizatriptan** (Maxalt®) are agonist for the 5-HT_{1D} and 5-HT_{1B} receptors and are used widely for the treatment of migraine headache. The latter are believed to act by increasing cerebral vascular constriction during the vasodilatory phase of a migraine headache.[82,83]

Drugs That Block the Reuptake or Prevent Enzymatic Degradation of 5-HT

It is clear that the most common way to increase serotonergic neurotransmission, clinically, is to use a reuptake blocker. The ones approved for clinical use include **fluoxetine** (Prozac®), **sertraline** (Zoloft®), **paroxetine** (Paxil®), **fluvoxamine** (Luvox®), and **clomipramine** (Anafranil®) — the first three of which are used as antidepressants, while the last two (fluvoxamine and clomipramine) are used for obsessive–compulsive disorder. In addition to their use in obsessive–compulsive disorder, the 5-HT reuptake inhibitors can be used to suppress appetite, although they are not approved for this use. Monoamine oxidase inhibitors, described above under norepinephrine, can also be used to enhance serotonergic neurotransmission since they will prevent the degradation of this amine as well.[8] However, the MAO inhibitors are not selective and could result in an increase in the synaptic content of NE, dopamine, and 5-HT.

Inhibitors of Serotonergic Neurotransmission

There are few drugs clinically available for interfering with serotonergic neurotransmission, and these fall into one of two categories: (1) drugs that interfere with storage of 5-HT and (2) drugs that block 5-HT receptors. The drugs that interfere with the storage of 5-HT are the same drugs that do this to NE and dopamine — namely, reserpine or **tetrabenazine**. The only one used clinically is reserpine, which is used to treat hypertension. A side effect of reserpine is depression with suicidal tendency, which apparently results from the depletion of brain NE and 5-HT.

There are a whole host of experimental drugs that block 5-HT receptors, but only a few are available for clinical use at the present time. These include **methysergide** (Sansert®), a nonselective (broad spectrum) 5-HT antagonist, which is used to prevent the onset of migraine headaches, and selective 5-HT_3 antagonists ondansetron (Zofran®) and granisetron (Kytril®) which are used to treat nausea and vomiting. Given the plethora of 5-HT receptors and the rate at which new ones are being discovered, it is clear that the

drug companies have a difficult road ahead; however, it is also clear that a wide variety of new and, it is hoped, selective 5-HT antagonists will be available in the near future.

Serotonin has been implicated in a wide variety of functions including anxiety, sleep states, pain perception, affective states (depression), food intake, thermoregulation, seizures, vomiting, neuroendocrine functions, and blood pressure. New drugs to treat disorders of these functions may well come from selective agents for modifying serotonergic neurotransmission.

Serotonergic Drugs in the TBI Patient

The role of 5-HT in brain injury and the recovery of function after injury is not clear. Studies done in animal models of TBI suggest that 5-HT synthesis increases after TBI and that this is associated with a decrease in local cerebral glucose utilization in the cerebral cortex.[84] Moreover, inhibition of 5-HT synthesis with *p*-chlorophenylalanine was found to reduce cerebral blood flow changes, cerebral edema, and cell injury following TBI in animals.[85] Such findings suggest that 5-HT contributes to the damage after TBI. However, several studies show that drugs that increase the concentration of 5-HT at its receptors in brain enhance recovery of function after TBI. For example, an agonist for the 5-HT_{1A} receptor has been shown to reduce learning deficits in rats following TBI.[86] The antidepressant fluoxetine has also been shown to facilitate cognitive function in rats following TBI.[87] Fluoxetine has also been found to reduce OCD in TBI patients.[88] The antidepressant effects of SSRIs are also seen in TBI patients, just as they are in the noninjured population. Thus, it would appear that enhancing serotonergic neurotransmission is beneficial in TBI patients. However, more studies are needed before definitive conclusions can be reached regarding the use of serotonergic drugs for TBI patients.

Gamma Aminobutyric Acid (GABA)

GABA is one of two amino acids (the other being glycine) that function as major inhibitory neurotransmitters in the mammalian brain. GABA is present in essentially all areas of the brain and has been implicated in the mechanism of action of several antiepileptic drugs, as well as in the action of hypnotics (sleeping aids) and antianxiety drugs. The concentration of GABA in the brain is much higher than that of the monoamine neurotransmitters. Studying the neurotransmitter role of GABA and other amino acids has not been easy for researchers because these amino acids also play a metabolic role and are structural components of proteins. Thus, within the neuron, there is both a metabolic and a neurotransmitter pool of GABA. Determining whether one is dealing with the metabolic pool or the neurotransmitter pool of GABA is crucial, but not always easy.

GABAergic neurons are widely distributed throughout the brain and spinal cord. In most areas of the brain, GABAergic neurons are short interneurons (inhibitory interneurons) rather than long projection cells. However, some GABAergic pathways have been mapped and these include the pathway from the striatum (caudate) to the substantia nigra and another from the globus pallidus to the substantia nigra. The purkinje cells of the cerebellum are also GABAergic and some of these project to the lateral vestibular nucleus in the medulla oblongata.[89]

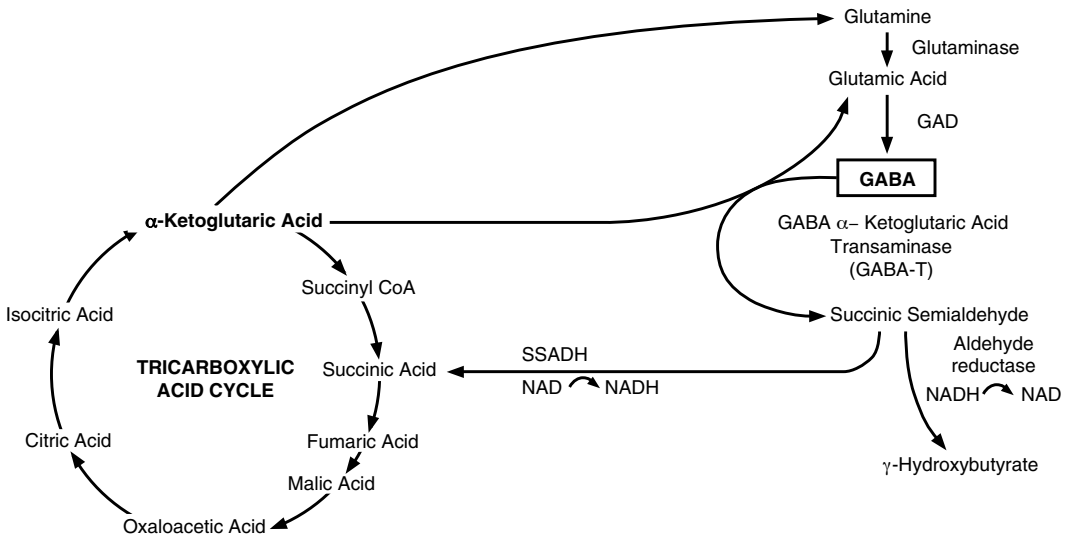

FIGURE 3.10
Synthesis and degradation of GABA via the GABA "shunt" of the tricarboxylic acid (Krebs) cycle. Note that glutamate is a precursor of GABA.

Synthesis, Storage, Release, and Inactivation of GABA

GABA is synthesized from glutamic acid by the enzyme glutamic acid decarboxylase (L-glutamate decarboxylase, GAD), which serves as a biochemical marker for GABAergic neurons.[90] The glutamate is formed from glucose via the glycolytic pathway and the Krebs cycle.[90,91] Pyruvate, formed from glucose, enters the Krebs cycle as acetyl CoA and is converted to alpha ketoglutarate, the first component of the "GABA shunt," which leads to the synthesis of GABA (Figure 3.10).[91]

The GABA shunt represents an alternative pathway between two intermediates of the Krebs cycle. In this shunt, alpha ketoglutarate is converted to glutamic acid in a transamination reaction involving GABA-alpha ketoglutarate transaminase. Some authorities have suggested the transamination of alpha ketoglutarate to glutamate may involve the enzyme aspartate amino transferase which is coupled to the conversion of aspartic acid to oxaloacetic acid.[92,93] The glutamate is then converted to GABA by glutamate decarboxylase (GAD).

GABA is degraded by GABA-transaminase (GABA-T) which converts it to succinic semialdehyde. In this process, a molecule of GABA can be broken down only if a molecule of precursor is formed (Figure 3.10).[90] The succinic semialdehyde is then converted to succinic acid by the enzyme succinic semialdehyde dehydrogenase (SSADH), returning the shunt to the Krebs cycle (Figure 3.10).

Released GABA may also enter the glutamine loop. In the latter case, the GABA is taken up by glial cells where it is converted back to glutamate by a reverse transamination involving GABA-T. The glia cannot convert glutamate to GABA because they lack GAD, but they convert the glutamate to glutamine with glutamine synthetase. The newly formed glutamine can diffuse out of the glial cells and into the GABAergic nerve endings where it can be converted back to glutamate by glutaminase. This provides another mechanism by which neurons can conserve GABA.[90]

GAD and GABA-T can be manipulated pharmacologically. Both enzymes require pyridoxal phosphate (vitamin B6) as a cofactor, but the subcellular location of the enzymes

differs for the two. GAD is a soluble enzyme found in cytoplasm and GABA-T is a mitochondrial enzyme.

Based on recent findings, it appears that there are two types of GAD, each of which is formed from a different gene. The two types of GAD are referred to as GAD_{65} and GAD_{67}.[81,94] These forms differ in molecular weight, amino acid sequence, interaction with pyridoxal phosphate, and expression in different parts of the brain. GAD_{65} appears to be localized to nerve terminals to a greater extent than GAD_{67}.

There is some controversy over whether or not GAD is saturated with glutamate. Some authorities suggest that it is[90] while others[94] suggest that it is not. However, all investigators agree that there is no evidence that GABA synthesis is controlled by the availability of glutamate, which should be the case if GAD is unsaturated with substrate. Of interest is the finding that GAD is the target of antibodies present in people who later develop insulin-dependent diabetes mellitus (Type 1 diabetes). In these patients, the antibody which destroys the beta islet cells of the pancreas is directed at GAD.[95,96]

GABA-T is also a pyridoxal phosphate-dependent enzyme which has been purified to homogeneity and was shown to have a molecular weight of about 109,000. The availability of alpha ketoglutarate may regulate the tissue levels of GABA. Variations in the concentration of alpha ketoglutarate could be responsible for the postmortem changes in GABA levels that are known to occur. For example, when respiration stops, the dependence of the Krebs cycle on respiration results in a marked decline in the availability of alpha ketoglutarate and the consequent reduction in GABA-T activity, which depends on alpha ketoglutarate for transamination. However, GABA synthesis can still occur from glutamate via GAD, which is an anaerobic enzyme.[90]

Whether GABA and other amino acid neurotransmitters are stored in and released from synaptic vesicles remains somewhat controversial. Both a vesicular and a cytoplasmic pool of GABA exist within the neuron and release occurs in both a Ca^{2+}-dependent and Ca^{2+}-independent manner.[97] However, synaptic vesicles isolated from the pig cortex contain a high concentration of GABA.[98] Based on differences in the rate of equilibration of ^{3}H-GABA between cytoplasmic and vesicular fractions, it has been concluded that the calcium-dependent release is from the vesicular fraction rather than the cytoplasmic fraction.[99]

As has been demonstrated for the uptake of NE and 5-HT into synaptic vesicles, GABA may be taken up into synaptic vesicles by a Na^{+}-independent mechanism that is driven by a proton gradient maintained by a Mg^{++}-ATPase.[100] Evidence also suggests that GABA is released from a cytoplasmic fraction,[101] both in a Ca^{2+}-dependent and Ca^{2+}-independent manner. The cytoplasmic release may involve an exchange transporter between cytoplasmic and extracellular compartments. The latter exchange system seems to be coupled to a Na^{+} transporter.[97]

It has recently been suggested that the amino acidergic exchange transporter is responsible for the Ca^{2+}-independent release of GABA that is known to coexist with the Ca^{+2}-dependent release.[102] Thus, the available evidence suggests that the release of GABA (and other amino acid neurotransmitters) can occur by either of two Ca^{2+}-dependent mechanisms, vesicular or cytoplasmic, and also by a Ca^{2+}-independent mechanism. How these three systems interact with each other and which system, if any, predominates is yet to be determined. (See detailed review by Nicholls.)[97]

Following release from nerve endings, high-affinity uptake by neurons and glial cells is believed to be responsible for terminating the neurotransmitter action of GABA since no rapid enzymatic destruction system similar to that for ACh has been identified. The plasma membrane transporter responsible for GABA uptake requires extracellular sodium and chloride ions. Two sodiums and one chloride ion are cotransported with each molecule of GABA.[81,103,104] The high-affinity uptake transporter of GABA is capable of moving GABA against a concentration gradient and, generally, concentrates the amino acid three

to four orders of magnitude higher in the intracellular compartment than in the extracellular compartment.

High affinity uptake of GABA and excitant amino acid into neurons and glial cells has also been demonstrated by several laboratories.[105] The operation of the glial transporter is similar to the neuronal transporter and is in the direction of net uptake.

Four distinct plasma membrane GABA transporters have been cloned. These are referred to as GAT-1, GAT-2, GAT-3, and BGT-1.[106] Such findings suggest a much greater heterogeneity of GABA transporters than was expected, and the significance of this heterogeneity is still unknown. Although it was hoped that these could be localized to either neurons or glia, this is not the case. However, some regions of the brain appear to contain a predominance of one type of transporter over another.[106] Of interest is the finding that certain drugs (e.g., hydroxynipecotic acid) appear to preferentially inhibit the glial vs. the neuronal transporter,[81] although the pharmacology of these transporters is still being determined.

GABA Receptors

Two subtypes of GABA receptor have been described in detail and are referred to as $GABA_A$ and $GABA_B$ receptors. The $GABA_A$ receptor has been more thoroughly investigated and is ligand-gated ion channel that functions as a channel for the chloride ion.[107,108] This receptor is usually placed in a gene family that also includes the nicotinic acetylcholine receptor and the glycine receptor. $GABA_A$ receptors are stimulated by GABA, **muscimol**, and **isoguvacine** and are blocked by the convulsants **bicuculline** (competitive antagonist) and **picrotoxin** (noncompetitive antagonist). The $GABA_A$ receptor has long been described as a macromolecular complex which consists of the GABA recognition site, the chloride channel, and the benzodiazepine binding site. Benzodiazepine anxiolytics (e.g., **diazepam**) and sedative–hypnotics (e.g., barbiturates) modulate the $GABA_A$ receptor by enhancing the action of GABA. Activation of the $GABA_A$ due to the binding of GABA to the receptor causes the chloride channel to open, which usually results in hyperpolarization unless the membrane potential is already greater than the chloride equilibrium potential, in which case GABA produces depolarization. In the adult nervous system, GABA almost always produces hyperpolarization (inhibition). However, in the developing brain, it can be excitatory.

Molecular cloning has indicated that there are five major types of polypeptide subunits for the $GABA_A$ receptor, which range in weight from 50 to 60 kDa (alpha, beta, gamma, delta, and rho). Like the nicotinic ACh receptor, each subunit has four membrane-spanning regions, one of which is believed to contribute to the walls of the ion channel. Molecular cloning studies have provided evidence for the existence of six alpha, four beta, three gamma, one delta, and three rho subunits. Scientists often use cells that do not normally express (contain) GABA receptors, like the Xenopus oocyte. By adding the genes for the GABA receptor to these cells, they can cause them to express GABA receptors, the function of which can then be studied. By examining recombinant receptors in Xenopus oocytes, it is possible to determine the importance of each subunit. It appears that while GABA-regulated chloride conductance, which is inhibited by bicuculline and picrotoxin, can be obtained with the expression of alpha and beta subunits only, full benzodiazepine sensitivity is only obtained if the neurons contain the alpha, beta, and the $gamma_2$ subunits.[109] Thus, recombinant receptors containing α, β, and γ_2 subunits most closely resemble $GABA_A$ receptors found in brain and the subtype of α and β subunits expressed determines the various affinities for benzodiazepines found in different parts of the brain.[109] As was the case with the ACh receptor, it is believed that five subunits (e.g., two alphas, two betas, and a $gamma_2$) form the ion channel.

The $GABA_B$ receptor is insensitive to bicuculline, 3-aminopropanesulfonic acid, and isoguvacine, but has a weak sensitivity to muscimol and is stereospecifically sensitive to (-)baclofen (Lioresal®). The $GABA_B$ receptor, unlike the $GABA_A$ receptor, is not a ligand-gated ion channel, but is, instead, linked through G-proteins to a second messenger system like the muscarinic cholinergic and the adrenergic receptors. Most of the early studies suggested that $GABA_B$ receptors were primarily presynaptic receptors involved in inhibiting the release of neurotransmitters; however, it is now clear that they may also mediate postsynaptic inhibition as well.[110,111] Basically, two membrane effects have been attributed to the $GABA_B$ receptors: (1) a decrease in Ca^{2+} conductance (usually a presynaptic effect leading to decreased neurotransmitter release) and (2) an increase in K^+ conductance (usually leading to postsynaptic hyperpolarization) as occurs in hippocampal pyramidal cells following the application of baclofen. It has been suggested that the reason for the different effects may be related to the fact that $GABA_B$ receptors are linked to different channels in different locations. Thus, they are probably linked via second messengers to Ca^{2+} channels on presynaptic terminals and to K^+ channels at postsynaptic sites.[111] The second messengers to which $GABA_B$ receptors have been suggested to be linked are cAMP (decreased) and phosphatidyl inositols.

The classical agonist for $GABA_B$ receptors is (-)baclofen. A number of studies have been carried out with baclofen to assess the function of $GABA_B$ receptors. However, one difficulty with the use of baclofen is that it crosses the blood–brain barrier rather poorly.[111]

A third subtype of GABA receptor called the $GABA_C$ receptor has recently been identified on the basis of its lack of sensitivity to bicuculline and baclofen and its sensitivity to *cis*-4-aminocrotonic acid (agonist). These receptors were first discovered in the retina, but have now been found in retina, cerebellum, optic tectum, hippocampus, and spinal cord. $GABA_C$ receptors form a chloride channel from five rho subunits and are, therefore, referred to as homomeric channels.[81,112] While many known drugs act on $GABA_A$ and $GABA_B$ receptors, we have no useful pharmacological agents for the $GABA_C$ receptor.

Clinically Useful Drugs That Alter GABAergic Neurotransmission

Facilitators of GABAergic Neurotransmission

GABA Agonists

Several experimental drugs are used as agonists for the $GABA_A$ receptor including **muscimol**, **THIP**, and **isoguvacine**. In fact, there are no clinically approved drugs that act as $GABA_A$ agonists per se. However, the **benzodiazepines** are allosteric modulators of the $GABA_A$ receptor which, when bound to their high-affinity site on the $GABA_A$ receptor, enhance the binding of GABA to its binding site and increase the frequency of chloride channel opening. The benzodiazepines are, by far, the most popular clinically used drugs whose mechanism of action involves the $GABA_A$ receptor. The latter compounds have a wide variety of uses, including the treatment of anxiety, seizures, insomnia, and muscle spasms. The benzodiazepines bind with high affinity to a site on the chloride channel and enhance the inhibitory action of GABA.

Benzodiazepines used to treat anxiety include **diazepam** (Valium®), **oxazepam** (Serax®), **alprazolam** (Xanax®), and **lorazepam** (Ativan®). Those used as antiepileptic drugs include diazepam, **clonazepam** (Klonopin®), and **nitrazepam**. Benzodiazepines used as hypnotics include **flurazepam** (Dalmane®), **temazepam** (Restoril®), **triazolam** (Halcion®), and **quazepam** (Doral®). Additionally, all of these drugs have muscle relaxant properties, but diazepam is, probably, most commonly used for this purpose.

There is another major class of drugs that act as positive allosteric modulators of the $GABA_A$ chloride channel. These are the barbiturates such as **phenobarbital**, **pentobarbital**,

and **secobarbital**. The barbiturates are widely used as hypnotic agents (sleeping pills) and as adjuncts to anesthetics during surgery. Moreover, some barbiturates find important use as antiepileptic drugs (e.g., phenobarbital and **primidone** [Mysoline®]). Barbiturates bind to a different site on the chloride channel than do the benzodiazepines, and they increase the duration of channel open time, rather than the frequency of opening.

$GABA_B$ receptors also mediate inhibition in the nervous system through the action of G-proteins and second messengers. Baclofen (Lioresal®) is a $GABA_B$ receptor agonist that has long been used to treat spasticity in patients with multiple sclerosis or other neurological diseases.

Drugs That Block GABA Degradation

There are a whole host of compounds used experimentally to block GABA-T, but only one of these is used clinically and that is gamma vinyl-GABA or **vigabatrin**, which is used as an antiepileptic drug in Europe but has not been approved for use in the United States.[113,114] Vigabatrin is an irreversible GABA transaminase inhibitor that has been shown to be of value in some drug-refractory epileptic patients. **Valproic acid** (Depakene®) has also been shown to elevate brain GABA levels by inhibiting GABA-T.[115] Valproic acid is used to treat a variety of seizure types including absence and generalized tonic–clonic. Whether the action of valproic acid in epilepsy is due primarily to an enhancement of the action of GABA is not known because it has another important effect that is probably responsible for its effect in tonic–clonic seizures — namely, it blocks sodium channels in a frequency- and voltage-dependent fashion.[113]

Drugs That Inhibit GABAergic Neurotransmission

Drugs That Block GABA Receptors

There are several GABA antagonists available for experimental use. However, because all the $GABA_A$ antagonists are convulsants, they have no clinical use, at the present time. The classical $GABA_A$ antagonist is bicuculline, but picrotoxin is also an antagonist. **Saclofen** and **phaclofen** are $GABA_B$ antagonists that are being used in experimental animals to help deduce the functional importance of the $GABA_B$ receptor. There are also a group of experimental compounds that bind to the benzodiazepine binding site on the chloride channel and cause a reduction in the effectiveness of GABA. The latter compounds, of which **beta-carboline-3-carboxylic acid** (and other beta carbolines) is an example, are called *inverse agonists.* Clearly, the GABA antagonists and the inverse benzodiazepine agonists are proconvulsant and have no clinical use in medicine.

GABAergic Drugs in the TBI Patient

GABA is the major inhibitory neurotransmitter in brain and, therefore, changes in GABAergic neurotransmission can have major consequences. In general, anything that reduces GABA neurotransmission can cause seizures and would be detrimental to the patient. Indeed, loss of GABAergic neurons following TBI may be responsible for posttraumatic epilepsy. However, immediately following TBI in animals, it appears that GABA release is increased.[116]

The increase in GABA release may represent a compensatory attempt to reduce seizures in the injured region. However, other studies have found a decrease in benzodiazepine receptor binding which may also reflect a reduction in GABA receptor function since the benzodiazepine binding site is on the same chloride channel as the GABA binding site (see text on GABA receptors).[117]

Drugs that facilitate GABAergic neurotransmission are widely used in TBI patients. For example, $GABA_B$ agonists, such as baclofen, are used to treat spasticity, while benzodiazepines, such as clonazepam and diazepam, are used to suppress seizures and anxiety. In general, however, drugs that facilitate neurotransmission at $GABA_A$ receptors (e.g., benzodiazepines, barbiturates, and some antiepileptics) may impair memory and cognition and could ultimately retard recovery of intellectual function in TBI patients.

Glycine

Glycine has the simplest chemical structure of any amino acid and it is not an essential component of the diet. It is believed to function as a neurotransmitter in spinal cord interneurons (e.g., Renshaw cell, which mediates recurrent inhibition) and in the brainstem.[8] Like GABAergic synapses, all of the glycinergic synapses appear to be inhibitory. The inhibition also seems to be mediated through a ligand-gated chloride channel which, as indicated above, places these receptors in a common family with the nicotinic ACh, $GABA_A$, 5-HT_3, and glutamate receptors.

The anatomical distribution of glycinergic neurons have not been extensively mapped. However, the concentrations of glycine found in the spinal cord (dorsal and ventral horn), medulla, and pons are higher than in other CNS regions. Neuronal pathways suggested to be glycinergic include spinal interneurons, a corticohypothalamic pathway, reticulospinal projections from the raphe and reticular formation, brainstem afferents to the substantia nigra, cerebellar golgi cells, and retinal amacrine cells.[89,118]

Synthesis, Storage, Release, and Inactivation of Glycine

Glycine is synthesized from glucose via the glycolytic pathway to produce 3-phosphoglycerate and 3-phosphoserine, which forms serine. Serine (the immediate precursor of glycine) is converted to glycine by the enzyme serine hydroxymethyltransferase (SHMT), which is found in the mitochondria. Radioactive tracer studies show that most of the glycine in brain is made from serine.[119] Serine hydroxymethyltransferase requires tetrahydrofolate, pyridoxal phosphate, and manganese ion for activity.[90]

Glycine appears to be abundant in the CNS and it is not clear what factors, if any, are rate limiting in the overall synthesis. Moreover, it is not clear whether neurons utilizing glycine as a neurotransmitter must synthesize it *de novo* or whether they accumulate existing glycine.[8] SHMT is inhibited by pyridoxal phosphate inhibitors, which also interfere with GABA synthesis and degradation. Enzymatic degradation of glycine can occur via a glycine cleavage pathway, which is also located in the mitochondria. Genetic mutations in the proteins of this pathway can cause metabolic disorders known as *nonketotic hyperglycinemias*.[120]

Whether glycine is stored in, and released from, vesicles has been somewhat controversial. Nevertheless, the evidence indicates that glycine (like GABA and glutamate) is taken up into synaptic vesicles by a Na^+-independent mechanism involving a low-affinity uptake system.[121]

The evidence suggests that glycine uptake (like that of GABA and glutamate) is driven by an electrochemical proton gradient, generated by an ATP-dependent proton pump (ATPase) located in the synaptic vesicle membrane. Kish et al.[121] have found that the glycine vesicle transporter has a different substrate specificity from that of the GABA

uptake system and a different regional distribution in the brain, suggesting they are in separate neurons. The likelihood that there is both vesicular and cytoplasmic release of glycine, as there appears to be for GABA (see text on synthesis and storage of GABA), remains very high.

After its release into the synaptic cleft, glycine is primarily inactivated by reuptake into the terminal of the releasing neuron or by uptake into glial cells. Glycine reuptake is carried out by a glycine transporter in the membrane. The Na^+ and Cl- electrochemical gradients assist in the movement of glycine against its concentration gradient.[120] Two glycine membrane transporters have been identified by molecular cloning: GLYT-1 and GLYT-2. It appears that GLYT-1 is found in both neurons and glial cells, while GLYT-2 is localized to neurons. Both transporters are expressed in the hindbrain, whereas GLYT-1 can also be found in forebrain areas even though there are few, if any, glycinergic terminals. Since glycine also functions as a coagonist with glutamate at NMDA receptors (see text on glycine receptors and EAA), there is speculation that the GLYT-1 transporter might regulate glutamate receptor function in forebrain areas.[120] Selective inhibitors of the glycine transporter are not yet available, but could become useful drugs in the future. It has been suggested that GLYT-1 is the glial transporter, while GLYT-2 is the neuronal transporter, but this remains somewhat controversial.[8]

Glycine Receptors

As indicated above, the glycine receptor is a member of a super family of ligand-gated ion channels where the ligand binding site and the ion channel are in the same molecule. In this regard, the glycine receptor, like that of the nicotinic ACh and $GABA_A$ receptors, has been classified as an ionotropic receptor.[89] The glycine receptor has been purified using affinity chromatography[122] and cloned.[123] It is a glycoprotein with two polypeptide subunits called *alpha* (48 kDa) and *beta* (58 kDa).

These polypeptides have four membrane-spanning hydrophobic regions (like the nicotinic ACh and GABA receptors) and it is believed that three alpha and two beta subunits are responsible for forming the ion channel.[122] One hydrophobic region of each subunit (probably M2) is believed to contribute to the walls of the chloride channel. The composition of the receptor appears to depend on development. In embryonic tissue, the receptors consist entirely of alpha-2 subunits, but in adults, glycine receptors are composed of 3α and 2β subunits.[120]

The glycine receptor is associated with, a 93 kD protein called *gephyrin*, which associates with the intracellular domain of the beta subunit. Gephyrin is believed to function as an anchoring protein that connects the membrane receptor protein with the protein tubulin in the cytoplasm.

Strychnine is the classical glycine antagonist, and radioactive strychnine was originally used to map the distribution of glycine receptors in the CNS. The strychnine binding site is on the 48-kDa subunit which is where glycine also binds.[122]

Glycine also has an action at a strychnine-insensitive receptor that has been linked to the NMDA excitatory amino acid receptor.[90] This is a high-affinity site that appears to increase the action of glutamate at its NMDA receptor.[124] This strychnine-insensitive glycine binding site has a widespread distribution in brain and seems to be similar to that of the NMDA receptors. Thus, glycine, in submicromolar concentrations, appears to enhance the action of excitant amino acid neurotransmitters and may even be necessary.[124] It appears to enhance excitant amino acid action by binding to a site within the channel and producing an allosteric modification. In this regard, it appears to be analogous to the interaction between the GABA receptor and the benzodiazepine binding site. The strych-

nine-insensitive glycine binding site also appears to have an endogenous antagonist. The tryptophan metabolite, kynurenic acid, is an antagonist of the glycine binding site on the NMDA receptor. However, 7-cholorkynurenic acid is a more selective and more potent antagonist and is now being widely used to study this glycine receptor.[124]

Clinically Useful Drugs That Alter Glycinergic Neurotransmission

At the present time, there are no clinically available drugs whose mechanism of action is mediated through glycinergic neurotransmission. However, there is an experimental drug called *milacemide* that is believed to increase glycine levels in the brain and is being tested as an anticonvulsant agent in experimental animals. Thus, we may have drugs available to enhance glycinergic neurotransmission in the future.

As far as antagonists are concerned, strychnine, which is a convulsant drug, was once used to treat a variety of disorders, as well as being a potent poison. This agent no longer finds any medical use. As indicated above, glycine appears to also bind to a site on the NMDA receptor (the so-called *strychnine-insensitive* receptor) to enhance the excitatory effects of glutamate or aspartate. Thus, at this site, glycine is proconvulsant. At the present time, there is considerable interest among drug companies to explore the use of strychnine-insensitive glycine antagonists (e.g., 7-chlorokynurenic acid) as potential antiepileptic drugs and it is conceivable that we will see such agents available in the future. The ability of glycine to enhance the excitatory effects of glutamate may stem from its ability to block NMDA receptor desensitization.[8]

Glycinergic Drugs in the TBI Patient

As indicated above, there are no drugs currently available that modulate glycine neurotransmission. However, the drug milacemide, which increases glycine levels in brain, may eventually be useful as an anticonvulsant. The antagonist at the strychnine-insensitive glycine receptor (7-chlorokynurenic acid) may also prove to be useful in the future. At present, there is no information on whether or not glycinergic drugs would be useful in the TBI patient.

L-Glutamic Acid

The major excitatory neurotransmitter in the CNS is glutamic acid or glutamate. Aspartate is also plentiful and may function as an amino acid neurotransmitter, but glutamate has been more widely studied and is considered to be the most important excitatory transmitter. Glutamate and aspartate are sometimes referred to as the excitant amino acids (EAAs). Glutamate is found in higher concentrations than any other free amino acid in the CNS, being three or four times higher than aspartate and six times higher than GABA.[125] The role of glutamate as an excitatory neurotransmitter is the subject of intense current investigation, in part, because of glutamate's abundance and importance in so many neural pathways and, in part, because of studies implicating it in such pathological conditions as epilepsy, postanoxic cell loss, and neurotoxicity. It has been suggested that the vast majority of the synapses in the mammalian brain use an excitatory amino acid (EAA) as their neurotransmitter.[126]

So, glutamatergic neurons are found throughout the CNS. There are, however, some specific pathways that have been mapped using lesion and biochemical analyses. These include the well-known corticostriate pathway from the cerebral cortex to the striatum, as well as many other corticofugal pathways.[89] In addition, the perforant pathway, from the entorhinal cortex to the dentate gyrus of the hippocampus, contains a heavy glutamatergic component, as do the Schaffer collaterals from CA3 to CA1 of hippocampus.[89] The dorsal horn of the spinal cord has a high concentration of glutamate, which disappears after cutting the primary sensory afferents, indicating that glutamate is an important neurotransmitter of the primary afferents.

Synthesis, Storage, Release, and Inactivation of Glutamate

Glutamate is a nonessential amino acid that does not cross the blood–brain barrier. Therefore, it must be synthesized in the brain.[89] However, unlike most other neurotransmitters, the synthesis of glutamate is far from straightforward. This problem arises, in part, because glutamate plays many roles in the brain and is available from many sources. For example, in addition to its neurotransmitter role, it is an important component of protein and peptide (e.g., glutathione) synthesis.[127] It also functions as an amino group acceptor to detoxify ammonia in the brain, and it is the immediate precursor of GABA for GABA synthesis. Glutamate can be synthesized from several sources, but it is not always clear which one contributes most to the neurotransmitter pool.[8]

Some investigators have suggested that the main pathways contributing to the transmitter pool of glutamate are from glucose via the Krebs cycle intermediates or from glutamine by the enzyme glutaminase (in the mitochondria). Although both glucose and glutamine are readily converted to glutamate, the pool derived from glutamine is preferentially released,[119] suggesting that this may be more important. However, *in vivo* studies using ^{14}C-glucose and ^{14}C-glutamine showed that released glutamate was derived equally from glucose and glutamine.[128]

The various routes of synthesis are shown in Figure 3.11. Some authors have suggested that the transmitter pool may utilize glutamate from several sources and that the critical factor is the transmitter–storing vesicle that can take it up irrespective of its source.[125] Glial cells probably also play a role in the synthesis of glutamate.[129] The latter cells can actively accumulate glutamate by a sodium-dependent process and convert the glutamate to glutamine by the enzyme glutamine synthetase. The glutamine can diffuse out of glial cells and into glutamatergic terminals where it is converted back to glutamate by glutaminase. This appears to be one of the mechanisms by which the neurotransmitter is recycled.

There has been some controversy over whether or not glutamate is stored in, and released from, synaptic vesicles. However, several lines of evidence indicate that vesicles do serve as storage organelles for glutamate, just as they do for other transmitters.[127, 130] Indeed, the protein (i.e., transporter) that moves glutamate from the cytoplasm into the vesicle was recently identified, after many decades of searching, by a team at the University of California at San Francisco. This vesicular glutamate transporter protein is apparently the same transporter that moves inorganic phosphate ions across the cell membrane, but the one found in synaptic vesicles of glutamatergic neurons has been called VGLUT1.[131] Glutamate is released from synaptosomes in a Ca^{2+}-dependent manner and is derived from a noncytosolic compartment.[97] Thus, the finding that glutamate can be taken up and stored in synaptic vesicles and that its calcium-dependent release from synaptosomes is from a noncytoplasmic compartment has led to the view that release occurs by exocytosis. At present, the view that glutamate is released from neurons by exocytosis is widely accepted.[120]

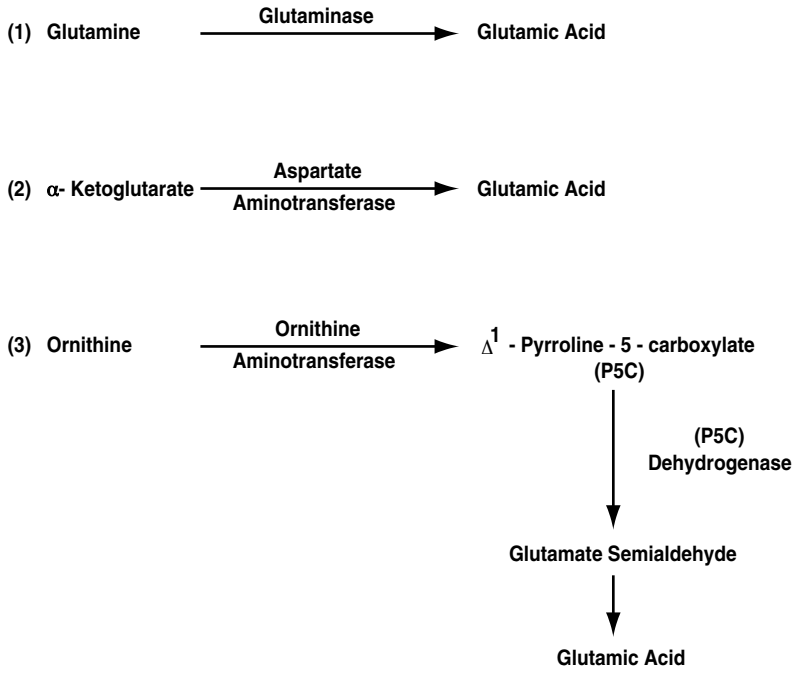

FIGURE 3.11
Three pathways that can synthesize glutamic acid in brain. The glutamine and α-ketoglutarate pathways are primarily responsible for synthesizing glutamate in nerve terminals

High affinity uptake is believed to be responsible for terminating the synaptic actions of glutamate and aspartate. The transporter(s) involved in terminating the actions of EAAs is a sodium-dependent, high-affinity transporter that has been studied in synaptosomes and brain slices. It does not distinguish between L-glutamate, L-aspartate, and D-aspartate.[127,132,133] This transporter has an uneven brain regional distribution consistent with a role in neurotransmission. However, glial cells also possess a high-affinity uptake for glutamate and aspartate which is believed to play an important role in terminating the action of the EAA neurotransmitters following their release from nerve endings, as was discussed above for GABA. Indeed, it has been shown that some glial cells possess receptors for glutamate which, when activated, lead to a transient increase in intracellular calcium (i.e., a Ca^{2+} wave) which may pass from one glial cell to another and function as a form of intercellular communication.[134] Molecular cloning studies have revealed at least four different high-affinity Na^{+}-dependent glutamate transporters, three of which are found in mammals.[120] These are referred to as **GLAST** (glutamate-aspartate transporter), **GLT-1** (glutamate transporter-1), and **EAAC1** (excitatory amino acid carrier-1). GLAT and GLT-1 are expressed in glial cells and are believed to be responsible for the majority of the glutamate inactivation in the CNS.[120]

Excitatory Amino Acid Neurotransmitter Receptors

The EAA receptors (i.e., receptors for glutamate and aspartate) have been actively investigated over the last 15 years and are still among the most vigorously targeted areas of research by drug companies seeking new compounds for epilepsy, stroke, psychiatric disorders, and degenerative brain disease.

These receptors have been found to occur in two large families referred to as (1) *ionotropic receptors* and (2) *metabotropic receptors*.

The ionotropic glutamate receptors are ion channels for sodium, potassium, and calcium similar to the nicotinic ACh, GABA, and glycine receptors. These channels are opened by glutamate and various synthetic chemicals with a similar structure. Three subtypes of ionotropic glutamate receptors have been identified, originally based on the chemicals that activate them: (1) *N*-methyl-*D*-aspartate or **NMDA**, receptor, (2) α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid, or **AMPA**, receptor, and (3) **kainate** receptor. Separate families of genes have been identified for each of these ionotropic receptor subtypes.[120] In the past, these receptors were separated into NMDA and nonNMDA because of the antagonists that blocked either the NMDA or nonNMDA (AMPA, kainate) receptors. A variety of protein subunits that comprise the excitant amino acid (EAA) receptors have been identified through molecular cloning. The subunits for the NMDA receptor are referred to as NR1, NR2A, NR2B, NR2C, and NR2D, while those for the AMPA receptor are designated as GluR1-4. The protein subunits that form the kainate receptor include GluR5-GluR7 and a KA1 and KA2.[120]

Of the ligand-gated EAA receptor channels, the NMDA receptor is unique in that it is voltage-dependent (as well as ligand-dependent), requiring some depolarization of the membrane to remove an Mg^{++} block within the ion channel.[125] The NMDA receptor also has several functional subcomponents with discrete binding domains, which make it similar to the $GABA_A$-benzodiazepine receptor complex.[126] In this regard, glycine has a binding site on the NMDA receptor and has been shown to facilitate the excitatory action of NMDA receptor agonists.[120,126,135] The latter has often been referred to as a strychnine-insensitive glycine binding site. Thus, glycine appears to be a coagonist at the NMDA receptor and there are now some selective antagonists for this glycine site (e.g., 7-Chlorokynurinate). The NMDA receptor is also unique in that it conducts calcium, as well as sodium, into the cell.

The agonist binding site on the NMDA receptor has several selective competitive antagonists (e.g., 2-amino-5-phosphonovalerate or **AP5**, 2-amino-7-heptanoate or **AP7**, and 2-carboxypiperazin propyl-1-phosphonic acid or **CPP**). In addition, some noncompetitive antagonists of the NMDA receptor have been discovered. These apparently bind to a site within the ion channel to inhibit neurotransmission. The latter compounds include such drugs as **phencyclidine** (PCP), **ketamine** (Ketalar®), and **MK-801** (dizocilpine).[120,126] The EAA receptors (especially the NMDA receptor) are believed to be important in learning and memory (see Chapter 10), which is believed to be mediated through their role in long-term potentiation (LTP).[125] Indeed, the NMDA receptor may be the primary receptor responsible for LTP. The distribution of the NMDA and nonNMDA glutamate (AMPA and kainate) receptors has been extensively mapped in the rat brain using radioactive ligands and autoradiography.[126]

However, excessive amounts of EAAs in the brain are believed to be responsible for excitotoxicity (leading to neuronal death) and seizures mediated through the ionotropic EAA receptors. The latter effect has led to the interest in EAA antagonists in neuropathological states such as those following stroke.[126] The excitatory amino acids have also been shown to play a role in posttraumatic brain injury,[136] and the neuropathology may be due to the excitotoxic effects of EAAs released after injury.

AMPA receptors can be blocked selectively by the quinoxaline diones such as 6-nitro-7-sulphamobenzo-quinoxaline 2,3-dione (**NBQX**). There are no selective antagonists at the kainate receptor except, perhaps, the experimental drug LY294486.

Eight different metabotropic glutamate receptors have now been cloned, which are designated as mGluR1 through mGluR8. Like other G-protein-coupled receptors, these have seven membrane-spanning regions, but are larger (i.e., contain more amino acids)

than most other G-protein coupled receptors. The mGluRs are classified into three groups, based on amino acid sequence homology, signal transduction mechanisms, and pharmacology: Group I includes mGluR1 and mGluR5; Group II includes mGluR2 and mGluR3; and Group III includes mGluR4, mGluR6, mGluR7, and mGluR8.[137] Several of the mGluRs are located on presynaptic nerve terminals and seem to decrease neurotransmitter release. Depending on the transmitter release, an agonist for the mGluR can produce either excitation or inhibition.[120] At present, there are no clinically approved drugs that act on the mGluRs, but selective antagonists for Group I, Group II, and Group III have been identified and it is likely that some of these drugs will be available for clinical use in the future. Group I mGluRs are linked to a Gq protein, leading to activation of the phosphatidylinositol pathway (described above), while Groups II and III appear to signal through the Gi/Go proteins leading to a decrease in cAMP.[137]

Clinically Useful Drugs That Alter Excitant Amino Acid Neurotransmission

Drugs That Enhance the Action of Glutamate

Basically, there are no clinically useful drugs that are known to enhance the action of excitant amino acids. Indeed, those that are available for experimental studies in animals (e.g., **glutamate**, **kainate**, **ibotenic acid**, etc.) are all convulsants which also cause excitotoxic lesions of neuronal cell bodies. Cycloserine and drugs developed for the treatment of tuberculosis are weak partial agonists at the NMDA receptor and there is some evidence that these drugs have antipsychotic effects that can be used to treat schizophrenia. Whether agents that selectively enhance LTP in the hippocampus can be developed without the dangers of killing neurons remains to be determined.

Drugs That Inhibit the Action of Glutamate

Several glutamate receptor antagonists are available for experimental work in animals and some of these have been described above, but again, none are available for clinical use at the present time. These drugs are of interest for treating such disorders as epilepsy, postischemic brain syndrome, and posttraumatic brain injury. Moreover, such drugs are believed to have some potential in various neurodegenerative diseases such as Huntington's chorea, Alzheimer's disease, Fredrick's ataxia, and stroke. Thus, a great deal of research time and money has been, and continues to be, invested in developing effective EAA antagonists. One disappointing aspect of this work has been the psychotic-like side effects that have accompanied the testing of some NMDA antagonists in humans.

It is of interest to note that the widely used drug **dextromethorphan** (marketed as a cough suppressant) has been shown to antagonize experimental seizures in animals and has been found to be an NMDA antagonist.[138–140] Because of all the modulatory sites on the NMDA receptors, several drugs are known to have some antagonist effects on this receptor. For example, phencyclidine (PCP, angel dust) and ketamine act as noncompetitive antagonists of the NMDA receptor and have psychotomimetic effects at low doses and function as dissociative anesthetics at higher doses. While both are still used in veterinary medicine, only ketamine is used in humans, at the present time, where it is mainly used as a pediatric anesthetic. Both are considered drugs of abuse in humans.[120]

Glutamatergic Drugs in the TBI Patient

Glutamate and other excitatory amino acids have long been known to produce excitotoxic damage to neurons and glial cells, and are believed to play a role in producing brain

damage in the hours immediately following TBI.[141,142] Indeed, it has been suggested that the EAAs contribute to CNS damage in a variety of neurological disorders such as epilepsy, stroke, and other neurodegenerative diseases.[143] Moreover, animal and human studies using microdialysis have shown the extracellular levels of glutamate are increased immediately following TBI.[143] Therefore, treatment with glutamate antagonists in the early hours following TBI should limit the damage and facilitate recovery.

Most of the evidence suggests that the NMDA subtype of glutamate receptor is responsible for the neuronal damage because of the increase in intracellular calcium that follows the opening of this channel. Calcium, in high concentrations, can damage and kill cells.[6] Thus, administration of NMDA antagonists immediately following injury has been shown to improve recovery in rats. The hallucinogen, phencyclidine (PCP), an NMDA antagonist, was found to attenuate long-term neurobehavioral deficits in rats receiving TBI.[143] Clearly, more studies are needed in this area.

Since glutamate is involved in normal cognitive processing and in learning and memory, it seems reasonable that NMDA agonists might improve cognitive function after TBI. Because too much glutamate receptor activation can lead to seizures and neuron cell death, moderate or controlled activation of NMDA receptors would seem to be more useful. In this regard, the chronic administration of D-cycloserine, an NMDA partial agonist acting at the glycine site, has been shown to improve cognitive function in rats following TBI.[144] Thus, weeks or months after the injury, it may be beneficial to augment glutamate neurotransmission and metabotropic glutamate agonists may turn out to be useful in this regard. On the other hand, the Group I metabotropic glutamate receptor agonists are known to potentiate excitation, and antagonists of these receptors have been shown to reduce brain damage and improve recovery of motor function after TBI.[145] Clearly, drugs acting on glutamate receptors can have profound effects in TBI patients and should provide some new therapeutic tools in the future.

Peptide Neurotransmitters

Until 1960, acetylcholine and the monoamines were the only well-recognized neurotransmitters. Then came the GABA and the amino acids in the 1960s and 1970s. The amine and amino acid neurotransmitters are sometimes referred to as the *classical* neurotransmitters. However, within the last 20 years, there has been an explosion in the number of candidate neurotransmitters due largely to the discovery of various peptides that may function as neurotransmitters or neuromodulators. Many of the neuroactive peptides were first discovered as hormones and were then found to also be present in neurons within the CNS. Another common finding was that many of the neuroactive peptides were also found in the gut where they served as gastrointestinal hormones (e.g., cholecystokinin).

Although one finds that the peptide neurotransmitters are not classified in any consistent manner, a common approach used by authors is based on localization. For example, peptide neurotransmitters have been grouped into the following categories: (1) the gut-brain peptides, (2) the pituitary peptides, and (3) the hypothalamic-releasing hormones.[146]

There are far too many candidate peptide neurotransmitters to cover here. Moreover, there are no clinically useful drugs to affect their action, except in the case of the opioid peptides, which mediate their effects through the receptors on which morphine and other potent narcotic analgesics act. Therefore, we will restrict this discussion to the opioid peptides.

However, substance P is also of interest because it was the first peptide neurotransmitter isolated from horse gut and brain by Euler and Gaddam,[147] although it was 40 years later

before its structure was determined. Substance P is of interest because, while there are no clinically available drugs to modify its action, it appears to be the neurotransmitter of primary sensory afferent fibers carrying pain sensation (i.e., C-fibers) and it can be released from such nerve terminals by the active ingredient in chili peppers (i.e., **capsaicin**).[148,149] Moreover, neurons containing opioid peptides appear to synapse on the terminals of substance P containing neurons in the dorsal horn of the spinal cord. Substance P is one of a group of interesting peptides known as *tachykinins* for which three receptors have been cloned and new antagonists are being developed. Cooper, Bloom and Roth[8] provide a review of further information on this subject.

Opioid Peptides as Neurotransmitters

The first discovered opioid peptides were the pentapeptides (containing five amino acids), leucine-enkephalin, and methionine-enkephalin, which were isolated by Hughes et al.[150] We now have three separate families of opioid peptides, each derived from a separate gene family.[151] These include (1) the enkephalins (pentapeptides derived from a proenkephalin precursor), (2) the endorphins (e.g., β-endorphin, a 31 amino acid containing peptide derived from proopiomelanocortin or POMC), and (3) the dynorphins (8–13 amino acid containing peptides derived from a prodynorphin precursor).

Extensive maps of the enkephalin, endorphin, and dynorphin containing neurons in the rat brain have been obtained using immunocytochemistry, but these will be only briefly described here (see Khachaturian, Lewis, Schafer, and Watgson[152] for more detail). In general, the enkephalinergic neurons are short interneurons widely distributed throughout the neuraxis. A high density of enkephalinergic neurons is found in the basal ganglia, cerebral cortex, amygdala, hippocampus, and in such brainstem areas as the periaqueductal gray, interpeduncular nucleus, parabrachial nucleus (concerned with respiration), and the nucleus tractus solitarius, as well as in the dorsal horn of the spinal cord.

The dynorphin-like immunoreactivity follows the distribution of the enkephalinergic neurons fairly closely and also appears to be found mostly in short local neurons rather than in long projection fibers. Thus, the enkephalin and dynorphin systems appear to be anatomically contiguous. The endorphin-containing neurons are, however, different in that they tend to be long projection neurons which arise from the arcuate nucleus of the hypothalamus. Another area containing a high density of endorphin (POMC) containing cell bodies is the pituitary gland from which β-endorphin is presumably released into the blood. However, the precursor of β-endorphin, POMC, is also the precursor for adrenocorticotrophic hormone (ACTH) and melanocyte stimulating hormone (α-MSH). Thus, depending on where in its structure POMC is cleaved by enzymes, one gets different biologically active peptides. It is little wonder, then, that the endorphins are intimately related to the endocrine system and are apparently released during stress.

Synthesis, Storage, Release, and Inactivation of Opioid Peptides

The synthesis of any peptide involves transcription of the information in the genetic code of DNA (the gene) into messenger RNA (mRNA), and the translation of the message in mRNA into the appropriate sequence of amino acids in the peptide chain to form a functionally important peptide or protein. A detailed description of protein synthesis is clearly beyond the scope of this chapter and the reader is referred to a basic textbook of biochemistry for more detail.

As indicated above, there are three families of opioid peptides derived from different genes which lead to the synthesis of precursor proteins from which the neuroactive peptide

is cleaved by the action of enzymes. Thus, proenkephalin, prodynorphin, or proopiomelanocortin (POMC) can be synthesized in the cell body of a cell that expresses these genes.

After the peptide precursors are formed, they are usually sent to the golgi apparatus where they are packaged into membrane-bound vesicles and then transported to the nerve terminals by axoplasmic transport. At the axon terminal, the opioid peptides are stored in vesicles from which they are released by exocytosis.[89] However, the mechanisms of peptide packaging, storage, and release are poorly understood at the present time. It is important to note that peptides cannot be synthesized at nerve terminals and must be made in the cell body and transported to the terminal for release, making them much more expensive in terms of energy expenditure.

Once the opioid or any other neuroactive peptide is released from a neuron, it is apparently degraded by peptidases (enzymes) and cannot be recaptured by reuptake. Thus, utilization of peptides is less efficient than that for the classical neurotransmitters and is, again, a more energy-expensive process. Moreover, once they are used, it will take a significantly longer time to replace them at the nerve terminal than it does for the classical transmitters.[89,153]

Another interesting aspect of peptide neurotransmitters is that they appear to be costored in neurons with other neurotransmitters, either other peptides or the classical neurotransmitters. Examples of a classical transmitter coexisting in a neuron with a peptide include (1) serotonin and substance P, (2) dopamine and cholecystokinin, and (3) acetylcholine together with vasoactive intestinal polypeptide (VIP). In some neurons, the classical transmitter and the peptide may even be stored within the same vesicle (e.g., 5-HT and substance P).[153]

Opioid Receptors

Opioid receptors were known to exist long before the discovery of the opioid peptides. Indeed, it was the discovery of opioid receptors using radioactive ligands that led to the search for the endogenous peptides by Hughes and Kosterlitz.[146] The distribution of opioid receptors was mapped before the distribution of the peptides. The opioid receptors are now divided into three main subtypes: (1) mu (μ) receptors, (2) delta (δ) receptors, and (3) kappa (κ) receptors, although some authors include the sigma (σ) receptors as a fourth subtype.

Mu receptors appear to be the primary receptors involved in mediating analgesia and, therefore, have a high affinity for morphine and related drugs. The endorphins have a higher affinity for μ receptors than for any other opiate receptor. Indeed, the rank-order potency of agonists for opioids binding to the mu receptor is β-endorphin > morphine > met-enkephalin > leu-enkephalin.

The mu receptor is believed to be a 65 kDa protein with a widespread distribution in the CNS.[154] The density of μ receptors is high in striatum, amygdala, cortex, periaqueductal gray regions of midbrain, and thalamus.[155] Mu receptors are also found in the periphery. The mu receptor appears to be a G-protein linked receptor that is negatively coupled with cAMP (i.e., a Gi protein) and is involved in mediating hyperpolarization by opening K^+ channels.[155]

The use of mu agonists can alleviate the opiate withdrawal syndrome. Beta-endorphin is probably the naturally occurring ligand for the mu receptor, although morphine and its analogs appears to mediate most of their effects through the mu receptor. **Naloxone** (Narcan®) is a potent antagonist of the mu opioid receptor.

The delta receptor binds leu-enkephalin with a greater affinity than met-enkephalin, β-endorphin, or morphine. Thus, the enkephalins are believed to be the natural ligands for

the delta receptor.[154] The distribution of δ receptors corresponds closely to the distribution of enkephalin neurons and, like the mu receptors, are linked to adenylate cyclase in a negative fashion via a Gi protein.[154] Naloxone is a less potent antagonist at delta receptors than it is at mu receptors so that higher concentrations of naloxone are required.

The kappa opioid receptors bind ketocyclazocine with high affinity. The latter compound, along with **pentazocine**, **bremazocine**, and **butorphanol**, is a kappa receptor agonists. The density of kappa receptors is highest in the spinal cord and brainstem and the dynorphins are believed to be the naturally occurring agonists for these receptors. Naloxone can act as an antagonist at kappa receptors, but it is less potent than at mu receptors. Kappa agonists cannot alleviate the symptoms of opioid withdrawal. However, stimulation of kappa receptors can alleviate pain, especially viscerally mediated chemical pain.[154] Dynorphin is believed to be the natural agonist for the kappa receptor and dynorphin levels are increased immediately following TBI. Indeed, kappa agonists may increase neurological deficits when administered following TBI (see Opioids in the TBI Patient section).

More recently, a new receptor related to the opioid receptors was cloned. Because it had a high degree of homology (similarity) to other opioid receptors, but was unresponsive to endogenous opioid peptides (enkephalins, endorphins, dynorphins), it was referred to as an orphan receptor. More recently, a novel endogenous peptide for the orphan receptor was isolated and sequenced. This peptide appeared to have antiopioid effects (i.e., cause pain) when bound to the orphan receptor. Thus, it was named nociceptin/orphanin FQ. Now, there appears to be a family of these peptides and they all bind to G-protein coupled receptors (i.e., Gi/Go).[156,157] The functional significance of the nociceptin/orphanin FQ system is not known, but there is interest in developing antagonists for these receptors because they could be useful in the treatment of pain.

Clinically Useful Drugs That Alter Opioid Neurotransmission

Drugs That Enhance Opioideragic Neurotransmission

Opioid Agonists

A comprehensive discussion of the pharmacology of opioid agonists and antagonists has been provided by Gutstein and Akil[158] and is beyond the scope of this chapter. The agonists are the only available drugs for enhancing opioidergic neurotransmission. These are the narcotic analgesics used to treat severe pain, such as that occurring postoperatively. **Morphine** is the prototypical drug in this class and has been around since 1806. It is a natural constituent of opium powder, but can now be made in the chemistry laboratory. **Meperidine** (Demerol®) is a synthetic analog of morphine widely used in hospitals for postoperative pain. Both of these are primarily mu agonists, but also have some agonist activity at delta and kappa receptors. **Codeine**, the *o*-methyl analog of morphine, has similar properties, but is a weaker agonist. Indeed, codeine is metabolized to morphine in the body. Pentazocine (Talwin®) is a kappa agonist and a mu antagonist and butorphanol (Stadol®) has similar properties. Pentazocine was originally marketed as a nonnarcotic analgesic, but this error was eventually corrected. **Buprenorphine** (Buprenex®) is a partial mu agonist and a kappa antagonist. The latter drugs are sometimes referred to as *mixed agonist–antagonists.*

Opioid analgesics have many side effects, not the least of which is respiratory depression, which can kill the patient in overdose. These drugs are also very useful to suppress the cough reflex and are commonly added to cough mixtures (syrups).

Drugs That Inhibit Opioidergic Neurotransmission

Opioid Antagonists

Naloxone (Narcan®) is a pure opioid antagonist that is used to treat life-threatening overdoses of opioid analgesics. It functions as an antagonist at mu, delta, and kappa receptors, but must be given by injection. The administration of 0.4 to 0.8 mg intravenously or intramuscularly can reverse the effects of mu opioid agonists in humans and will precipitate a withdrawal syndrome in addicted individuals.[158] **Naltrexone** (Trexan®) is also a pure narcotic antagonist with greater oral efficacy and a longer duration of action allowing it to be administered orally.

Opioids in the TBI Patient

An increase in dynorphin has been demonstrated following TBI in an animal model of brain injury[159] and kappa receptor agonists have been shown to increase neurologic deficits after experimentally induced spinal cord injury in rats. Moreover, kappa antagonists have been found to reverse deficits associated with spinal cord injury.[160] Kappa agonists may, in fact, facilitate neuronal damage via an action through glutamate, since NMDA antagonists were found to reverse the neurotoxicity associated with dynorphin in the spinal cord injury model.[161]

While activation of kappa receptors appears to enhance neurologic damage, activation of mu and delta opioid receptors may be neuroprotective rather than neurotoxic.[162] Thus, it appears that, immediately following injury, administering a kappa antagonist or a mu agonist could be beneficial in reducing neurological damage associated with TBI. However, more research is needed to determine the appropriate timing and dose needed to reduce neurological deficits.

Other uses of opioids in the TBI patient obviously includes their use as analgesics to alleviate pain while recovering from multiple injuries. However, when using opioids as analgesics, it is important for practitioners to be cognizant of possible detrimental effects that can also occur. Knowledge of the specific receptors on which the drugs act and the selection of specific mu or delta agonists may prevent such detrimental effects.

Summary

The preceding pages provide considerable detail concerning the process of neurotransmission in the nervous system. It is clear that this is a major form of communication between neurons and the principal site of controlling neuronal function. It is also clear that neurotransmission is the principal target for drugs that affect the nervous system. Although it is impossible to provide a concise summary of the broad array of topics covered in this chapter, the editor felt that some type of summary of the clinically relevant drugs showing the neurotransmitters through which they exert their action would be useful for the busy practitioner and, I fully agree. Therefore, an appendix (see Appendix 3A) has been provided at the end of this chapter to summarize these relationships and to give the reader a quick mechanism for linking the drugs to the neurotransmitters. It should be noted, however, that, in the interest of space, we have only included those drugs discussed in this chapter. Although they represent some of the more popular ones in use today, they are by no means the only ones available. Practitioners of rehabilitation, as well

as other specialties in medicine, must be aware that pharmacology is a constantly changing field with new drugs being introduced every day. It is hoped that this chapter also provides a foundation that will allow the reader to appreciate and understand the mechanism of action of new (undiscovered) drugs that will be introduced in the future.

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Appendix 3A
Summary of Relationship between Therapeutically Used Drugs and Various Neurotransmitters

Drug Name	Brand Name*	Neurotransmitter	Receptor	Drug Action
Alpha-methyltyrosine (metyrosine)	Demser	Dopamine; NE	—	Blocks synthesis of dopamine and NE
Acebutolol	Sectral	NE	Beta-1	Beta-1 receptor blocker
Acetylcholine	Miochol (Ophthalmic)	ACh	Nicotinic and muscarinic-cholinergic	Agonist for muscarinic and nicotinic receptors
Albuterol	Proventil	Epinephrine (hormone)	Beta-2	Beta-2 receptor agonist
Alprazolam	Xanax	GABA	Benzodiazepine-$GABA_A$ complex	Agonist for benzodiazepine receptor
Amantadine	Symmetrel	Dopamine	—	Increases release and blocks reuptake of dopamine
Amphetamine	Obetrol	Dopamine; NE	—	Increases release and blocks reuptake of NE and dopamine
Apomorphine	Apomorphine HCl	Dopamine	D-1 and D-2 dopamine	Agonist for D-1 and D-2 receptors
Atenolol	Tenormin	NE	Beta-1	Blocks beta-1 receptors
Atropine	Atropine Sulfate	ACh	Muscarinic-cholinergic	Blocks muscarinic receptors
Baclofen	Lioresal	GABA	$GABA_B$	Agonist for $GABA_B$ receptors
Benztropine	Cogentin	ACh	Muscarinic-cholinergic	Blocks muscarinic receptors
Bethanechol	Urecholine	ACh	Cholinergic-muscarinic	Agonist for muscarinic receptor
Botulinum toxin A	Botox	ACh	—	Blocks release of ACh
Bretylium	Bretylium Tosylate	NE	—	Blocks release of NE
Bromocriptine	Parlodel	Dopamine	Dopamine (D-1, D-2, etc.)	Nonselective dopamine receptor agonist
Buprenorphine	Buprenex	β-endorphin; enkephalin	Opioid (mu)	Partial agonist for mu receptor and a kappa antagonist
Bupropion	Wellbutrin; Zyban	Dopamine	—	Blocks reuptake of dopamine
Buspirone	Buspar	Serotonin (5-HT)	$5\text{-}HT_{1a}$	Partial agonist for $5\text{-}HT_{1a}$ receptor
Butorphanol	Stadol	β-endorphin; enkephalin	Opioid (kappa)	Kappa agonist and mu antagonist
Capsaicin	Zostrix-HP	Substance P	—	Depletes C-fibers (pain fibers) of Substance P; used as topical analgesic
Carbachol	Isopto Carbachol	ACh	Muscarinic-cholinergic; nicotinic-cholinergic	Muscarinic and nicotinic agonist
Chlorpromazine	Thorazine	Dopamine	Dopamine D_2	Blocks dopamine receptors

Drug Name	Brand Name*	Neurotransmitter	Receptor	Drug Action
Cimetidine	Tagamet	Histamine (not covered in chapter)	H_2 histamine receptors	H_2 blocker
Clomipramine	Anafranil	Serotonin	—	Blocks serotonin reuptake
Clonazepam	Klonopin	GABA	Benzodiazepine-$GABA_A$ complex	Facilitates action of GABA
Clonidine	Catapres	NE	$Alpha_2$	Alpha-2 agonist
Clozapine	Clozaril	Dopamine	Dopamine D_4	D_4 antagonist
Cocaine	Cocaine HC1	NE; dopamine	—	Blocks reuptake of NE and dopamine
Codeine	Found in many cough syrups and analgesics containing acetaminophen	Opioid	β-endorphin; enkephalin	Agonist for mu and delta opioid receptors
d-tubocurarine	Tubocurarine chloride	ACh	Nicotinic-cholinergic	Nicotinic receptor blocker
Desipramine	Norpramin	NE	—	Blocks NE reuptake
Dextroamphetamine	Dexedrine	NE; dopamine	—	Increases release of NE and dopamine and blocks reuptake
Dextromethorphan	Found in many cough syrups (e.g., Robitussin-DM)	Glutamate	NMDA	Blocks glutamate NMDA receptor
Diazepam	Valium	GABA	Benzodiazepine-$GABA_A$ complex	Agonist for benzodiazepine receptor
Disulfiram	Antabuse	NE	—	Blocks synthesis of NE
Dobutamine	Dobutrex	NE	B_1 adrenergic receptor	Agonist for B_1 receptors
Donepezil	Aricept	ACh	—	Blocks enzymatic breakdown of ACh
Edrophonium	Tensilon	ACh	—	Cholinesterase inhibitor; prevents degradation of ACh
Entacapone	Comtan	NE; dopamine	—	Blocks enzymatic breakdown of NE and dopamine by blocking COMT
Esmolol	Brevibloc	NE	B_1	Blocks B_1 receptor
Fenfluramine	Pondamin	Serotonin	—	Increases the release of serotonin
Fluoxetine	Prozac	Serotonin	—	Blocks reuptake of serotonin
Flurazepam	Dalmane	GABA	Benzodiazepine-$GABA_A$ complex	Facilitates the action of GABA
Fluvoxamine	Luvox	Serotonin	—	Blocks serotonin reuptake
Galantamine	Reminyl	ACh	—	Blocks enzymatic breakdown of ACh
Gallamine	Flaxedil	ACh	Nicotinic-cholinergic	Blocks nicotinic receptors at neuromuscular junction
Granisetron	Kytril	Serotonin	5-HT_3	Blocks 5-HT_3 receptors

Guanabenz	Wytensin	NE	$Alpha_2$	Alpha-2 agonist
Guanadrel	Hylorel	NE	—	Blocks the release of NE
Guanethidine	Ismelin	NE	—	Blocks the release of NE
Guanfacine	Tenex	NE	$Alpha_2$	Alpha-2 agonist
Haloperidol	Haldol	Dopamine	Dopamine D_2	Blocks dopamine receptors
Ipratropium	Atovent	ACh	Muscarinic-cholinergic	Muscarinic blocker
Isocarboxazid	Marplan	NE; dopamine; serotonin	—	Inhibits degradative enzyme (monoamine oxidase)
Isoproterenol	Isuprel	NE	B_1 and B_2	Agonist for all beta receptors
Ketamine	Ketalar	Glutamate	NMDA	Noncompetitive blockers of NMDA receptor
L-DOPA and carbidopa	Sinemet	Dopamine	—	Increases synthesis of dopamine
Levodopa	Larodopa	Dopamine	—	Increases synthesis of dopamine
Lorazepam	Ativan	GABA	Benzodiazepine-$GABA_A$ complex	Agonist for benzodiazepine receptor
Maprotiline	Ludiomil	NE	—	NE reuptake inhibitor
Mecamylamine	Inversine	ACh	Nicotinic-cholinergic	Blocks neuronal nicotinic receptors
Meperidine	Demerol	β-endorphin; enkephalin	Opioid (mu)	Agonist for mu opioid receptors
Metaproterenol	Metaprel	NE	$Beta_2$	Selective agonist for beta-2 receptor
Metaraminol	Aramine	NE	$Alpha_1$	Agonist for alpha-1 receptors
Methacholine	Provocholine	ACh	Muscarinic-cholinergic	Agonist for muscarinic receptors
Methamphetamine	Desoxyn	NE and dopamine	—	Increases release of NE and dopamine
Methoxamine	Vasoxyl	NE	$Alpha_1$	Agonist for alpha-1 receptor
Methylphenidate	Ritalin	Dopamine and NE	—	Increases release of dopamine and NE
Methysergide	Sansert	Serotonin	Serotonin	Nonselective serotonin receptor blocker
Metoclopramide**	Reglan	Dopamine; serotonin	Dopamine D_2; 5-HT_3	Blocks dopamine D-2 and 5-HT_3receptors
Metoprolol	Lopressor	NE	$Beta_1$	Blocks beta-1 receptors
Molindone	Moban	Dopamine	Dopamine D_2	Blocks dopamine receptors
Morphine	Morphine Sulfate	β-endorphin	Mu opioid	Agonist for mu receptor
Naloxone	Narcan	β-endorphin; enkephalin	Opioid	Nonselective opioid receptor blocker
Naltrexone	Trexan	β-endorphin; enkephalin	Opioid	Nonselective opioid receptor blocker
Naratriptan	Amerge	Serotonin	5-$HT_{1D/1B}$	Serotonin receptor 1B/1D agonist
Neostigmine	Prostigmin	ACh	—	Blocks degradation of ACh by cholinesterase
Nicotine	Nicoderm (patch); Nicorette (gum)	ACh	Nicotinic-cholinergic	Agonist for nicotinic receptor
Nitrazepam	Mogadon	GABA	Benzodiazepine-$GABA_A$ complex	Agonist for benzodiazepine receptor
Norepinephrine	Levophed	NE	$Alpha_1$, $alpha_2$, $beta_1$	Agonist for adrenergic receptors
Nortriptyline	Aventyl	NE	—	Blocks reuptake of NE
Olanzapine	Zyprexa	Dopamine; serotonin	Dopamine $D_{3/4}$, 5-HT_{2A}	Blocks dopamine and serotonin receptors

Drug Name	Brand Name*	Neurotransmitter	Receptor	Drug Action
Ondansetron	Zofran	Serotonin	5-HT_3	Blocks 5-HT_3 receptor
Oxazepam	Serax	GABA	Benzodiazepine-$GABA_A$ complex	Agonist for benzodiazepine receptor
Pancuronium	Pavulon	ACh	Nicotinic-cholinergic (at neuromuscular junction)	Blocks nicotinic receptor
Paroxetine	Paxil	Serotonin	—	Blocks serotonin reuptake
Pentazocine	Talwin	β-endorphin; enkephalin	Mu opioid; kappa opioid	Mu antagonist; kappa agonist
Pentobarbital	Nembutal	GABA	$GABA_A$	Facilitates action of GABA
Pergolide	Permax	Dopamine	Dopamine D_1 and D_2	Agonist for D_1 and D_2 receptors
Perphenazine	Trilafon	Dopamine	Dopamine D_2	Blocks dopamine receptors
Phenelzine	Nardil	NE; dopamine; serotonin	—	Blocks monoamine oxidase to prevent degradation of monoamine transmitters
Phenobarbital	Luminal	GABA	$GABA_A$	Facilitates action of $GABA_A$
Phenylephrine	Neo-Synephrine	NE	$Alpha_1$	Alpha-1 agonist
Phenoxybenzamine	Dibenzyline	NE	$Alpha_1$, $alpha_2$	Irreversibly blocks alpha-1 and alpha-2 receptors
Phentolamine	Regitine	NE	$Alpha_1$, $alpha_2$	Reversibly blocks alpha-1 and alpha-2 receptors
Physostigmine	Eserine Sulfate	ACh	—	Blocks enzymatic breakdown of ACh
Pilocarpine	Pilocarpine HC1	ACh	Muscarinic-cholinergic	Muscarinic agonist
Pindolol	Visken	NE	$Beta_1$ and $beta_2$	Blocks beta adrenergic receptors
Pirenzepine	Gastrozepine	ACh	M_1 muscarinic	Blocks M-1 receptors
Pramipexole	Mirapex	Dopamine	Dopamine D_1, D_2	Agonist for dopamine receptors
Prazosin	Minipress	NE	$Alpha_1$	Blocks alpha-1 receptor
Primidone	Mysoline	GABA	$GABA_A$	Facilitates action of $GABA_A$
Prochlorperazine	Compazine	Dopamine	Dopamine D_1 and D_2	Blocks D-1 and D-2 receptors
Propranolol	Inderal	NE	$Beta_1$ and $beta_2$	Blocks beta-1 and beta-2 receptors
Protriptyline	Vivactil	NE	—	Blocks reuptake of NE
Pyridostigmine	Mestinon	ACh	—	Blocks enzymatic breakdown of ACh
Quazepam	Doral	GABA	Benzodiazepine-$GABA_A$ complex	Agonist for benzodiazepine receptor
Quetiapine	Seroquel	Dopamine; serotonin	Dopamine $D_{3/4}$, 5-HT_{2A}	Blocks dopamine and serotonin receptors
Reserpine	Serpasil	NE; dopamine; serotonin	—	Blocks storage of monoamine transmitter and depletes nerves
Risperidone	Risperdal	Dopamine; serotonin	Dopamine $D_3/_4$, 5-HT_{2A}	Blocks dopamine and serotonin receptors
Rivastigmine	Exelon	ACh	—	Blocks enzymatic breakdown of ACh
Rizatriptan	Maxalt	Serotonin	5-$HT_{1D/1B}$	Serotonin receptor 1B/1D agonist

Ropinirole	Requip	Dopamine	Dopamine D_1, D_2	Dopamine receptor agonist
Scopolamine (hyoscine)	Isopto Hyoscine	ACh	Muscarinic-cholinergic	Muscarinic blocker
Secobarbital	Seconal	GABA	$GABA_A$	Facilitates action of $GABA_A$
Selegiline	Eldepryl	Dopamine	—	Inhibits monoamine oxidase Type B which degrades dopamine
Sertraline	Zoloft	Serotonin	—	Serotonin reuptake inhibitor
Sotalol	Betapace	NE	$Beta_1$ and $beta_2$	Beta-1 and beta-2 blocker
Succinylcholine	Anectine	ACh	Nicotinic-cholinergic (at neuromuscular junction)	Nicotinic receptor blocker
Sumatriptan	Imitrex	Serotonin	$5\text{-}HT_{1D}$	Agonist for $5\text{-}HT_{1D}$ receptors
Tacrine	Cognex	ACh	Nicotinic and muscarinic-cholinergic	Cholinesterase inhibitor; partial agonist at muscarinic receptors
Temazepam	Restoril	GABA	Benzodiazepine-$GABA_A$ complex	Agonist for benzodiazepine receptor
Terazosin	Hytrin	NE	$Alpha_1$	Alpha-1 blocker
Terbutaline	Brethine	NE	$Beta_2$	Agonist at beta-2 receptor
Thioridazine	Mellaril	Dopamine	Dopamine D_2	Blocks dopamine receptors
Tiagabine	Gabitril	GABA	—	Blocks GABA uptake
Tolcapone	Tasmar	NE; dopamine	—	Blocks enzymatic breakdown of NE and dopamine by blocking COMT
Tranylcypromine	Parnate	NE; serotonin; dopamine	—	Inhibits degradation of monoamines by MAO
Triazolam	Halcion	GABA	Benzodiazepine-$GABA_A$ complex	Agonist for benzodiazepine receptor
Trimethaphan	Arfonad	ACh	Nicotinic-cholinergic (at autonomic ganglia)	Blocks nicotinic receptor
Valproic acid	Depakene	GABA	—	Increases synthesis and blocks degradation of GABA
Vecuronium	Norcuron	ACh	Nicotinic-cholinergic (at neuromuscular junction)	Blocks nicotinic receptor
Ziprasidone	Geodon	Dopamine; serotonin	Dopamine $D_{3/4}$, $5\text{-}HT_{2A}$	Blocks dopamine and serotonin receptors
Zolmitriptan	Zomig	Serotonin	$5\text{-}HT_{1D/1B}$	Serotonin receptor 1B/1D agonist

* Includes only one example of a brand name.
** See Table 3.4 for other dopamine receptor antagonists.

Abbreviations: ACh = acetylcholine, NE = norepinephrine, GABA = gamma aminobutyric acid, NMDA = *N*-methyl-*D*-aspartate, 5-HT = 5-hydroxytryptamine.

4

Heterotopic Ossification in Traumatic Brain Injury

Douglas E. Garland and Arousiak Varpetian

CONTENTS

Heterotopic Ossification

The designation *heterotopic ossification* (HO) is preferred to such terms as *ectopic ossification, paraosteoarthropathy,* or *myositis ossificanse* when discussing the formation of new bone around joints as a consequence of traumatic brain injury (TBI). *Heterotopic* refers to the occurrence of bone in more than one location. Microscopically, the bone is a true "ossific" process arising *de novo* to new bone formation rather than calcification of soft tissue.

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Heterotopic ossification associated with TBI is labeled *neurogenic HO* because the stimulus to form the new bone is the cerebral insult.

The majority of HO associated with TBI is around joints, although it may also occur in the thigh. Neurogenic HO is commonly para-articular and usually occurs in a single plane around a joint, although it may occur in multiple sites. The bone itself lies within a well-defined tissue plane and usually does not involve the joint capsule or muscles. Patients exhibiting marked spasticity, especially extensor rigidity, are most likely to develop this bone. Multiple sites are common in patients with marked spasticity. The HO frequently forms in the vicinity of the spastic musculature. The position of the extremity often permits early prediction of the future location of the HO. It is uncommon for a patient with only cognitive dysfunction to develop neurogenic HO.

Genetic and Patient Predisposition

Strong evidence for some type of genetic predisposition to HO formation comes from the hereditary disorder fibrodysplasia ossificans progressiva (FOP).[1] FOP is inherited as an autosomal dominant trait with full penetrance and variable expression. FOP was recently mapped to human chromosome 4q 27–31.[2] It is a disorder of connective tissue with skeletal malformations and HO. The natural history of HO from FOP has similarities to the natural history of HO from other causes, especially neurogenic HO. Although the majority of cases of FOP-associated HO are spontaneous, some cases also occur after trauma. A predilection of HO for certain locations (i.e., the axial musculature and proximal limbs) that is similar in both traumatic and neurogenic HO is documented. Heterotopic ossification frequently recurs after surgical resection. Recurrence is also noted after resection of neurogenic HO and, occasionally, after traumatic HO resection.

The association of human leukocyte antigens (HLAs) with neurogenic HO has been noted. An increased prevalence of HLA-B18 and HLA-B27 antigens has been reported in patients with HO in comparison to normal subjects.[3,4] However, follow-up studies from other centers have not confirmed these findings, and this system does not appear capable of predicting susceptibility to HO.[5–7]

Prevalence and Onset

The reported prevalence varies for most types of HO, but much of this difference may be the result of methodology and institutional variations. The type of center (acute care vs. rehabilitation) and the type of impairment (hemiplegia, paraplegia, or quadriplegia) influence the incidence. Methodology also affects study outcomes. Prospective vs. retrospective studies, whole-body radiographs vs. hip only, and 6 month vs. 1 year follow-ups have the potential to influence final data.

The prevalence of clinically significant HO — that which limits joint motion, as opposed to HO of purely academic interest, or that which is solely a radiographic observation — is similar when studies from similar institutions and methodologies are compared. The most commonly reported prevalence of clinically significant HO in TBI is 10 to 20%.[8–11] Joint ankylosis occurs in less than 10% of HO lesions.

Diagnosis

Physical Examination

Limited joint motion is the most common physical finding and, frequently, the earliest sign of HO. An increase in spasticity usually occurs. Joint erythema, or warmth, occasionally requires differentiation from a septic joint. Although low grade fever may be present with HO, temperatures greater than 101˚F are uncommon. Erythrocyte sedimentation rate (ESR) also assists in the differentiation. ESR values in septic joint are in the range of 50 to 100 mm/hour while in HO they would never be above 50 mm/hour. Lower limb swelling may mimic thrombophlebitis which should be ruled out. The two conditions also do coexist. HO has also been mistaken for hematoma and cellulitis. The most common symptom of HO is pain. An increase in pain, spasticity, or muscle guarding should alert the examiner to the impending onset of HO.

Serum Alkaline Phosphatase Determination

Serum alkaline phosphatase (SAP) is a marker of osteoblastic and osteogenic activity, which increases with bone deposition. Early reports on HO failed to associate elevated SAP levels. However, follow-up studies have demonstrated that elevated levels of SAP are present with clinically significant HO. SAP levels begin to rise, although remaining in the normal range, within 2 weeks of injury.[12] Elevated levels may occur by 3 weeks, and the duration of persistently high titers averages 5 months. The majority of patients who develop clinically significant HO about the hip will have an elevated SAP level. This may not be true at the elbow where small amounts of HO may decrease motion. SAP titers do not correlate with inactivity, peak activity, or number of HO lesions. SAP determination is nonspecific and not absolute, but it may constitute the earliest and, certainly, the most convenient and inexpensive laboratory test for early detection of HO. Many patients are in intensive care units and cannot undergo special studies. Medicinal treatment may be initiated solely on the basis of SAP elevation if fractures are not present.

Radionuclide Bone Imaging

Radionuclide bone imaging (RNBI) became effective as a diagnostic tool in the late 1960s and early 1970s. Early bone scan techniques employed injection of technetium-99m polyphosphate with follow-up scans obtained approximately 4 to 5 hours after injection. Presently, the "three-phase" bone scan is the best method for early detection, as well as confirmation, of HO.[13] This test involves injection of Tc-labeled methylene diphosphonate followed by imaging in three phases:

- Phase I — A dynamic blood flow study with frequent photoscans during 1-minute frame
- Phase II — A static scan for blood pool after the completion of phase I
- Phase III — A 2- to 4-hour bone scan to determine the amount of the labeled radionuclide in bone

The first two phases are the most sensitive for early detection of HO and may show abnormal results within 2 to 4 weeks after TBI. The period of positive uptake in Phases I and II with a negative Phase III may range from 2 to 4 weeks. Likewise, Phase III may be positive up to 4 weeks before HO is observed radiographically.

A large prospective, or even retrospective, study of the RNBI Phase III evaluation of HO is not available. Correlation of RNBI with evolution of radiographic features has not been performed. The majority of bone scans return to baseline within 7 to 12 months, while a slowly downward activity occurs in many of the remainder of the scans. A few scans remain fully active during the first year. The RNBI may become reactivated after a quiescent period.

Quantitative radionuclide bone scans compare the ratio of uptake in normal ossification vs. HO. Since HO uptake decreases with time, it is assumed that serial decreases or a steady state in the ratio of uptake between normal and heterotopic bone indicates HO maturity. It is proposed that the incidence of recurrence of HO is decreased after resection if HO is removed during a radionuclide steady state. Unfortunately, this premise has not been adequately verified in a large homogeneous series. Our large surgical resection series demonstrated that this steady state was not a predictor of recurrence.[14] Patients with persistently active scans predictably had recurrence, whereas in patients with negative scans, recurrence was not always predictable. Consequently, it seems that neither the natural history of HO nor treatment guidelines based on RNBI activity have been adequately established.

Radiography

Before RNBI became available, radiographs provided confirmatory evidence of HO. Although plain films may detect HO as early as 3 weeks after injury, radiographic detection is usually not confirmatory until 2 months after the stimulus.

Radiographs offer other benefits. They identify the site of HO at the joint and are an easy, inexpensive, and reliable method for evaluation of treatment. Radiographs permit evaluation of maturation of HO, especially when coupled with results of SAP determinations and physical examination (decrease in spasticity).

Computed Tomography

The precise role of computed tomography (CT) scanning as a clinical tool for diagnosis and a measure of maturation of HO is not established.[15] Computed tomography may aid in preoperative surgical planning. Multiple sites of HO at a joint may be more readily delineated by CT. CT scan more clearly defines HO and its relation to muscle, vessel, and nerve.

Bone Markers

Active research is ongoing in an attempt to identify newer bone markers in blood and urine in order to detect early HO.[16–19] Bone markers are not used widely yet. When available, their use is encouraged because early diagnosis allows earlier treatment.

Location

Our retrospective review of 496 patients revealed 57 patients (11%) with 100 joints involved with neurogenic HO.[20] Of these patients, 30 had single joint involvement, while 27 patients had multiple joint involvement. The ratio of the involved male to female patients was similar to the ratio of male to female in the total population. This is significant since some people suggest that, based on spinal cord injury (SCI) patients wherein HO in females is uncommon, HO is a disease of males. We found that 81 of the involved joints were located on spastic extremities. We think the other extremities may have been previously spastic but had no spasticity at transfer to our unit.

The 11% incidence may not indicate the true incidence. A routine radiographic survey of major joints was not undertaken. Only clinically significant HO, in a joint associated with pain and decreased range of motion, was detected. Although the series was consecutive, the population was selected. Patients with mild head injuries are not transferred to our unit. The incidence of HO in these patients may be low or may occur in a mild, clinically insignificant form. Patients with severe neurologic involvement are frequently not candidates for rehabilitation and are not transferred to our unit. The incidence in this group, as well as the amount of HO, may be increased.

Hip

In 33 patients, 44 hips developed HO. Three main locations were detected. The site of HO could frequently be predicted from the abnormal posture of the extremity. Occasionally, HO developed in more than one plane.

Heterotopic bone anterior to the hip may result in swelling of the thigh with a palpable and visual mass (Figure 4.1). The hip often assumes a mildly flexed position with external

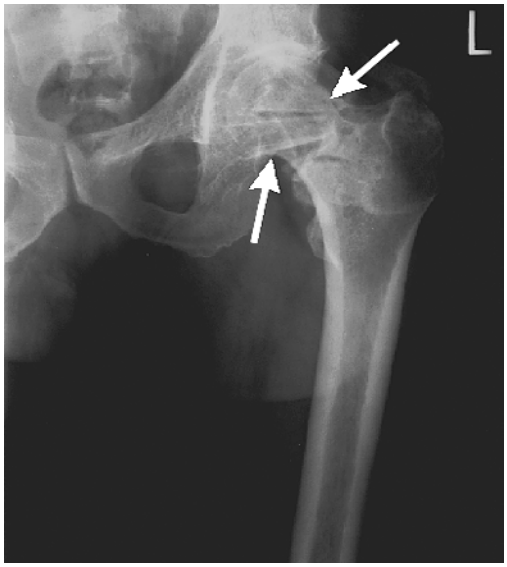

FIGURE 4.1
Left hip. HO (arrows) is posterior to the femoral neck.

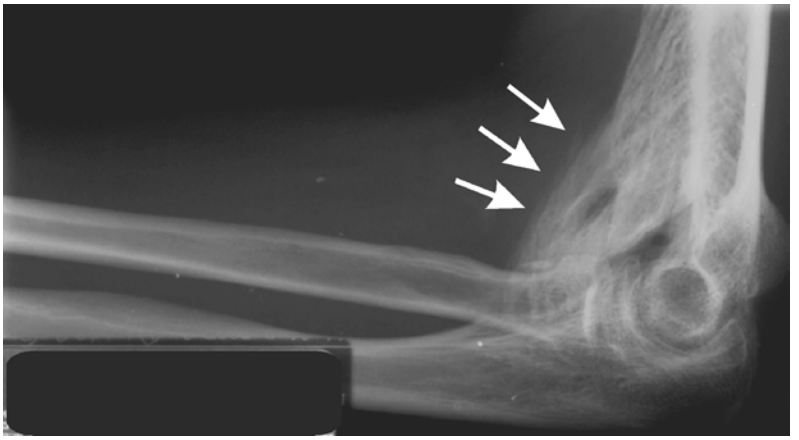

FIGURE 4.2
Left elbow. Anterior HO (arrows) is present with complete ankylosis.

rotation of the leg. The massive amount of HO present in SCI patients at this location is seldom observed in TBI patients.

HO occurring posterior to the hip may be associated with hip flexion contractures. This location of HO may not result in great limitation of motion.

The most common location of HO at the hip was the inferomedial location. HO, in this location, is frequently associated with adductor spasticity. Ankylosis is uncommon, unless the patient had a severe neurologic insult. Some loss of hip flexion and extension normally occurs. If a large amount of HO is present, adduction range is compromised due to a mechanical block.

Elbow

Two sites of HO generally occur in the elbow, although HO may form in any or all planes, especially in the traumatized elbow. HO, anterior to the elbow, is often associated with flexor spasticity, as noted in the hemiplegic limb (Figure 4.2 and Figure 4.3). If ankylosis results, the bone usually bridges the distal humerus and proximal radius.

New bone occurring posteriorly at the elbow is often associated with extensor posturing (rigidity). Since extensor rigidity resolves with neurologic improvement, the elbow may assume a more flexed position at the time ankylosis is occurring. This explains the paradox of posterior HO in a normal, hemiplegic, or flexed extremity. Ankylosis most commonly occurs posteriorly at the elbow. Ankylosis is usually between the distal humerus and olecranon.

Shoulder

The rate of occurrence is similar to the elbow. The new bone is generally located inferomedial to the joint (Figure 4.4). The shoulder position is internal rotation and adduction. Ankylosis is uncommon, unless the patient sustains a severe neurologic insult.

Knee

HO about the knee and the quadriceps muscle is uncommon. It may appear anywhere in the distal thigh or about the knee (Figure 4.5 and Figure 4.6).

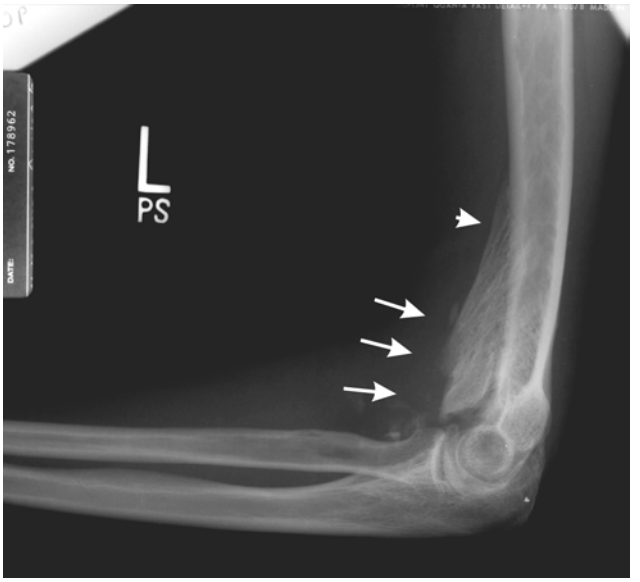

FIGURE 4.3
Left elbow. The HO has been resected (arrows). Removing all the HO is not necessary (arrowheads).

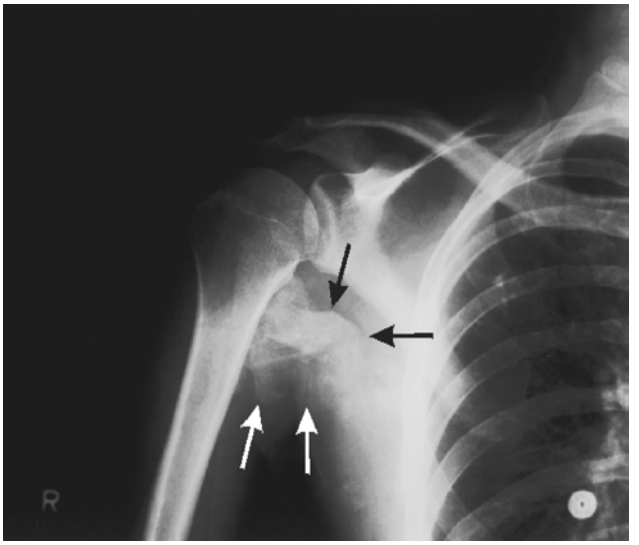

FIGURE 4.4
Right shoulder. Traumatic brain injury neurogenic HO (arrows) is usually at the inferomedial location. Some shoulder motion is usually maintained.

Natural History

HO in TBI probably begins shortly after injury. Serum alkaline phosphatase begins to rise in the third week. Bone scan is positive and symptoms are present by the fourth week. Radiographs become positive 6 to 8 weeks after injury.

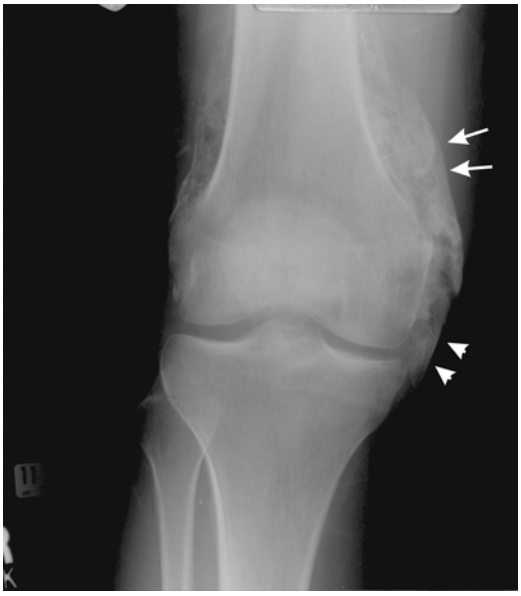

FIGURE 4.5
Right Knee. HO is located at the distal femur and knee medially (arrows) and laterally. The medial side is crossing the joint (arrowheads).

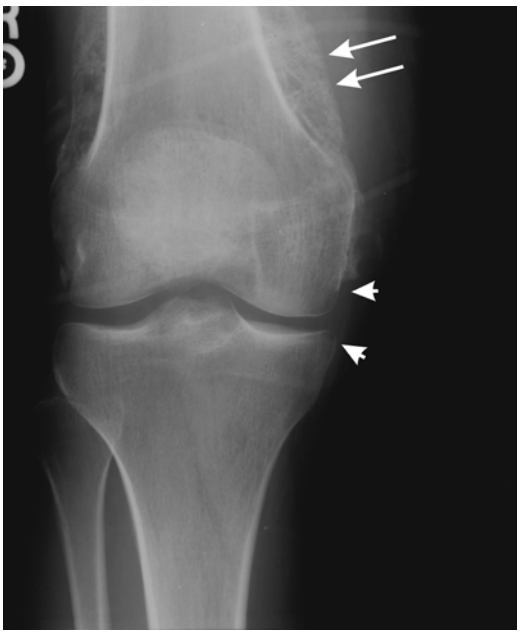

FIGURE 4.6
Right Knee. The HO about the medial joint has been removed (arrowheads). The HO attached to the femur was not removed (arrows).

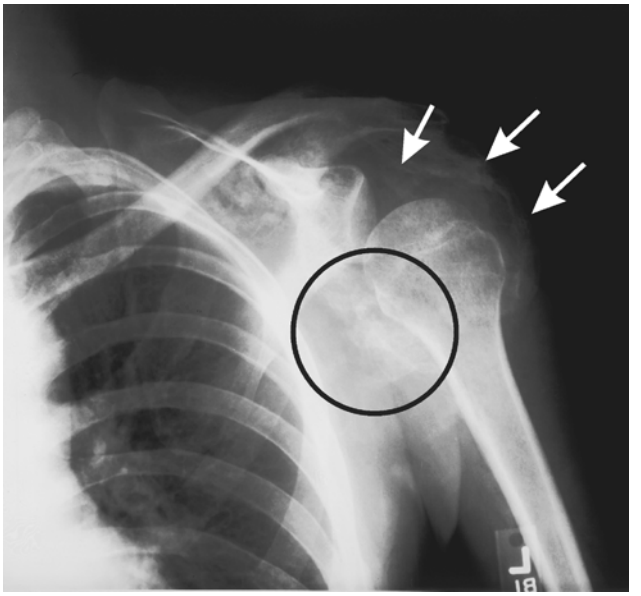

FIGURE 4.7
Left Shoulder. The shoulder is dislocated (arrow). HO is circumferential (circle). This occurs because of the combination of trauma to the shoulder plus traumatic brain injury.

The natural history of HO is defined through radiographs and not frequently emphasized.[21–23] The natural radiographic history is similar and predictable in the majority of patients. It also closely parallels the elevation of SAP level and the presence of spasticity.

Our retrospective review of 23 TBI patients who underwent resection of HO at an average of 28 months after injury allowed classification of patients from I to V according to their neurologic recovery. Class I patients had near-normal neurologic recovery, whereas Class V patients had severe cognitive deficits and spasticity. Class I patients rarely had recurrence after resection. In contrast, every Class V patient had recurrence regardless of the site of HO. Radiographic progression subsided by 6 months, and SAP levels and RNBI activity were normal, or significantly decreasing, in patients who made an early, normal neurologic recovery (Class I). Patients with severe motor compromise had larger amounts of HO. This HO progressed, in some instances, for more than 1 year, with elevated SAP levels for 2 years or longer and, occasionally, persistent activity on RNBI.

Complications of HO include ankylosis in 10% of HO lesions. Joint dislocations are seen occasionally (Figure 4.7). Pressure sores occur on bony prominences. Vascular, lymphatic, and peripheral nerve compression and injury have been reported due to abnormal growth of bone.[24–26] Limb fractures may result from vigorous ranging exercises.

Treatment

HO runs a gamut from being undetected, and therefore untreated, to having a poor response to all treatment modalities. Some patients with minimal HO require no specific treatment, whereas others may require physical therapy, medicine, manipulation, surgical excision, or all of these (Figure 4.8). The majority of patients with HO maintain functional

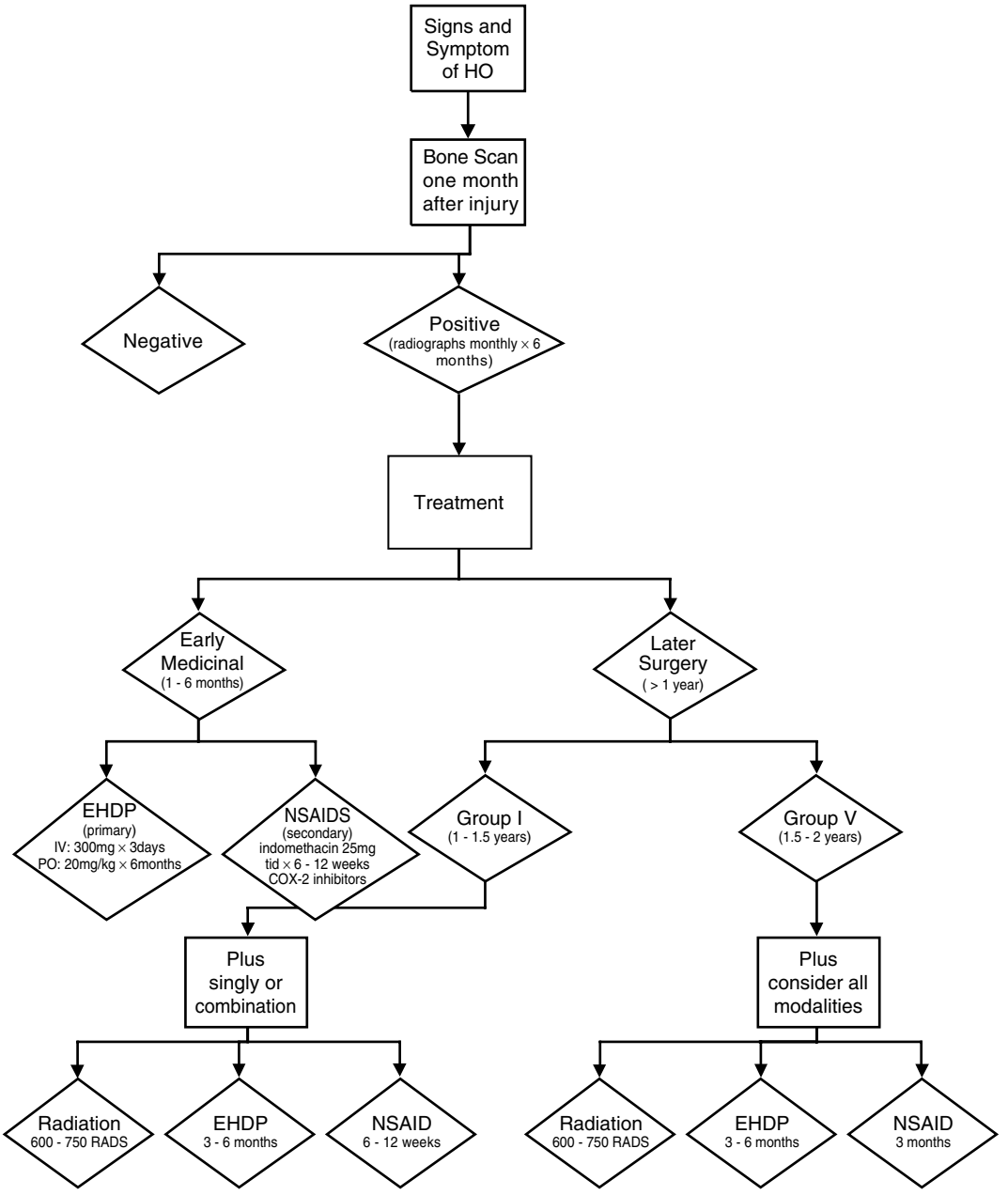

FIGURE 4.8
Diagnosis and treatment of HO.

joint motion with standard physical therapies, medicines, and, occasionally, forceful manipulations. A small group requires surgery, with some developing recurrence after surgery.

Medical treatment, including radiation, is used prophylactically in two general situations: (1) to prevent HO formation after the primary insult and (2) to prevent recurrence of HO after surgical resection.

Ethylhydroxybisphosphonate (Ethidronate Disodium)

In the early 1960s, research with polyphosphates and their inhibitory activity on calcium phosphate precipitation led to evaluation of bisphosphonates, specifically ethylhydroxybisphosphonate (EHDP), for similar effects. Definitive studies demonstrated that bisphosphonates inhibited the precipitation of calcium phosphate from clear solutions, delayed aggregation of apatite crystals into layer clusters, blocked the transformation of amorphous calcium phosphate into hydroxyapatite, and delayed dissolution of crystals. All effects seemed related to their affinity for hydroxyapatite. The ability of EHDP to inhibit experimental soft tissue ossification, as well as normal mineralization of bone, led to the clinical use of EHDP to prevent HO.[27,28]

For optimal effects, EHDP must be used at proper dosage and duration of treatment. As noted above, EHDP prevents conversion of the amorphous calcium phosphate compounds into hydroxyapatite crystals, which is one of the final stages of bone formation. The majority of HO evolves radiographically over a period of 6 months; therefore, the conclusion is that EHDP should generally be given over this 6-month span.[21–23] A lower EHDP dose is adequate to inhibit crystal resorption, but it is less effective in inhibiting crystal growth. The 20-mg/kg dosage is necessary to prevent HO formation. Treatment for this duration and at this dosage should prevent HO lesions in the majority of patients and also decrease the incidence of the so-called rebound calcification. Prolonged treatment with EHDP produces undesirable side effects such as long bone fractures in dogs.[29] Therefore, dosages of 20 mg/kg for longer than 6 months may not be warranted, and continued treatment may be deleterious. EHDP will not be effective for the persistent neurologically compromised patient regardless of dosages and duration of treatment.

The present method of etidronate treatment is derived from the SCI literature.[30–32] No definitive study exists in the TBI literature. Etidronate 300 mg is diluted in 300 ml of 5% dextrose and water and given over 4 hours for 3 consecutive days. The patient is then given etidronate orally at a dose of 20 mg/kg for 6 months because this drug acts at the last phase of ossification. Preferably, it is given once daily in the morning with water or juices. If gastrointestinal disturbances occur, the dose may be lowered. The medicine is stopped at 6 months after initiation, even if HO progresses radiographically. The drug should not be given for more than 6 months; with prolonged treatment at this dosage, osteoporosis and fractures may occur.

Quantitative histomorphometry demonstrates an increased number of osteoclasts, as well as osteoblasts, in the HO lesion compared to normal bone.[33] EHDP, at a much lower dosage than that necessary for the inhibition of ossification, interrupts osteoclastic function but does not destroy the osteoclasts. They eventually recover full function over a prolonged period. The impairment of osteoclast function is extremely undesirable. Resorption is the final aspect of HO maturation and involves partial, or even complete, resolution of the HO lesion. With cessation of treatment, the osteoid may ossify immediately, yet the resorptive capability remains impaired until osteoclastic function returns. This may influence the rebound phenomenon as well as resorption. The effect of EHDP on osteoclasts, the recovery of rebound phase, the length of treatment, patient compliance, and the cost

of the medication may eventually contribute to the selection of another drug for treatment of HO.

Nonsteroidal Antiinflammatory Agents (NSAIDs)

Dahl is generally credited with demonstrating the prophylactic effects of indomethacin on HO formation after total hip replacement.[34] Other studies have verified its effectiveness.[35,36] A recent study showed that indomethacin was helpful in preventing HO in patients with spinal cord injury.[37] The ability of indomethacin to inhibit prostaglandin synthetase is proposed as the primary mechanism of HO prevention, although many effects on bone formation are known. Prostaglandins are mediators of inflammation, and part of NSAIDs' effect is inhibition of the inflammatory response or suppression of mesenchymal cell proliferation. It has also been observed early postoperatively that NSAIDs may inhibit differentiation of pluripotential stem cells into osteoblasts. Because of its potency among NSAIDs, indomethacin was used early for treatment of HO. Indomethacin dosage is 25 mg, 3 times a day for 6 weeks, after total hip replacement. Ibuprofen and aspirin may also be effective when used in a similar fashion. The effectiveness and the duration of treatment of nonsteroidal, antiinflammatory drugs to prevent HO in the neurologic patient have not been established. Since it prevents bone formation in its early phase, its use could be for 3 months and not the entire 6 months that etidronate is used. The newer COX-2 inhibitors are probably a better choice due to their fewer gastrointestinal side effects and similar mechanism. Both etidronate and NSAIDs may be necessary in a patient with aggressive HO.

Radiation

The ability of radiation to inhibit bone growth has been known by radiotherapists for years. Irradiation prevents conversion of precursor cells to bone-forming cells. Early reports of irradiation in the treatment of myositis ossificans were often anecdotal. Now it appears that 1000 rads or less, immediately after total hip replacement, is effective in preventing HO.[38,39] However, one study, comparing radiation to indomethacin, showed both methods used as prophylaxis were equally effective in this population.[40] The location of HO formation in the neurologic patient cannot be predicted. Because radiation is relatively ineffective once HO is detected, its use in prevention and early treatment of initial neurogenic HO may be limited. It may have some use after HO resection but its effectiveness in the follow-up of patients with neurogenic HO has not been demonstrated.

Forceful Manipulation

The role of ranging joints involved with HO for maintenance or increasing joint motion is controversial. Some authors have suggested that ranging increases the amount of HO, whereas others have reported beneficial gains or maintenance of joint motion. A review of patients who underwent forceful manipulation under anesthesia demonstrated its usefulness in maintaining motion in most patients and actually increasing motion in others.[41] Traumatic brain injury patients frequently have spasticity, intolerance to pain, and voluntary muscle guarding. Consequently, anesthesia is usually required for manipulation. Examination under anesthesia allows differentiation of spasticity and true ankylosis. If spasticity is determined to be a major factor, treatment may also be directed toward it.

Large increases in motion are sometimes achieved under anesthesia, but motion may be gradually lost thereafter. If neurologic improvement continues, joint manipulation may be repeated as necessary. If the patient remains at a low level of neurologic recovery, repeated manipulations are not beneficial. We have not manipulated a joint more than three times. Final arc of motion is closely related to the amount of neurologic recovery. Of 28 joints, 23 (82%) gained motion with anesthesia. Further motion was maintained or gained by 18 joints (64%) with rehabilitation. Review of the radiographs did not reveal an exacerbation of the ossific process.

Surgery

Surgery is indicated for joint mobility, limb positioning, or sitting. Various operative procedures have been described.[14,22,23,42] Precise timing for surgery is mentioned infrequently but is determined in respect to the quiescent state, indicated by normal SAP levels, mature radiographic appearance, and baseline RNBI. Postoperative complications are common when compared to standard orthopedic procedures.

The natural history of neurologic recovery is the best indicator for time of surgical excision, recurrence, and functional outcome. The majority of motor recovery occurs by $1\,1/2$ years and resection should be considered at that time. Excision in the patient with a rapid neurologic recovery may be undertaken earlier when alkaline phosphatase is normal and no spasticity is present. Surgery should be delayed longer than $1\,1/2$ years if the motor recovery is prolonged. Recurrence is common in the presence of normal or abnormal laboratory values in the neurologically-compromised patient. Investigators have shown that continuous passive motion, postoperatively, decreases recurrence and achieves greater range of flexion.[43,44] Delaying excision because of abnormal laboratory values is not warranted: surgery is indicated for limb positioning in neurologically-compromised patients.

No currently available studies have defined the role of medical prophylaxis after resection. The stimulus to form HO has subsided in the normal recovery group and medical prophylaxis may not be necessary for these patients. Since the neurologically-compromised patient continues to form HO after resection, present prophylaxis methods may be inadequate. A mildly to moderately neurologically-compromised patient should respond to prophylaxis after resection. This would include any of the three treatment methods described singly or in combination.

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5

Rehabilitation for Posttraumatic Vestibular Dysfunction

Peter S. Roland, Debbie Eaton, and Erik Otto

CONTENTS

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Introduction

Vestibular injury is frequently overlooked in the diagnostic evaluation of the traumatically brain-injured individual. Many of the patients we see in our postacute setting have never been formally evaluated for vestibular dysfunction. Yet, an important percentage of these patients suffer from vestibular dysfunction.

The complaint of vertigo is not the only symptom of vestibular injury. Other symptoms may include decreased ability to balance, visual complaints (double vision, blurriness), or nausea. Complaints that may or may not be symptoms of vestibular injury per se, but often accompany a vestibular lesion after a head injury, are: headache, irritability, oversensitivity to sounds and/or lights, and decreased attention and concentration span. These symptoms are often seen as a psychological response following a head injury and not related to organic damage. In addition to the vestibular and associated complaints, there is the issue of litigation that can cloud the mind of the patient and caregiver alike. Only following a complete evaluation can the process of treatment begin. Treatment may include exercise, medication, and/or a surgical procedure. Finally, when complete rehabilitation is not expected, the role of a counselor can be crucial in dealing with adjustment to disability. This process should also include patient education about the extent of the lesion and its consequences. Patient education is critical to help bring under control a process that otherwise might lead to a degree of disability not warranted by the lesion itself.

Recovery from head injury is now recognized to be a complex process which progresses over many months. The patient recovering from a head injury is frequently afflicted with more than a single area of difficulty or dysfunction. Many of these areas are the focus of specific chapters in this book. Such problem areas frequently cross disciplinary boundaries and, in practical clinical situations, symptoms outside the specialty area of the primary caregiver may receive less than adequate attention. Comprehensive care is, therefore, improved when the post–head-injury patient is served by a multidisciplinary team whose efforts are orchestrated by a designated coordinator.

Review of the literature suggests that dizziness or disequilibrium following a head injury represents an area which requires considerably more attention and postinjury rehabilitation than it has received to date.

Demographics

Although previous investigations are few in number, the evidence presented by available studies argues powerfully that postconcussive balance disturbance is the primary cause

of very substantial morbidity and long-term disability. Indeed, Healy asserted in the *Journal of the American Medical Association* that "cochlear and vestibular dysfunction represent the largest group of delayed complications of head injury."[1,2]

Berman and Fredrickson[3] evaluated 321 head injury patients within the Canadian Workman's Compensation System. In this group, 40% complained of postinjury vertigo and, of those complaining of vertigo, 50% had objective electronystagmographic (ENG) findings of organic dysfunction. When the 140 patients with complaints of vertigo were evaluated 5 years after injury, only 14% had returned to their preaccident or equivalent work. In this group, 46% had not returned to any work at all. Vertigo, together with headache, was of prime importance in determining long-term work status. Although no long-term studies exist for U.S. populations, since social, cultural, and compensation variables are quite similar, it seems reasonable to extrapolate these results to the United States.

Rantanen et al.[4] evaluated 41 patients within several days of head injury. In this group, 60% complained of vertigo. When eye movement was evaluated by physical examination alone (even with Frenzel lenses), only 20% had observable nystagmus. However, when electronystagmography (ENG) was performed with eyes closed, nystagmus was detectable in over 60%. Elimination of "visual fixation" by eye closure releases pathological nystagmoid eye movement in a significant percentage of injured people, and Rantanen et al. emphasize that formal ENG evaluation is important in the objective evaluation of postinjury patients complaining of dizziness.

Saito et al.[5] evaluated 22 patients who complained of dizziness after head injury. All had positional nystagmus on ENG, and 11 had ENG findings suggestive of central nervous system injury. Of the 11 patients with ENG findings suggestive of CNS injury, only four recovered in 2 months or less, and four were still unrecovered after 3 months. Patients with ENG indicators of peripheral vestibular dysfunction recovered much more quickly. By differentiating between central and peripheral pathology, ENG was helpful in establishing a prognosis.

Tuohimaa[6] carefully studied 82 patients who had sustained only "mild" head injuries (duration of unconsciousness less than 2 hours or not at all) and compared them to a matched control group. Of the postinjury patients, 78% complained of vertigo. Central ENG disturbances were observed immediately after injury in 60% of the patients, but the incidence fell to 12% at 6 months postinjury. The incidence of persistent central ENG changes increased with increasing age of the post–head-injury patient. Tuohimaa's group of patients demonstrated a dramatic impairment of the ability to suppress nystagmus by deliberate visual fixation. He argues that diminished fixation suppression indicates that reduced central inhibition is a frequent consequence of mild head injury. The incidence of both spontaneous and positional nystagmus was significantly higher in mild-head-injury patients immediately after injury than in normal controls.

Grimm and his colleagues[7] studied 102 patients with mild craniocervical trauma who experienced positional vertigo. This group displayed a set of symptoms often referred to as *postconcussion syndrome.* Over 95% of these patients suffered from disequilibrium and 70% from vertigo. Headache, memory loss, tinnitus, nausea, confusion, clumsiness, alteration of subjective visual perception, and stiff neck were all present in over 50% of this group of patients. Their conclusion that all of these patients had a perilymphatic fistula is highly controversial, but their work does highlight the importance of balance disturbance in patients with even mild head injury. Moreover, they have documented well the pattern of characteristic symptomatology found so frequently after head injury.

Vartiainen et al.[8] examined 199 children after blunt head trauma. In this group, 50% had positional or spontaneous nystagmus and 50% had central ENG disturbances. The incidence of abnormalities dropped rapidly after 2 to 8 years but was somewhat higher in the peripheral group (18%) than in the central group (12%). Clinically, when compared to

adults, a much lower percentage of these children (1.5%) remained symptomatic at 2 to 8 years.

Evator, Bergtraum, and Randel[9] evaluated 22 children, ages 6 to 18 years, for posttraumatic vertigo. Children with hearing loss were excluded. Five pathologically distinct etiologies were identified, including posttraumatic migraine (five), seizure disorders (four), postconcussion syndrome (four), whiplash injury (four), and posttraumatic neurosis (five). Their work emphasizes the variety of processes which can produce posttraumatic disequilibrium and emphasizes the value of objective ENG testing in distinguishing among various etiologies.

Anatomy and Physiology of the Vestibular System

The anatomy of the vestibular system is complex and, especially in its ramifications within the central nervous system, poorly understood. Anatomically speaking, one may divide the vestibular system into four parts: (1) the peripheral vestibular end-organ enclosed within the bony labyrinthine capsule, (2) the vestibular nerve, (3) the brainstem vestibular nuclei together with their vestibulo-ocular, vestibulo-cerebellar, vestibulo-spinal radiations and feedback loops, and (4) vestibular cortex (Figure 5.1).

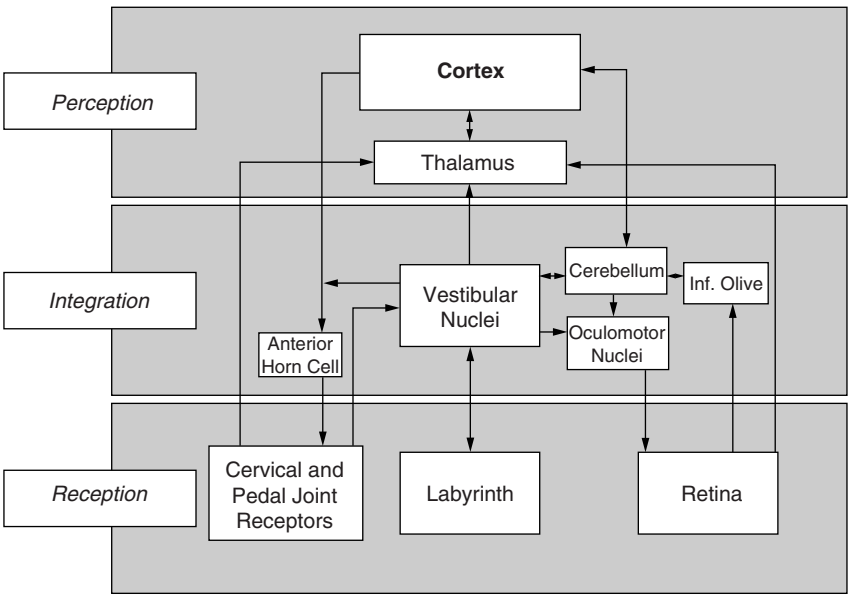


FIGURE 5.1
Conceptual schema of the vestibular system. This subdivides the various components of the vestibular system into a vertically oriented hierarchy with receptor organs at the bottom and perception at the top. Lateral organization distinguishes between various different receptors at the lowest level and brainstem nuclei at higher levels. A fully functional vestibular system requires coordination and integration of sensory receptor information. Plasticity of the vestibular system arises from the fact that deficiencies in information provided by receptors can be compensated for at the integrative or perceptive level by reorganizing input from residual receptors. (From Brown, J. J., A systematic approach to the dizzy patient, *Neurol. Clin.*, 1991; 8(2), 210. With permission.)

Vestibular End Organ

The *labyrinth* (inner ear) consists of a folded, fluid filled tube (membranous labyrinth or endolymphatic space) which lies within the bony labyrinthine capsule. The membranous labyrinthine is suspended in and cushioned by a second fluid compartment (perilymphatic space). Anteriorly within the bony labyrinth is the spirally shaped cochlea, the organ of hearing. Posteriorly are the three semicircular canals. Between the cochlea and semicircular canals is a central chamber, the vestibule, which contains the utricle and saccule (Figure 5.1 and Figure 5.2).

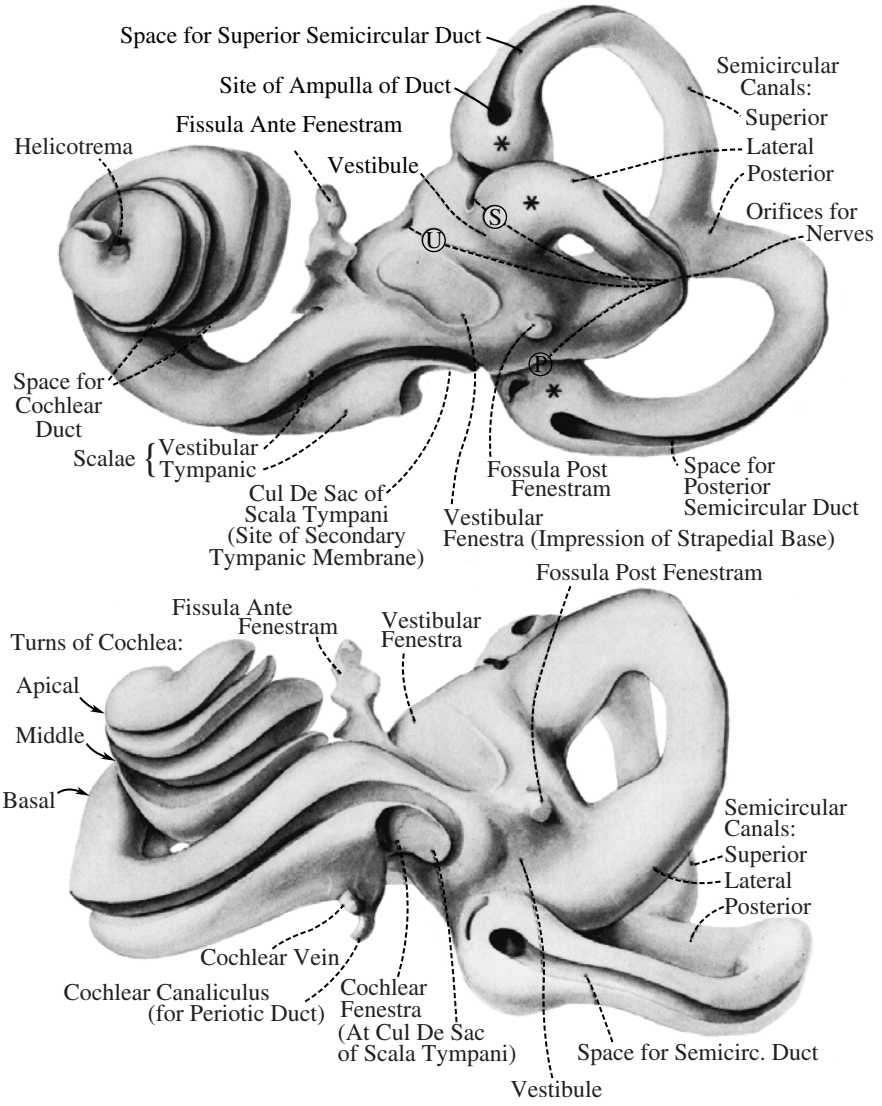


FIGURE 5.2
The labyrinth is seen from the lateral position (top) and from below (bottom picture). The bony labyrinth has been opened to show the position of the membranous endolymphatic duct. Asterisks indicate the cupular dilatations of the semicircular canals. S = saccule, U = utricle. (From Lindermann, H. H., *Studies on the Morphology of Sensory Regions of the Vestibular Apparatus*, Springer-Verlag, New York, 1969. With permission.)

The two inner fluids are chemically distinct. Endolymph (like intracellular fluid) contains a relatively high concentration of potassium and a relatively low concentration of sodium. Perilymph (like extracellular fluid) contains much sodium but relatively little potassium. The difference in electrolyte composition between these two fluids is essential in maintenance of the resting electrical potential, which is critical to normal functioning of the receptor cells.

The composition of endolymph is thought to be regulated by a vascular structure within the lateral wall of the endolymphatic duct called the *stria vascularis*. The production and composition of endolymph may, therefore, be altered by conditions and substances that alter blood flow, vascular permeability, or systemic fluid balance. Perilymph is, at least partially, an ultrafiltrate of spinal fluid. The perilymphatic space is connected with the subarachnoid cerebrospinal fluid space via the cochlear aqueduct. Changes within the subarachnoid space may alter the perilymphatic compartment. Increased intracranial pressure produced by disease or by straining may be transmitted to the perilymphatic space and produce chronic or acute perilymphatic hypertension. Chemicals, toxins, and viral and bacterial infectious agents may all pass from the cerebrospinal fluid to the perilymph via the cochlear aqueduct.

Alterations in the chemical composition, relative volumes, or mixing of the inner ear fluids may incapacitate both the vestibular and hearing end organ. Depending upon the anatomic extent and severity of the alteration, various combinations of balance disturbance, hearing loss, aural fullness, and tinnitus may result.

The common sensory receptor within the inner ear is the *hair cell*. Its function is to translate fluid motion into a pattern of neuronal electrical discharge. The labyrinthine fluids first translate both head acceleration and sound waves into fluid movement. Movement of fluid across the stereocilia of receptor hair cells deflects the stereocilia and changes the resting rate of discharge in the nerve attached to the hair cell (Figure 5.3). Movement in one direction may increase the rate of discharge and movement in the opposite direction may decrease the rate of discharge. It is this change in rate of neuronal activity which is processed by the central nervous system into conscious and subconscious information about spatial orientation and sound.

The vestibular end organ consists of five separate structures, each with its own specialized sensory epithelium. The three semicircular canals are at right angles to each other: one in the horizontal, one in the sagittal, and one in the coronal plane. The receptor organ of the semicircular canals is the *crista ampullaris* (Figure 5.1 and Figure 5.2). Each crista consists of a group of hair cells, the stereocilia of which protrude into a dilated portion of the membranous labyrinth called the *ampulla*. The stereocilia of the hair cells are embedded in a gelatinous matrix that fills the ampulla (Figure 5.4). Head acceleration in the plane of the semicircular canals results in the bending of stereocilia due to inertial lag in the movement of endolymph. The same "bending" event occurs when head movement is stopped because the endolymph will "keep going" for a few milliseconds after the head comes to a complete rest. The semicircular canals, therefore, respond exclusively to angular acceleration. They do not respond to constant velocity — only to changes in velocity. This distinction is important. Once constant velocity is achieved, the sense of motion is eliminated. A pilot in a rolling airplane may, absent visual clues, lose all sense of rotation if the rotation continues at constant velocity for more than a few seconds.

The saccule and utricle are the two otolithic end organs. They sense linear acceleration and static tilt. They are gravity sensitive and maintain the ability to distinguish "up" from "down." Each otolithic end organ consists of an outpouching of the endolymphatic duct on one wall of which rests a collection of hair cells called the *macula*. The hair cells are covered with a gelatinous matrix in which are embedded crystals of calcium carbonate called *otoconia* (Figure 5.5). The otoconia (Figure 5.6) are acted upon by gravitational forces

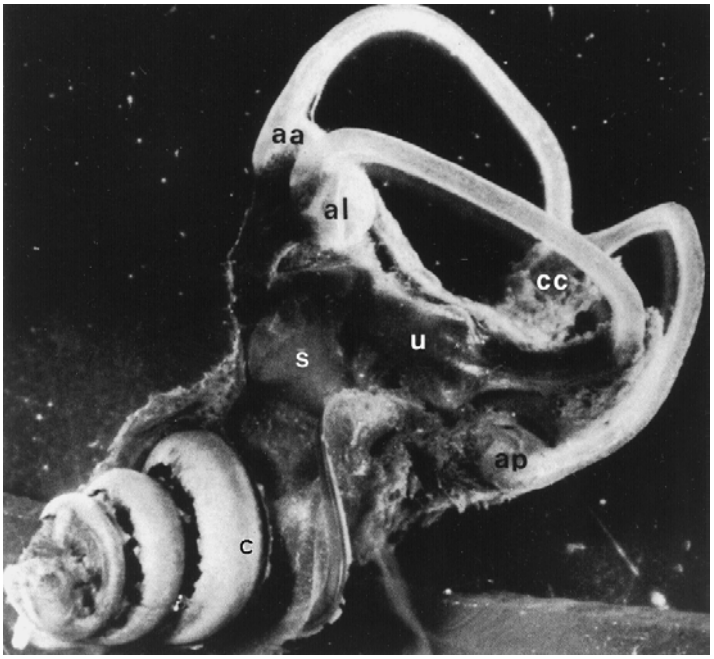


FIGURE 5.3
This is an actual microdissection. The bone has been completely removed leaving only the membranous endolymphatic duct system. The microdissection is oriented in approximately the same position as the top drawing in Figure 5.2. AA = cupula of the superior canal, AL = cupula of the lateral semicircular canal, AP = cupula of the posterior semicircular canal. CC = crus communis, U = utricle, S = saccule, and C = cochlea. (From Lindermann, H. H., *Studies on the Morphology of Sensory Regions of the Vestibular Apparatus*, Springer-Verlag, New York, 1969. With permission.)

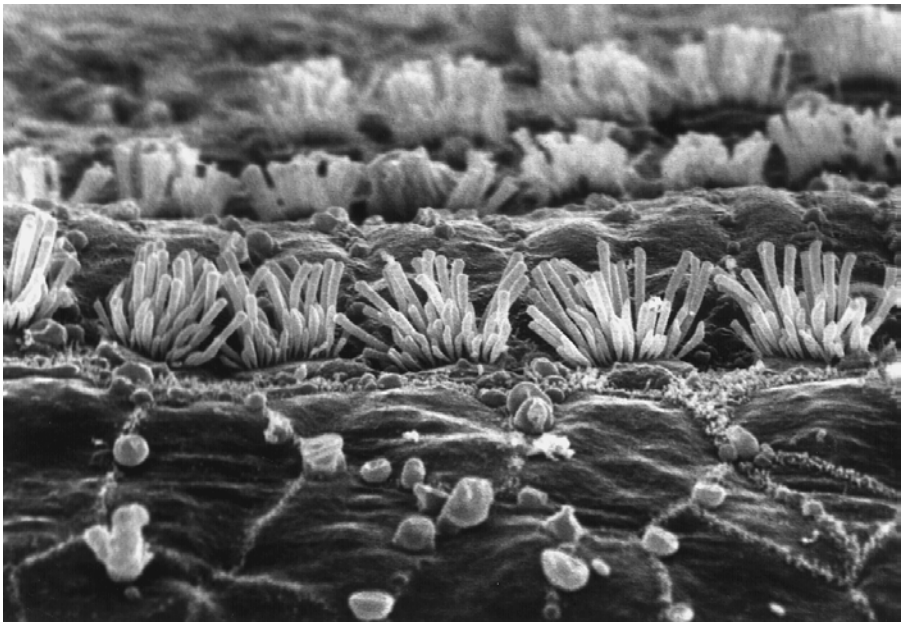


FIGURE 5.4
This is a scanning electron micrograph of the stereocilia from the cochlear hair cells. (Photomicrograph courtesy of C. Gary Wright.)

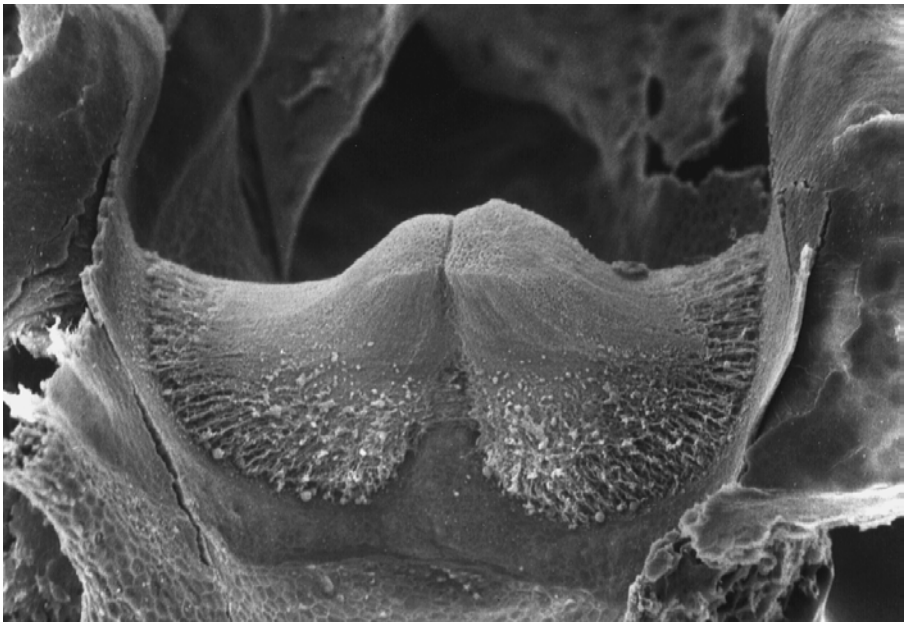


FIGURE 5.5
The open cupula of a semicircular canal reveals the underlying otogenous matrix into which hair cells protrude. (Photomicrograph courtesy of C. Gary Wright.)

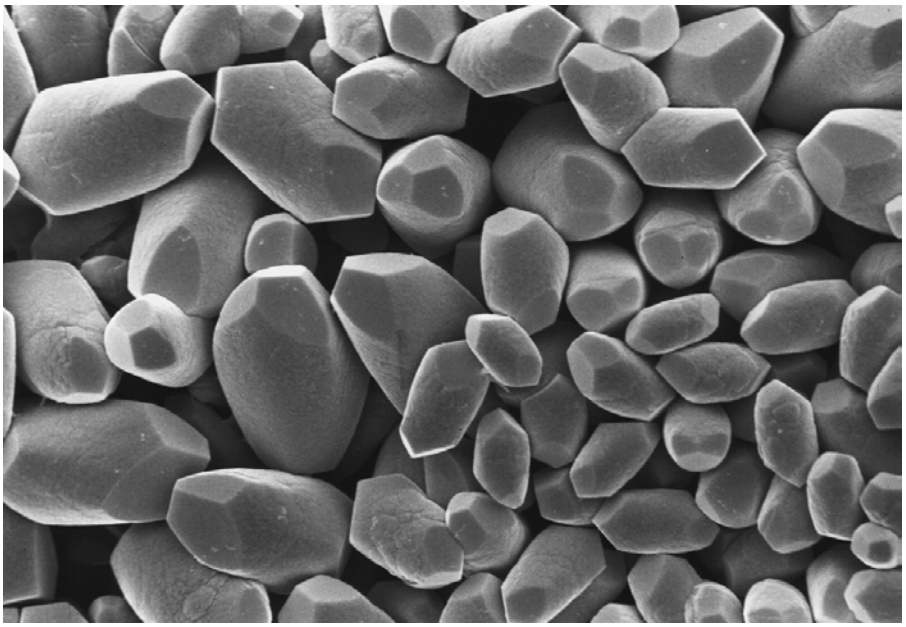


FIGURE 5.6
Scanning electron micrograph of calcium carbonate otoconia. (Photomicrograph courtesy of C. Gary Wright.)

as well as linear acceleration. A change in head position alters the direction in which the otoconia are pulled by gravity and bends the stereocilia of the macular hair cells in that direction. Thus, any change in head position produces a sense of head movement. Since resting head position produces constant otoconial displacement and stereociliar "bending," the otolithic organs are also sensitive to static "tilt"and help maintain orientation to "up and down."

Vestibular Nerve

Information from the vestibular labyrinth is carried to the brainstem by the vestibular nerve. The superior vestibular nerve carries fibers originating from the superior and horizontal semicircular canals, utricle, and a small portion of the saccule. The inferior vestibular nerve carries fibers originating from the posterior semicircular canal and from most of the saccule. Within the internal auditory canal, the superior and inferior vestibular nerves join together, first with each other and then with the auditory nerve, and form a single cochleovestibular nerve. The facial nerve also travels through the temporal bone within the internal auditory canal in close proximity to the vestibular and auditory nerves. The vestibulocochlear nerve crosses the subarachnoid spinal fluid space to the brainstem where the vestibular fibers synapse within the vestibular nuclei. The anterior inferior cerebellar artery, or one of its branches, is often closely associated with the vestibulocochlear nerve either within the internal auditory canal or within the subarachnoid space between the temporal bone and the brainstem.

The Central Vestibular System

The first-order vestibular neurons constitute the vestibular nerves synapse with one or more of the four brainstem vestibular nuclei. The neurons from one labyrinth will often synapse within the vestibular nuclei on both sides of the head, thus providing bilateral representation of the vestibular system even at the brainstem level. The wide-ranging ramifications of the vestibular system within the central nervous system are very complex and poorly understood. Four principal areas can be conceptually distinguished even if they cannot always be precisely anatomically delineated: vestibulo-ocular, vestibulo-spinal, vestibulo-cerebellar, and vestibulo-cortical.

Vestibulo-ocular connections form the basis of the vestibulo-ocular reflex (VOR).[10–12] Each semicircular canal has an elaborate pattern of both direct and indirect synaptic connections to the oculomotor nuclei that control eye movements. The vestibular nuclei on each side are connected to the oculomotor nuclei of both eyes in such a way that stimulation of each semicircular canal can produce eye movements in the plane of that canal, i.e., stimulation of the horizontal semicircular canal can produce horizontal eye movement. These complicated connections are responsible for the production of nystagmus. Stimulation of one labyrinth produces slow movement of the eyes in the opposite direction from the direction of head movement and of roughly equal magnitude. Eye movement continues until a predetermined amount of lateral deviation is reached. Ocular centers within the brain are able to recognize that no further eye movement is appropriate. In order to prevent "pinning" of the eyes in extreme lateral gaze, the eyes are returned to the neutral "straight ahead" position from which lateral deviation can begin again. The eye movement perceived by an observer, therefore, is of slow lateral deviation followed by a very "quick" return movement which, in turn, is followed by another slow movement phase. The rapid return phase is a *saccade*. Saccades are the mechanism of eye movement utilized during volitional change of focus when we "look around." Saccades may occur

with speeds of up to 800°/seconds. During each saccade, reflex brainstem activity suppresses vision so that the visual field is prevented from constant "jumping." During the fast phase of nystagmus (a saccade), vision is suppressed as it occurs. Since this is not true of the "slow" phase, which is controlled by the labyrinth, some patients will complain that their visual field "jumps" in the direction opposite to slow phase when they have nystagmus. The slow phase of nystagmus is about equal to, but in the opposite direction of, head movement, so it appears to be a mechanism which reflexively permits retention of visual fixation during head movement or when falling.

Vestibulo-Cerebellar

There are extensive direct and indirect descending (efferent) and ascending (afferent) pathways between the midline cerebellar nuclei (principally the vermis and fastigial nucleus) and the brainstem vestibular nuclei and associated integrative centers. These extensive connections permit precise modulation of equilibrium both at rest and during complex body movements. Since most of the pathways discussed have a pattern of inhibitory connections as complex as the excitatory ones, brainstem centers subserving the vestibular system are capable of making very fine discriminations and executing highly precise adjustments of movement and balance.

Cortical Projections

The vestibular system (via the thalamus) projects onto the superior temporal gyrus near the auditory cortex. Stimulation of this cortical area can produce a sense of movement often described as "spinning." Input from proprioceptive and visual centers is integrated to produce the final conscious "sensation." Occasionally, epileptiform discharges or neoplasms produce "vertigo" by direct stimulation of these areas of cerebral cortex.

Pathophysiology: Specific Disease Processes

While the pathophysiologic mechanisms of posttraumatic vertigo are frequently obscure, several specific injuries with reasonably well-described mechanisms are recognized.

Temporal Bone Fracture

Because the largest portion of the skull base is made up of the temporal bone, most basilar skull fractures involve some portion of the temporal bone. Such fractures are loosely categorized into two types: longitudinal and transverse. Longitudinal fractures are more common and, fortunately, are accompanied by a low incidence of fracture into the labyrinthine capsule and facial nerve paralysis. Transverse temporal bone fractures are less common (5 to 10% of temporal bone fractures) but are much more likely to fracture into the labyrinthine capsule despite the labyrinthine bone being the hardest bone found anywhere within the human body.[13] When fracture lines extend into the labyrinthine capsule, complete ipsilateral hearing loss and total ablation of ipsilateral vestibular function is the rule. If normal vestibular function is retained in the contralateral ear, then, following several days of overwhelming rotational vertigo with nausea and vomiting, normal functioning will likely return. The rate of improvement depends on the presence

or absence of associated injuries and on the age of the injured subject. Younger patients recover at a much faster rate than older patients. An individual in his twenties may be expected to be able to ambulate unassisted in 3 to 4 days. He may be able to resume fairly demanding activities like bicycle riding and ladder climbing in 3 to 4 weeks. (Ultimately, clinical recovery in this age group is usually complete, although subtle testing will continue to uncover abnormalities of the vestibular system.) The pattern of recovery will be quite different in more elderly persons; it will be slower. A person who is in his 60s or 70s may not be able to ambulate unassisted for several weeks and may be able to perform demanding tasks only after several months. Recovery of fine balance skills may never be complete in the older person. Although vestibular rehabilitation therapy will hasten recovery in the younger individual, many younger patients will do well without a formal rehabilitation program. The outcome in persons over 40, even if the vestibular loss is an isolated disability, may depend critically on the early implementation of a comprehensive, individualized rehabilitation program. This may also be so in younger patients if the vestibular injury is accompanied by other motor, sensory, or neurologic deficits.

Perilymphatic Fistulas

Head injury may produce rupture of the membranes which seal the inner ear and prevent escape of perilymphatic fluid into the middle ear space (Figure 5.7). When perilymph is removed from the labyrinth, inner ear function is degraded. A combination of otologic symptoms may result and symptoms may fluctuate in complex ways that are difficult for the patient to explain. In obvious cases, trauma is accompanied (or followed within a few minutes) by rapid, severe hearing loss, loud roaring tinnitus, and severe rotational vertigo. Vertigo is often incapacitating and accompanied by visceral autonomic symptoms (sweating, pallor, nausea, vomiting). Even cursory examination will demonstrate marked instability and nystagmus. Audiometric evaluation reveals sensorineural hearing loss. Platform posturography will confirm disequilibrium with a vestibular pattern and the platform fistula test will be positive. Vertigo and, to a lesser degree, tinnitus and hearing loss are sometimes exacerbated by straining or Valsalva maneuver. Repair of the fistula by grafting the round and oval windows often produces immediate and complete elimination of vertigo. Infrequently, hearing will be improved as well.

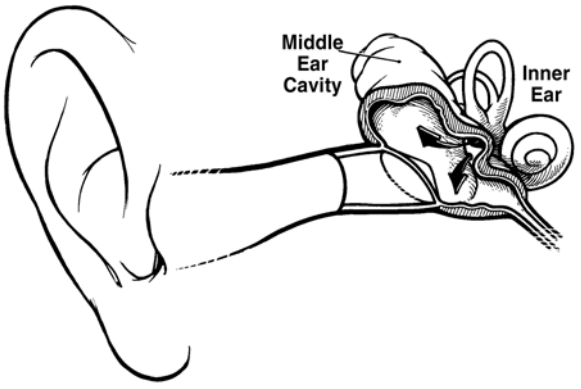


FIGURE 5.7
Diagrammatic representation of a perilymph fistula. Perilymph can escape from either the oval window (upper arrow) or round window (lower arrow). Since the amount of fluid is extraordinarily small, the patient has no subjective sense of fluid within his middle ear space. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

Unfortunately, many perilymph fistulas do not manifest themselves in this straightforward manner.[7,14] Onset of symptoms may be delayed for several days or the acute phase may be masked by more serious injuries in other areas. Rotational vertigo may be entirely absent and disequilibrium may be mild, vague, and episodic. Hearing loss, tinnitus, and aural fullness may come and go unpredictably. Such protean and elusive symptomatology has lead to controversy. Opinions differ widely among credible otologists about how frequently perilymph fistulas occur, what types of injuries and forces produce them, and what sorts of ancillary symptoms (headache, concentration defects, phobias, and impaired mentation) accompany them. Although one might hope that middle ear exploration could resolve this controversy by establishing the actual frequency with which perilymph fistulas occur, it has not. The average human inner ear contains only 0.07 cc (70 μl) of perilymph and, therefore, even relatively rapid leaks will, in absolute terms, be quite small. Even with magnification, leaks involving only 5 to 10% of the perilymph will be difficult to see in an operative field where local anesthetics have been injected, irrigating fluids have been used, and where there is even minimal bleeding.

Because no reliable method of proving the absence or presence of perilymph fistula is yet available, reliable incidence and prevalence figures do not exist. At the present time, considerable effort at the national level is being expended to clarify the perilymph fistula controversy, but at this time, it remains unresolved.

Posttraumatic Ménière's Syndrome

In 1861, Prosper Ménière described a syndrome of episodic rotational vertigo accompanied by tinnitus and fluctuating neurosensory hearing loss. A sense of aural fullness or pressure is now also considered an important part of this syndrome. Attacks generally last 15 to 100 minutes and are followed by several hours of asthenia, nausea, and disequilibrium. When no cause (i.e., syphilis, acoustic tumor, or viral labyrinthitis) can be established, the syndrome is idiopathic and may be termed Ménière's Disease. Histopathologic evidence demonstrates that this syndrome arises as a consequence of excess amounts of endolymph which produce distension of the endolymphatic space. Both Ménière's syndrome and perilymph fistula share a common factor — the ratio of endolymph to perilymph is altered in the same direction (relative excess of endolymph compared to perilymph). In Ménière's, it results from excess endolymph, whereas in perilymph fistula, it results from loss of perilymph. While these conditions are clinically separable in their typical or classical presentations, they are indistinguishable in their atypical manifestations. Ménière's disease may, like perilymph fistula, manifest as a highly variable and changing combination of aural fullness, disequilibrium, hearing loss, and tinnitus. No physical finding, laboratory test, or radiographic or audiometric study can definitively separate these two conditions. Although uncommon, the development of Ménière's syndrome after traumatic brain injury (posttraumatic Ménière's syndrome) is well established and not rare.[15] It usually appears weeks or months (perhaps even years) after the original injury. Diagnosis depends on history, documentation of fluctuating neurosensory hearing loss, positive electrocochleography, and/or positive dehydration audiometry and electrocochleography.

Treatment for Ménière's syndrome, whether idiopathic or posttraumatic, should begin with attempted medical management. Surgical intervention should be limited to patients who fail aggressive medical therapy. Rigorous adherence to a salt restricted diet (2000 mg daily) and diuretic therapy are the mainstays of medical treatment. A vestibular suppressant should be added during symptomatic periods. If aggressive medical management is inadequate or poorly tolerated, then consideration should be given to one of the many surgical options available.

Benign Paroxysmal Positional Vertigo

Traumatic injury may dislodge an otoconia from the macula of the saccule or utricle. Two hypotheses have been developed to explain how dislodged otoconia can produce the clinical phenomenon of benign paroxysmal positional vertigo (BPPV). The *cupulolithiasis* theory proposes that these loose otoconia migrate and become attached to the ampulla of the semicircular canal. The additional mass added to the ampulla makes it gravity sensitive. Consequently, cupular deflection occurs with a variety of head movements and not only as a result of angular acceleration.

The *canalithiasis* theory proposes that otoconia are floating freely in the endolymphatic fluid of the vestibule. Provocative positioning results in displacement of these mobile otoconia into the fluid of the semicircular canal, producing unilateral movement of labyrinthine fluid, cupular deflection, and a sensation of movement.[16] BPPV may arise from a combination of these two mechanisms.

BPPV is a common cause of vertigo. Many cases are idiopathic, but this entity is often seen after upper respiratory infection, trauma, Ménière's disease, surgery, otologic infection, and in combination with other inner ear disorders.

BPPV classically presents with intense, brief, rotary vertigo, which occurs when rolling from side to side while in the supine position (such as in bed). The rotary sensation itself typically lasts for about 30 seconds, but patients frequently describe a second component consisting of persistent dysequilibrium. BPPV will cause vertigo and nystagmus with five characteristic features: (1) latency of onset, usually 2 to 6 seconds, (2) short duration, usually less than 30 seconds, (3) reversibility, (4) fatigability, and (5) direction. The nystagmus is typically rotational in nature with the fast phase directed toward the undermost side. Many patients experience mild vertigo and nystagmus to the opposite side when brought back to the upright position; this is referred to as *reversibility*.

BPPV constitutes a specific pathophysiologic entity with characteristic ENG findings and should not be confused with benign positional vertigo from other causes.

BPPV can be diagnosed during physical examination if the "Dix–Hallpike" maneuver is performed. For Dix–Hallpike testing, the patient starts in the sitting position. He is then rapidly moved into a supine position with head turned to the side.[12] When this maneuver is performed to the affected side, vertigo and nystagmus will be induced after a latency of a few seconds and will continue for 15 to 40 seconds, after which it will disappear. The nystagmus is away from the undermost ear. If the patient is returned rapidly to the sitting position, the nystagmus may reappear (again, with a brief latency), beating this time in the opposite direction. The response fatigues quickly and repeated Dix–Hallpike maneuvers will eliminate the phenomenon within a few repetitions at most. ENG evaluation is always helpful and frequently essential in clarifying and documenting these classic characteristics.

Most cases of BPPV are self-limited, resolving over a 2- to 6-month period. Published reports of treatment outcomes focus on patients with symptoms persisting beyond 6 months. There are three different bedside treatments for BPPV: the canalith repositioning procedure (CRP), the liberatory maneuver, and Brandt–Daroff habituation exercises.[17–19] Each has specific indications, but CRP is the most widely used because it is well tolerated by patients and is easy to perform.

CRP is based on the theory of canalithiasis and is effective for either superior or posterior semicircular canal involvement. This treatment involves a five-position cycle in which the patient is taken through a series of head positions to move the head around the debris (Figure 5.8). This is repeated until no nystagmus is observed during the last cycle. The patient is first moved into the Dix–Hallpike position with the head rotated 45 degrees toward the side of the affected ear. The head is then slowly rotated (while extended) toward the unaffected side, kept in that position briefly, and then the head and body are rotated

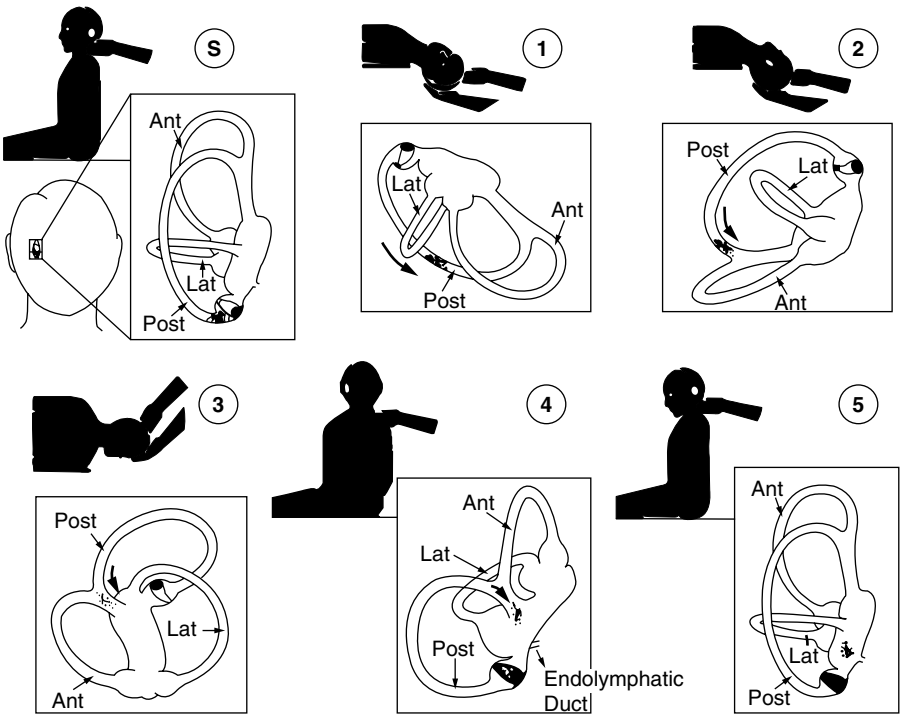


FIGURE 5.8
Positions for canal repositioning, targeting left posterior semicircular canal (PSC). S (Start) — Patient is seated, operator behind. (1) Head is placed over the end of the table, 45 degrees to the left (canaliths gravitate to center of PSC). (2) While head is kept tilted downward, it is rotated to 45 degrees right (canaliths reach common crus). (3) Head and body are rotated until facing downward 135 degrees from supine position (canaliths traverse common crus). (4) While head is kept turned right, patient is brought to sitting position (canaliths enter utricle). (5) Head is turned forward, chin down 20 degrees. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

together into a side-lying position with the head turned 45 degrees down. While the head is kept turned, the patient is brought to a sitting position. Lastly, the head is turned forward, with chin down 20 degrees. At each position, the operator should pause until induced nystagmus approaches termination. Reversal of nystagmus during the second portion of the maneuver suggests that debris is moving back toward the cupula and has been identified as a factor predicting poor response by Parnes et al.[20] Most authors recommend a soft cervical collar and neutral head position for at least 48 hours postmaneuver.

The liberatory maneuver is a more aggressive repositioning sequence where the patient begins by lying on the involved side with the head turned 45 degrees up. The patient is rapidly rotated through the sitting position to lie on the contralateral side with the head turned 45 degrees down. This is an awkward manipulation, especially in the elderly population, and has fallen out of favor.

Brandt–Daroff exercises require the patient to move repeatedly into the provoking side-lying position several times per day. Recovery is reported in approximately 95% of patients but often requires several weeks.[16] Patient compliance issues make CRP preferable to the Brandt–Daroff exercises.

In general, approximately 80 to 85% of patients with BPPV will experience remission of vertigo with just one episode of repositioning.[16,18] Many patients with BPPV, however, have persistent balance problems lasting several weeks after resolution of the episodic

vertigo. An exercise program directed by a physical therapist is recommended for those patients.

The role of medications in the treatment of BPPV is limited to vestibular suppressants and antiemetics. Benzodiazepines (such as diazepam and alprazolam) are effective vestibular suppressants but have sedative side effects and must, therefore, be used with caution. Promethazine is a commonly used antiemetic which is available in oral and intravenous formulations but may also cause sedation. Cases refractory to repositioning maneuvers have been successfully treated surgically with posterior semicircular canal occlusion.[20] The first published reports of posterior semicircular canal occlusion were in 1990 by Drs. Parnes and McClure.[21] This procedure is based on the theory of cupular deflection and endolymph displacement. The goal of the technique is to occlude the semicircular canal, thereby creating a closed, fluid-filled space and causing the cupula to become fixed. In this procedure, a mastoidectomy is performed and the posterior semicircular canal is punctured. Various materials, including bone dust, bone wax, fibrin glue, and fascia, may then be used to occlude the semicircular canal.

Labyrinthectomy, vestibular neurectomy, and singular neurectomy are further surgical options that have largely been replaced by posterior semicircular canal occlusion.

Labyrinthine Concussion

Labyrinthine concussion is an imprecise term which subsumes a variety of symptoms, complaints, and, possibly, etiologies. Generally, it is assumed that the injury arises from bleeding within the labyrinthine capsule, but mechanical membrane disruption caused by acceleration and deceleration effects may also occur.[13,14] Diagnosis depends on detecting objective vestibular abnormalities in the vestibular laboratory. ENG testing is the most frequently helpful diagnostic test and pathologic positional nystagmus is the most common abnormality. Unilateral weakness on ENG testing occurs less commonly but is compelling when identified. Platform posturography showing reduced function with a vestibular pattern is confirmatory. Sinusoidal harmonic acceleration (SHA) may show asymmetry with or without phase lag depending on the extent of the injury and the degree of compensation.

Symptoms may include vertigo and disequilibrium, with or without hearing loss, tinnitus, or aural fullness. Recovery depends upon the extent of the injury and the presence or absence of associated abnormalities. Often, recovery is complete within a few weeks. When recovery is slow, vestibular rehabilitation can hasten its arrival and often improve the final outcome. If unilateral weakness can be demonstrated on ENG, consideration should be given to surgical ablation of the injured labyrinthine end organ.

Posttraumatic Vascular Loop

From time to time, head injury may displace one of the posterior fossa intracranial vessels and cause it to come to rest against the eighth cranial nerve in the cerebello-pontine angle. Generally, the anterior inferior cerebellar artery or one of its branches is involved. Vascular compression of the cochleovestibular nerve produces a characteristic syndrome. The afflicted individual is overwhelmed by an almost constant, severe positional vertigo often associated with visceral symptoms. While actual severity may vary over a fairly wide range, the patient is frequently not able to function. Motion usually results in marked exacerbation of symptoms. Unilateral tinnitus and hearing loss may accompany the vestibular symptoms but are frequently absent. Diagnosis depends on the presence of typical abnormalities seen during auditory brainstem response audiometry (ABR). Specifically, changes in interpeak latency suggestive of cochlear-vestibular nerve pathology will be

noted. Radiographic demonstration of the juxtaposition of the nerve to the vessel is helpful but not essential. When present, surgical decompression is curative.

Cervical Vertigo

Since cervical position sense receptors and muscle stretch receptors provide information to the central nervous system about the orientation of the head in space, musculoskeletal abnormalities of the neck and cervical spine may result in "dizzy" sensations.[22–25] Most commonly, myofascial pain dysfunction syndromes involving either the lateral or posterior cervical muscles are responsible. Since cervical proprioception is not the most important sensory modality subserving equilibrium, disorders of the cervical musculoskeletal system usually produce symptomatology that is relatively mild. Patients typically complain of a vague disquiet and uneasiness about their balance. They resist free movement and frequently use support structures (wall, handrails, etc.). "Spinning" is not experienced and falls do not, in fact, occur, although the patient is ever fearful that he *will* fall. Frequent headaches occur commonly. Physical examination will generally detect muscle spasms and tenderness. Tenderness is frequently focal and of the "trigger point" variety.[26] Common focal points are the spinous process of the seventh cervical vertebrae and along the posterior nuchal line where the posterior cervical muscles insert into the periosteum of the skull or at the insertion of the sternocleidomastoid and splenius capitis muscles into the mastoid tip. Aggressive physical therapy, exercises, and antiinflammatory medications must be combined regularly for several weeks in order to achieve relief.

Central Vertigo

Dizziness and disequilibrium originating within the nervous system and not from the labyrinth or eighth nerve is a relatively common component of posttraumatic head injury. Vertigo which arises within the CNS itself is accompanied more often by other cranial neuropathies and neurologic deficits than is peripheral vertigo. Dysarthria, dysphagia, oculomotor deficits, numbness and tingling in the extremities, and focal motor weakness are common.[13,22,27–31] A significant number of these individuals have been severely injured so that they have been in prolonged coma. Many have significant long tract signs.

Involvement of the cerebellum produces "dizziness" and disequilibrium only in the standing position and when attempting to walk. Subjective rotational vertigo is notably absent. Ambulation, however, may be severely impaired and is no better with eyes open than with eyes closed. Nystagmus will also be as vigorous with eyes open as with eyes closed. Indeed, nystagmus may be so pronounced as to be apparent from several feet away but, when queried, the patient will often deny subjective vertigo.

Frequently, disorders of balance are recognized relatively late in the rehabilitation of these individuals. Early in treatment, other injuries are more apparent and need to be addressed more urgently. As consciousness returns, mentation improves, motor weakness resolves, and efforts can be directed toward beginning ambulation and resuming normal activities. It may be when such retraining is begun and proceeds poorly that balance disturbance is first recognized.

The pathophysiology of central balance disturbance remains unclear. Windle et al. have demonstrated punctate hemorrhage and degeneration within the vestibular nuclei of head-injured guinea pigs.[13] Much evidence of central involvement comes from ENG evaluation. Many investigators have shown a high incidence of central ENG findings in the head-injured population. Tuohimaa has argued cogently that ENG findings imply that vestibular dysfunction may be the result of impaired cortical inhibition and not solely the result of

disruption of brainstem nuclei or pathways.[6] Subjective vertigo from stimulation or injury to the temporal cortical projections of the vestibular system is uncommon but may occur as a component of a seizure disorder.

There are no medical or surgical methods for managing central vestibular injury. Indeed, the presence of a central component is frequently cited as a cause for the reduced effectiveness of eighth nerve section in head-injury patients even when a clear-cut peripheral component is present. Vestibular rehabilitation will continue to be the mainstay of treatment for patients who have a significant central component, but medical and surgical treatment may be of significant ancillary assistance when there is a concomitant peripheral vestibular injury.

Clinical Evaluation

History

An adequate history is frequently the key to both diagnosis and management of vestibular disorders. This can be a difficult undertaking in the individual recovering from brain injury. However, every effort should be made to elicit as much information as possible even though this may be taxing to the evaluator.

Patient's History

Questions about premorbid leisure activities can give important information regarding physical impairment, including vestibular injury. Did the patient return to sports and leisure after his injury and, if not, why? Are there any close relatives or friends able to substantiate this information?

Does the patient's direct family report any changes regarding the patient's participation in the family circle? Specifically, are there complaints of balance (i.e., in darkness or with leisure activities)? Has the patient become less physically active at all? Are there any complaints of visual or auditory overstimulation that can be associated with a vestibular lesion?

When balance dysfunction is present, it should first be established whether or not the patient suffers from a subjective sense of vertigo or disequilibrium. Individuals with central dysfunction and cerebellar disorders, although clearly impaired by balance dysfunction, may have no associated sense of disequilibrium or vertigo. When present, such sensations are frequently referred to as feeling "dizzy." It is astonishing how frequently this term may remain unclarified and ill-defined even though treatment persists for months. It is critical to clarify, in as much detail as possible, what the individual means by the term *dizzy*. Often, the patient will protest that he is unable to further elucidate the experience, but, if pressed, this is almost never the case and important information can almost always be obtained with perseverance. *Vertigo* is a technical term which refers to the illusion of movement when no movement is in fact present. The most obvious example of such a sensation is the sense of rotation when one is still. However, a sense that one is falling when one is not falling, or the sense that one is "veering" when one is not, also constitute an illusion of movement when none is present. These sensations are appropriately subsumed under the term *vertigo*. It will turn out that a goodly number of patients do not have an illusion of movement even when they use the term *dizzy*. Such patients may be referring to a sense of lightheadedness, giddiness, a vague feeling of nausea, a sense that they are walking on air, a feeling of being "closed in," of weakness, disorientation, or a general sense of "confusion."

After clarifying the character of the dizzy sensation, it is crucial to determine if the sensation is invariably present or present only episodically. If present episodically, how frequently and how long it persists will be important data to gather. Whether or not the symptoms are always of the same severity needs to be ascertained and, if the severity is variable, a search for exacerbating or remitting factors needs to be made. The relationship of the symptoms to movement is crucial. Many patients either have their symptoms only in certain head or body positions or the act of moving into certain positions precipitates symptomatic episodes. The patient should be questioned as to whether there is any relationship between his symptoms and diet, exercise, or situational stress. One should determine if the symptoms are reliably reproduced in a given place. Individuals suffering from anxiety disorders, for example, will frequently have their symptoms very reliably "place associated." They may experience symptoms in open places, or closed places, or in church, or in the car. When symptoms are closely linked to a specific place or situation, organic vestibular dysfunction is improbable. On the other hand, certain types of visual stimuli will reliably produce symptoms in patients with vestibular disease. Complex geometric patterns and rapid movement in the peripheral visual field are two such common stimuli. A surprising number of patients will complain of disequilibrium when shopping in the grocery store because of the rapid movement of the high, grocery laden shelves in their peripheral visual field as they move down the aisle.

A search for associated symptoms should be made. The patient must be carefully queried as to the presence or absence of dysarthria, dysphagia, visual change, numbness or tingling in the extremities or around the mouth, and focal motor weakness. He should be questioned about the presence or absence of headache and syncopal episodes.

Physical Examination

A complete neurotologic examination must be performed. It should start with close examination of the external auditory canals and tympanic membranes. Such an examination will not only determine the stigmata of temporal bone fracture or serious head injury but also the more mundane findings of middle ear effusion, cholesteatoma, or tympanic membrane perforation. It must always be remembered that the traumatically brain-injured individual is not immune to the commonplace afflictions of everyday life. The pneumatic otoscope should be utilized in order to assure adequate tympanic membrane mobility. A complete cranial nerve examination is mandatory. Eye movement abnormalities should be noted prominently because they will affect interpretation of the electronystagmogram. Similarly, evaluation of the facial nerve must be compulsive because it travels so closely with the vestibular nerve that it is an invaluable localizing sign. Evaluation of hearing is compelling for the same reasons and should include Rinne and Weber tests as well as a complete audiometric battery. Abnormalities of the lower cranial nerves, including swallowing dysfunction and disorders of voice, may indicate significant brainstem injury.

Coordination is evaluated using standard tests of cerebellar function such as the finger-tip-to-nose test, test for dysdiadochokinesia and rebound phenomenon which are performed for the upper extremities, and the heel–shin maneuver for the lower extremities.

Cerebellar ataxia in gait comprises a widened base of support, an irregular step length, and weaving from side to side. Vestibular dysfunction can also result in an ataxic gait quite similar to the one described above but does not result in positive cerebellar tests. Gait and station should be evaluated using the Romberg test and tandem gait, as well as heel and toe walking. A severely disabled individual might not be able to perform some of these tests and they will have to be omitted in such cases.

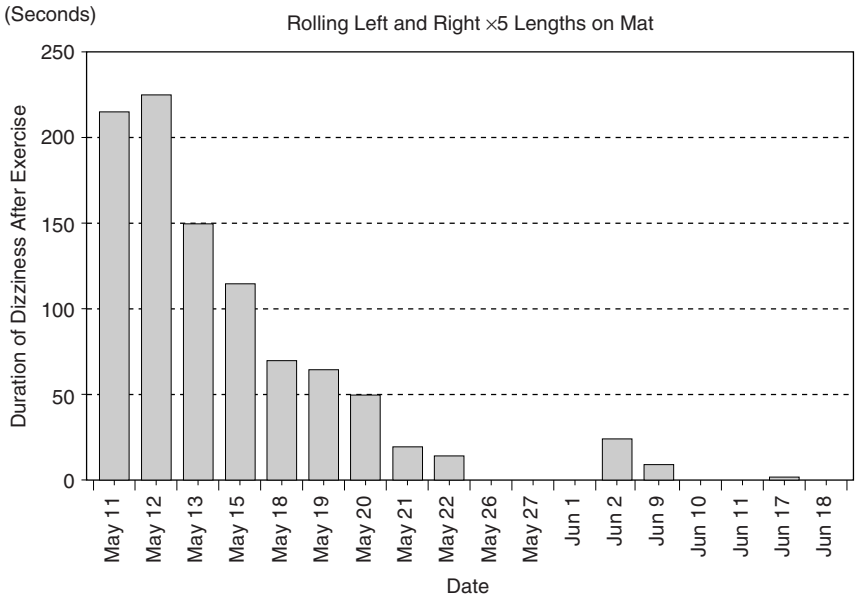


FIGURE 5.9
Mat rolling is an effective general technique for desensitization. The patient is asked to roll back and forth along a mat. The duration of dizziness after exercise is then measured. This patient's graph shows progressive improvement over a period of 2 weeks. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

Clinical Testing

Clinical evaluation of head-injury patients suspected of vestibular dysfunction will have to go beyond the administration of a few clinical tests as, in addition to the suspected vestibular dysfunction, other symptoms of CNS injury might compromise overall physical functioning. Also, clinical vestibular tests are not pathognomonic for specific lesions but only indicators. Additionally, the vestibular patient will not always be able to clearly discuss/communicate the changes that are a result of the vestibular injury.

The evaluation of a brain-injured individual comprises, next to taking the patient's history, a number of standard tests of range of motion, muscle strength, and cardiorespiratory conditioning. In addition, we evaluate coordination, weightbearing, weight-shift with rolling, quadruped crawling, and crawling on the knees, balance in standing, during ambulation, and more complex balance activities, reflexes, and sensation.

Preambulatory Activities

Rolling on a 10-foot long, floor-placed exercise mat for a number of repetitions (usually five times left and right) regularly provokes dizziness to the extent that clients spontaneously stop the activity with complaints of dizziness and/or nausea (Figure 5.9).

This response can be seen as vestibular sensitivity toward angular repetitious movement without lower extremity weightbearing. Such sensitivity can be a result of general deconditioning or be the first clinical sign of vestibular pathology.

Balance

A total of 14 balance tests are used to evaluate the spectrum from simple static balance to complex dynamic balance (Table 5.1A and Table 5.1B). Balance can be affected by a

TABLE 5.1A

Clinical Balance Testing — Test and Score Sheet

	Attempts	Score
Static and Dynamic Balance Test List		
Static Balance		
1. Romberg, eyes open	1 2 3 4 5	_____ sec
2. Romberg, eyes closed	1 2 3 4 5	_____ sec
3. One foot balance left, eyes open	1 2 3 4 5	_____ sec
4. One foot balance right, eyes open	1 2 3 4 5	_____ sec
5. Sharpened Romberg, eyes open, left foot posterior	1 2 3 4 5	_____ sec
6. Sharpened Romberg, eyes open, right foot posterior	1 2 3 4 5	_____ sec
Dynamic Balance		
7. Heel–toe ambulation, 50 ft, eyes open, straight line	(errors)	_____ ft
8. Balance beam forward, 50 ft, eyes open	(errors)	_____ ft
9. Balance beam backward, 50 ft, eyes open	(errors)	_____ ft
10. Hop both feet, times 10, maintain one rhythm	1 2 3 4 5	_____ reps
11. Hop left foot only, times 10, maintain one rhythm	1 2 3 4 5	_____ reps
12. Hop right foot only, times 10, maintain one rhythm	1 2 3 4 5	_____ reps
13. Jump rope, times 10, maintain one rhythm, jump both feet	1 2 3 4 5	_____ reps
14. Jump alternately on 10 inch elevation, maintain one rhythm, times 20	1 2 3 4 5	_____ sec

Notes: _____

Source: From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.

vestibular deficit, but also by generalized weakness, dyscoordination, spasticity, rigidity, decreased vision, or lack of sensation.

A vestibular deficit can be expected when any of the following indicators of vestibular involvement are present:

- Difficulty with any balance task that either limits or excludes vision. Example of the first is walking backwards on a balance beam; of the latter, the classic Romberg test with eyes closed. Vestibular patients rely heavily on visual input to compensate for the loss of (reliable) vestibular information. When this is denied in a testing situation, they score poorly.
- Difficulty with postural adjustment with static balance tests such as one foot balance or the sharpened Romberg test. The tests require a period of 30 seconds for a normal score. Normal subjects can adjust smoothly to balance disturbance. Vestibular patients can perceive gravitational effects sometimes, but not accurately, and therefore overcorrect, ultimately leading to a loss of balance or excessive weaving.
- Difficulty with complex, repetitious dynamic balance tasks. An example is hopping 10 times on both feet. Vestibular patients have difficulty with this test because of poor gaze stabilization or because they are unable to make the quick postural adjustment necessary to maintain balance.

Clinical Vestibular Testing

The vestibular system is generally tested in two steps. The vestibulospinal and cerebellar systems are examined by testing balance, posture, coordination, and fine motor skills as

TABLE 5.1B

Clinical Balance Testing — Explanation of Test Procedure

How the Balance Test is Performed

Static Balance

Tests 1–6: Client is tested barefoot on a wooden, circular (25 in. diameter) surface and needs to stay in one place. Five attempts are given; only the best effort is entered. A normal score is 30 sec.

Tests 1–2: A comfortable base of support, chosen by client, on the support surface.

Dynamic Balance

Tests 7–9: Client is instructed to perform each of the tasks at leisurely pace, barefoot.

Test 7: Mistakes are counted and entered. A mistake is stepping out of the straight line or not placing the feet heel to toe.

Tests 8–9: Client is instructed to walk forward (8)/backward (9) the 4 in. wide beam. Heel-to-toe placement is not necessary. A mistake is when client steps off the beam. Total number of mistakes is entered. We use a 10 ft long, 4 in. wide beam. Client travels the beam × 5 forward/backward.

Tests 10–14: These are the most complex of this test. Tests 10–13 are performed on the floor. Client is allowed to hop "around," as long as a sequence of 10 repetitions is maintained. Five attempts are given, with the best result entered.

Test 14: One foot is placed on the floor, the other on a 10 in. high support surface (e.g., first step of exercise stairs of physical therapy department). Client is instructed to alternate this foot placement while jumping straight up, again for a sequence of 10 smooth repetitions.

This test moves from simple to complex balance tasks. The more complex balance tasks are sometimes too strenuous for deconditioned clients. The therapist needs to be attentive to this and can stop the test when necessary. An explanation can be entered at the bottom of the score card in the "Notes" section.

Testing is repeated after 1 month, following therapy. Therapy excludes any of the tests used for evaluation to avoid "teaching the test."

Testing is performed in a quiet corner of the gym. Movement of others should be excluded from the visual field of the client, as it might interfere with performance.

Source: From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.

discussed previously. The vestibulo-ocular system is examined by observing ocular motility and assessing the vestibulo-ocular reflex (VOR). The vestibulo-ocular system is evaluated separately from other parts of the vestibular system.

The oculomotor examination includes an assessment of ocular alignment and range of motion. Misalignment may result in complaints of diplopia, vertigo, or oscillopsia. Subtle misalignments may be detected by alternately covering each eye while having the patient fixate on a distant object. If movement is noted in one eye after covering the other, an ocular misalignment is present. Misalignment, which is variable in different fields of gaze, may be due to an abnormality of an extraocular muscle. Obvious misalignment in a patient with no complaints likely represents long-standing strabismus. Vertical misalignment is associated with brainstem or cerebellar lesions. Three different types of eye movement should be assessed: vergence, saccades, and smooth pursuit. Vergence movements can be elicited by asking the patient to follow a finger toward and away from the nose; these movements are normally slow and smooth. Abnormal oscillation is suggestive of a functional disorder. Saccades are evaluated by having the patient fixate alternately on two stationary targets. Velocity, accuracy, and initiation time of the saccades should be assessed, and any abnormality points to a central etiology. Smooth pursuit movements are assessed by having the patient track a target, such as a pen, without head movement. Asymmetry in horizontal smooth pursuit movement is suggestive of central nervous system pathology. Mild impairment, however, may be seen in the elderly or as a side effect of medications. Only very gross abnormalities can be detected on physical examination. Subtle dysfunction, which is much more common, can only be detected by electro-oculography.

Clinical vestibular testing can be divided into two categories, namely functional testing and provocation of specific deficits. Provocation of specific deficits can be done if the patient's history indicates a specific lesion. A good example is the Dix–Hallpike maneuver done when a patient's complaints are suspect for benign paroxysmal positional vertigo. Routinely, we perform several functional vestibular tests. If any is positive, a vestibular lesion should be suspected.[32,33]

Several bedside tests may be used to evaluate the VOR. These are based on a unilateral reduction of the VOR causing motion of the visual surround during head movement (oscillopsia), primarily with movements toward the affected ear. A bilateral reduction results in oscillopsia with all head movements.

The head thrust test assesses the Doll's eye reflex and is performed by rapidly rotating the patient's head to midline from an initial position 30 degrees off midline. This is performed with the patient maintaining fixation on a target and is considered positive if the eyes have to make a saccade to refixate.

Testing visual acuity during head movement is another method of assessing the VOR. This can be done by rotating the patient's head through a 60-degree arc at a frequency of one to two cycles per second while testing visual acuity with a Snellen chart. Normal individuals lose one line of acuity. Patients with a unilateral loss of vestibular function may lose two to four lines and those with bilateral loss may lose five to six lines.

Post–head shake nystagmus may be elicited by passively or actively rotating the patient's head at a high frequency for 10 to 20 seconds and then stopping abruptly. Patients with severe unilateral vestibular loss will have nystagmus with the initial slow phase directed toward the affected side and a subsequent reversal phase toward the unaffected side. Bilateral vestibular hypofunction and acute unilateral hypofunction do not produce nystagmus after head shaking.

Tests for positional and positioning nystagmus help to separate peripheral from central pathology and often localize peripheral pathology. Positional nystagmus is assessed by placing the patient in each of the upright, supine, right-ear-down, and left-ear-down positions for at least 30 seconds and observing for nystagmus. Nystagmus that lasts longer than 1 minute and changes direction typically indicates central pathology. Positional nystagmus that lasts longer than 1 minute but does not change direction can be seen in peripheral or central disorders. Transitory nystagmus that lasts less than 1 minute is usually described as positioning nystagmus and indicates peripheral pathology (usually benign paroxysmal positional vertigo).

The Dix–Hallpike maneuver is the most commonly performed positioning test and is designed to elicit nystagmus during dynamic head movement. The test is performed by starting with the patient in the seated upright position, head turned 30 degrees toward the examiner. The patient's head is held between the examiner's hands and the patient is rapidly moved into the supine position, with head extended 30 degrees over the edge of the table. The patient's eyes are observed for nystagmus as this position is held for at least 30 seconds before returning to the upright position. This maneuver is then repeated for the opposite ear, with the head turned in the opposite direction. Observed nystagmus is generally horizontal–rotary, beating toward the side of the lesion.

A vestibular lesion may be classified as peripheral or central based on the nystagmus elicited during positioning (Table 5.2). In general, peripheral nystagmus has a latency period, short duration, and fatigability. Central nystagmus is often vertical or direction changing and lacks fixation suppression.

None of these tests is pathognomonic for a particular type of vestibular lesion, but the entire evaluation can give strong indicators of vestibular dysfunction that can be clarified by an in-depth laboratory evaluation. A vestibular evaluation by an otolaryngologist specializing in vestibular dysfunction is often requested.

TABLE 5.2

Charasteristics of Central and Peripheral Positioning Nystagmus

	Central	Peripheral
Latency	None	2–15 sec
Duration	30–120 sec	5–30 sec
Fatigability	+/–	+
Vertigo	Absent	Present
Fixation	No suppression	Suppression
Direction	Vertical, horizontal	Horizontal, rotary
Characteristic	Direction changing	Direction fixed

Unterberger test: The patient is asked to make 50 steps in place with the eyes closed. A positive test is turning to either side of more than 45 degrees. The patient will turn to the side of the lesion.[34]

Babinski–Weil test: The patient is asked to walk five steps forward and backward five times with the eyes closed, maintaining an imaginary straight line. A positive outcome is seen when the patient constantly drifts to the affected side walking forward and away from that side walking backward.

Unterberger and Babinski–Weil tests are done while the patient listens to music through headphones to prevent spatial orientation through environmental sounds.

None of these tests are pathognomonic for a type of vestibular lesion or localization of a lesion, but the entire evaluation can give strong indicators necessitating further laboratory evaluation. A vestibular evaluation performed by a neurotologist or otolaryngologist specializing in vestibular dysfunction should be added to these clinical evaluation tools.

Laboratory Evaluation

Auditory Testing

Because the vestibular system and auditory system are so closely interrelated at the level of the labyrinth, the eighth cranial nerve, and within the brainstem, complete audiometric testing is essential in the evaluation of any patient with balance disturbance. This should include a formal audiogram which tests pure tone reception at octave intervals from 125 Hz (cycles per second) to 8000 Hz. Both air conduction and bone conduction should be tested. Speech discrimination scores should be obtained and the speech reception threshold measured. If inconsistent or ambiguous information is developed within the pure tone audiogram or speech testing, then this information should be confirmed or expanded using auditory brainstem response audiometry (ABR).[35] The initial pure tone evaluation should be accompanied by immittance testing which measures not only tympanic membrane compliance but also assists in identification of ossicular disarticulation and assesses the stapedius reflex at several frequencies. Stapedius reflex testing is sensitive to a variety of different sorts of retrocochlear pathology. Abnormalities of stapedius reflex testing, if not explained by known difficulties, should be considered indications for further evaluation with auditory brainstem response audiometry or radiographic imaging. Based on the history and the pure tone audiogram, further evaluation with electrocochleography, vestibular testing, middle latency response evaluation, or central auditory testing can be considered.[29,36,37] The results of auditory testing should be consistent with the results of tuning fork tests as determined in the physical examination. If there are inconsistencies between these test results, these inconsistencies need to be resolved. This subject is further discussed in Chapter 8.

The Electronystagmogram

Nystagmus is the only sign on physical examination uniquely linked to the vestibular system. Therefore, the electronystagmogram plays a crucial and pivotal role in evaluating the vestibular system and offers a number of advantages. First and foremost, it is capable of detecting nystagmus with eyes closed. The vast majority of peripheral nystagmus is effectively suppressed by visual fixation and will not be apparent to the examiner with the patient's eyes open. Frenzel lenses are thick 20-diopter lenses used to assist in the detection of nystagmus on physical examination. These lenses make the detection of pathologically significant nystagmus easier in two ways. First, they prevent visual fixation by the patient since they make it virtually impossible to see anything but light. Second, they magnify the cornea and iris when the examiner views the patient's globe through the Frenzel glasses. Frenzel lenses will permit the detection of clinically significant nystagmus which would be otherwise inapparent. But even with Frenzel lenses, about half of pathologically significant nystagmus will be missed.[38,39]

The electronystagmogram is capable of detecting subtle abnormalities of both volitional and reflex eye movement controlled at the brainstem and even higher levels. These abnormalities cannot be detected by any other method. Their detection can be the most significant and easily documented evidence for brainstem dysfunction.

An additional advantage to electronystagmography is the ability of this testing method to test each labyrinthine end-organ separately. No other clinical test of vestibular function permits unequivocal isolation of one labyrinth from its contralateral partner.

Electronystagmography produces a permanent objective record of labyrinthine function. Such a record can be reviewed months or years after it was made and compared with new tracings to determine the evolution of a pathological process or to document improvement.

There are some disadvantages to ENG. The stimulus is not physiologic, and stimulus intensity is subject to a variety of variables only partially under the examiner's control. These include the shape and nature of the external auditory canal, the size of the tympanic cavity, and the thickness and position of the tympanic membrane. The test requires a compulsive and meticulous examiner who is willing to recalibrate his equipment before every examination, remove any cerumen impeding the flow of air/water into the canal, and assure good contact between the electrodes and the skin. A first-rate ENG technician will also interact with the patient in a tactful, compassionate, and sympathetic fashion. Not only is this an intrinsically desirable end in itself, but it will also encourage maximum effort from the patient and procure the most consistent and reliable tracings.

Electronystagmography requires relatively intact extraocular muscle function. Thus, individuals with certain intrinsic abnormalities of the extraocular muscles or paresis of Cranial Nerves III, IV, or VI may generate tracings that are uninterpretable.

Electronystagmography is perhaps more properly termed *electro-oculography* (EOG). Although generally used to measure and detect nystagmus in the evaluation of individuals with vertigo, the test actually measures the movement of the globe within the orbit. The positively charged cornea and the negatively charged retina together create a dipole whose movement can be detected when electrodes are placed around the orbits. The testing apparatus is calibrated so that eye deviations to the right produce an upward deflection and eye deviations to the left produce a downward deviation of the pen. In the vertical channel, upward eye movements create an upward deviation of the pen and downward movements generate a downward movement of the pen. The system is calibrated so that each degree of eye movement produces a 1 mm deflection of the pen. The system needs to be recalibrated before each test.

The complete electronystagmogram consists of a set of seven different subtests: (1) Saccade Test, (2) Gaze Test, (3) Tracking Test, (4) Optokinetic Test, (5) Positional Test, (6) Hallpike Maneuver, and (7) Bithermal Caloric Test.

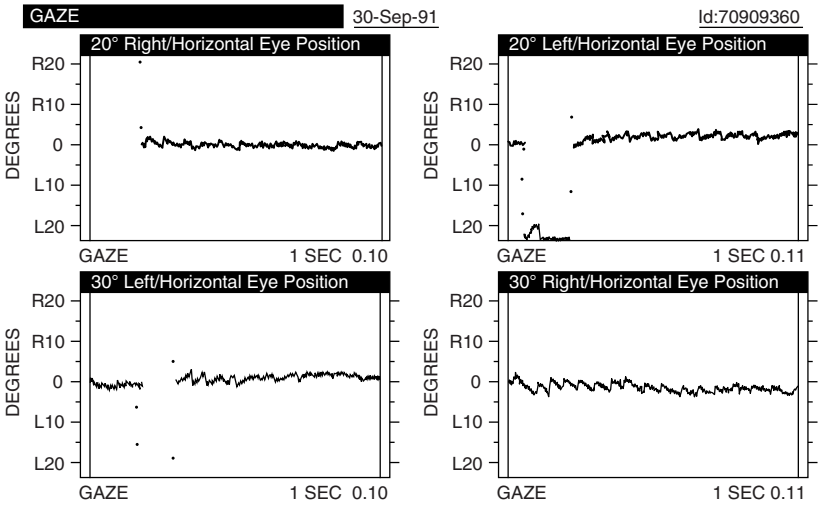


FIGURE 5.10
Gaze nystagmus is present in all gaze positions. It is most obvious in the 30 degree left and right deviations (lower tracings) than in the upper 20 degree eye deviation tracings. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

The saccade test is usually done first because the system can be calibrated at the same time the test is performed. With lights on, the patient is instructed to look back and forth between two spots located on the wall directly in front of him/her without moving his head. An arbitrary distance of about 6 feet is selected so that the patient's eyes move about 20 degrees in the horizontal and vertical plane as he looks back and forth, as directed, between spots. The spots on the wall are then selected to produce a 20 mm pen deflection. The speed and accuracy with which these movements are produced is inspected and measured. Normal individuals can perform this test with great rapidity and with very high degrees of accuracy. Brainstem dysfunction produces well-recognized abnormalities including systematic "overshoot" and "undershoot." These abnormalities may occur in one or in both directions of gaze.

Gaze testing is performed by having the patient look straight ahead and then 30 degrees to the right, left, up, and down. Gaze in these positions is maintained for at least 20 seconds with eyes open, and then an additional 20 seconds with eyes closed. Any nystagmus present during these sustained eye deviations is recorded. Gaze nystagmus can arise from both central and peripheral vestibular pathology as well as a consequence of normal variations such as endpoint nystagmus or congenital nystagmus (Figure 5.10). Frequently, one can distinguish between various etiologies by carefully examining the eye position in which the nystagmus occurs and the morphology of typical nystagmoid beats. Nystagmus which occurs with eyes open and disappears with eyes closed is reliably attributed to central nervous system pathology.

Sinusoidal tracking or pursuit testing is also performed in a lighted room. The patient is asked simply to visually track an object moving back and forth in front of his visual field. This may be a ball suspended on a string from the ceiling or a sophisticated computer-driven light bar. Normal individuals can track such sinusoidal motions with amazing accuracy. A variety of possible abnormalities can be detected (Figure 5.11). Certain of these are characteristic of central nervous system (particularly, brainstem) pathology and others may simply represent the superimposition of peripherally-induced nystagmus on the tracing.

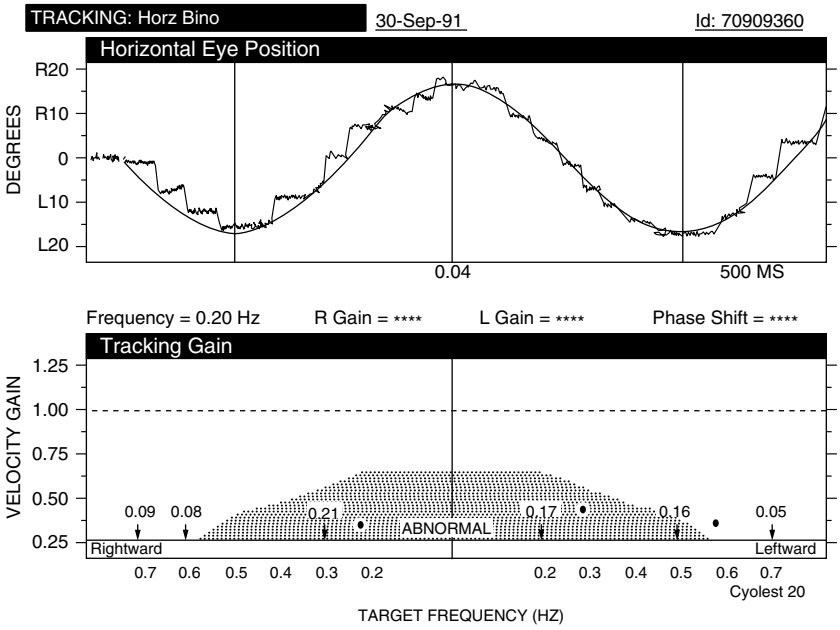


FIGURE 5.11
Horizontal tracking is illustrated in this computerized electronystagmographic tracing. Most subjects can follow a sinusoidal pattern very accurately. This patient follows it in a step-like "saccadic" fashion which is usually pathognomonic for central nervous system pathology. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

Optokinetic testing is performed by moving a series of alternating black and white stripes in front of the patient's visual field. This reliably induces nystagmus in normal individuals. Typically, the stripes are moved first to the right and then to the left in front of the patient's visual fields at 20 and then 40 degrees per second. Comparisons are then made between the resulting tracings. Several possible abnormalities can occur. Optokinetic nystagmus can be effectively and normally induced in one direction but not in the other. Occasionally, the system breaks down under stress and individuals whose optokinetic nystagmus is normal at lower speeds produce abnormal optokinetic nystagmus when the speed is increased. Virtually all abnormalities of optokinetic testing arise from central pathology, most commonly within the brainstem.

Positional testing is important not only to document pathological eye movements in patients whose chief complaint is positional nystagmus but also because abnormal test results occur in individuals who complain of nonpositionally related disequilibrium and vertigo. The test is performed by examining electronystagmographic tracings produced in four positions: with the patient sitting up, looking straight ahead; with the patient lying supine, looking straight ahead; with the right ear down; and with the left ear down. Not only does the tracing need to be examined for the presence of nystagmus produced in one position or another, but in patients with preexisting spontaneous nystagmus, the record needs to be carefully examined to see if positional changes produce any alteration in the underlying nystagmus pattern. A large variety of different patterns of positional nystagmus have been detected. These include direction-fixed and direction-changing varieties. Among direction-changing varieties are those which beat consistently away from the ground (ageotropic) and those which beat consistently toward the ground (geotropic). Although direction-fixed nystagmus is more characteristic of peripheral disorders and

direction-changing more characteristic of central disorders, so many exceptions to these rules have been identified that it is not possible to make definitive statements about the etiologic significance of particular positional patterns.[40–42] An exception is the individual in whom the direction of the nystagmus changes while in a single head position. Such a pattern is invariably associated with central nervous system pathology.

An objective record of fistula testing can be made using the electronystagmogram and the impedance bridge. In order to accomplish this, the immittance probe is placed into first one ear and then the other. The pressure in the external auditory canal is varied between +200 and –200 mm of mercury. The electronystagmogram is then examined for induced nystagmus. Each ear is tested separately. A positive test result is identified by the production of nystagmus associated with a change in pressure on the tympanic membrane. In some cases, the nystagmus can seem to change direction as the pressure changes from positive to negative. One would expect that the patient's subjective symptoms of vertigo, with or without nausea, would be induced during the presence of nystagmoid eye movements in positive tests. The results of the ENG fistula test can then be compared (when available) to platform fistula test results.[11,29,43]

Dix–Hallpike testing is a test of positioning nystagmus. In this test, the patient is rapidly moved from a sitting position to the supine position with first the right ear and then the left ear down. The test is specifically designed to identify benign paroxysmal positional nystagmus. The test is positive when, after latency of 10 to 15 seconds, bursts of horizonto–rotary nystagmus lasting 20 to 30 seconds are observed. The response fatigues rapidly so that, when the maneuver is repeated, the response will be much less vigorous. Usually, several repetitions in rapid succession are sufficient to eliminate any detectable response whatsoever. Positive Dix–Hallpike testing is classically associated with cupulolithiasis. Cupulolithiasis is not an uncommon consequence of blunt head injury. Since the response fatigues rapidly, Dix–Hallpike testing should precede other forms of positional testing. If it follows conventional positional testing, the expected response may actually have been inadvertently "fatigued out" by the previous positioning maneuvers.

Bithermal caloric examination permits quantification of the "strength" of the response obtained from each labyrinth separately. Although the strength of the bithermal caloric response is generally assumed to represent the activity of the individual labyrinth as a whole, it is important to remember that, in actuality, only the horizontal semicircular canal is stimulated. Careful evaluation of patients and comparison of electronystagmographic and SHA responses clearly demonstrate that it is possible to have residual function in the superior and posterior semicircular canals even when no response can be generated using bithermal caloric testing in the horizontal canal.

The test depends on the production of convection currents within the horizontal semicircular canal. Warmed and cooled air or water is systematically irrigated through the external auditory canal. This produces a raising or lowering of the temperature of the tympanic membrane and produces a temperature change within the middle ear space. As air is cooled or heated in the middle ear space, that portion of the horizontal semicircular canal which protrudes effectively into the middle ear space is also cooled or warmed. Since the nonexposed portions of this canal do not suffer the same temperature change, convection currents are produced within the endolymphatic space of the horizontal semicircular canal. This fluid movement will produce cupular deflection, discharges within the vestibular nerve, and nystagmus which can be measured. Thermal stimuli reliably produce nystagmus in a specific direction. Cold water will produce nystagmus with its fast component away from the irrigated ear. Warm stimuli, on the other hand, will produce nystagmus with the fast component toward the stimulated ear. A useful pneumonic for these relationships is COWS (cold opposite, warm same). The simplest clinical application of this principle is seen in the utilization of ice water caloric examination which can be

performed at the bedside or in the emergency department. Ice water calorics are performed by putting 10 to 20 cc of ice water into the external auditory canal. This will produce an extremely vigorous response in normal individuals with easily detected gross nystagmus away from the irrigated ear. Unfortunately, nausea and vomiting often accompany such intense stimulation. The vigorous response produced by ice water caloric examination is poorly accepted by patients, and therefore, current testing protocols use stimuli which produce a less violent response. When water is used, the temperature is usually adjusted to 30ºC for the cool irrigation and 44ºC for the warm irrigation. If air is chosen as the stimulating medium, then temperatures of 24ºC and 50ºC are generally utilized. Understanding the mechanics of the test makes it obvious that certain types of ear pathology invalidate or change test results. An individual with a unilateral tympanic perforation can be expected to have a much more vigorous response on the perforated side than on the intact side because the irrigant will pass through the perforation and stimulate the horizontal semicircular canal directly. Individuals with stenoses, mass lesions, or other types of obstruction of the external auditory canal can be expected to produce little or no response on the affected side. This, however, does not mean that the examination should not be performed. It means that the interpreter must be aware of the condition and make his interpretation in light of the existing pathologic process. Should, for example, an individual have no response in an ear with a perforated tympanic membrane, the perforation does not invalidate the pathological finding. Indeed, the presence of the perforation makes one even more secure that this labyrinth lacks appropriate physiologic function.

Normal individuals produce a fairly typical nystagmus response to caloric irrigation. There is generally a latency of 20 to 30 seconds followed by the onset of nystagmus which rapidly peaks in intensity at 60 to 90 seconds. The response then gradually diminishes over the next 3 to 4 minutes. In order to compare one labyrinth to the other, it is crucial that comparisons of nystagmoid response be made between peak responses for each irrigation. This is done by examining the tracing and picking out the strongest beats on each irrigation. Three or four of these beats should be measured and then averaged in order to obtain a typical "peak" response. The magnitude of the response is quantified in terms of eye speed in degrees per second. One should note that this is a different measurement than the assessment of total amplitude of the response. Very large deviations can be obtained at slow speeds. A variety of calculations can then be made to assess labyrinthine integrity. The most useful measurement is that which detects unilateral weakness (UW). This measurement compares the total response from the right ear to the total response from the left ear using the formula below when all of the responses are measured in degrees per second:

$$\frac{(RW + RC) - (LC + LW)}{(RW + RC + LC + LW)} \times 100 = \text{Percent Unilateral Weakness (UW)}$$

Using this formula, negative values indicate weakness on the right and positive values indicate weakness on the left. Convention dictates that the weakness is expressed according to the weaker side in absolute magnitude (i.e., one would say that there is a left unilateral weakness of 28%).

Most practitioners utilize a 20% difference between ears as the threshold for abnormality. Some examiners, however, use a more stringent 25 or 30% difference.

In addition to evaluating the strength of an individual labyrinth, one can also compare the total strength of all beats in one direction to all the beats in another (i.e., one can compare the strengths of right-beating nystagmus to that of left-beating nystagmus). In order to make such a calculation, one uses the following formula:

$$\frac{(RW + LC) - (RC + LW)}{(RW + LC + RC + LW)} \times 100 = \text{Percent Directional Preponderance (DP)}$$

When there is an apparent preference for the eyes to beat in the right or left direction, this is referred to as a *direction preponderance*. As a general rule, directional preponderances are a reflection of spontaneous nystagmus. Although directional preponderances can occur in the absence of spontaneous nystagmus, one should be suspicious that there has been some technical error in the irrigations whenever directional preponderance occurs in the absence of spontaneous nystagmus.

The significance of directional preponderance when not associated with spontaneous nystagmus remains unclear and, for that reason, some evaluators do not make this calculation.

An important part of the caloric examination is the test for visual fixation suppression. At some point, when the induced nystagmoid response is still brisk, the patient should be asked to open his eyes. Eye opening should produce a marked reduction in the intensity of nystagmus (Figure 5.12). Indeed, the strength of the response should be reduced by at least 60%. When this is not the case, central nervous system pathology is implied.

Computed Sinusoidal Harmonic Acceleration

An alternative method of assessing the vestibular ocular reflex utilizes a motorized chair to produce a back and forth (sinusoidal) movement (Figure 5.13). In response to such movement, the vestibular ocular reflex will induce compensatory eye movements in the opposite direction to body movement. These eye movements can be measured and compared to the rotational stimulus. Since the stimulus which initiates the vestibular ocular

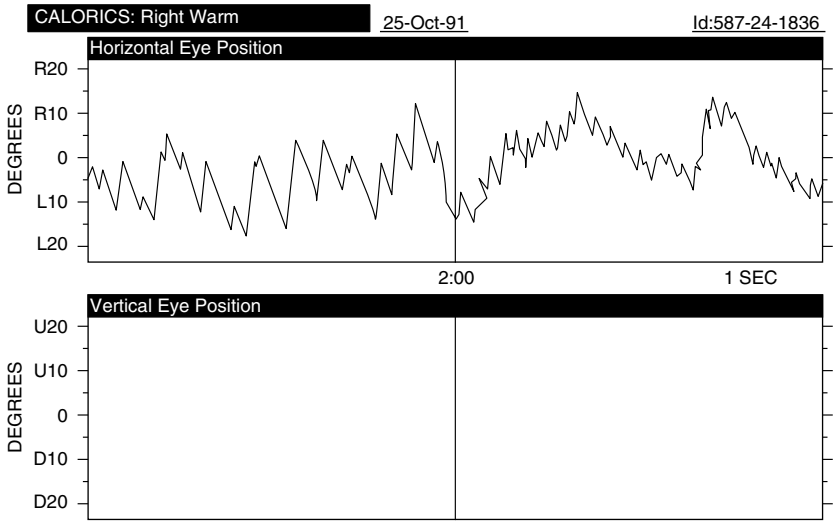


FIGURE 5.12
Electronystagmographic tracing taken from a patient with a central nervous system tumor. The right warm caloric is shown. At the vertical bar in the middle of the tracing, the patient was asked to open his eyes and fixate on a mark on the wall. Visual fixation produced only very slight decrease in the velocity of his nystagmus. Failure of visual fixation is a reliable sign of central nervous system pathology. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

FIGURE 5.13
A rotational chair. The subject is seated in the chair and is seen through the open door. With the door closed, the patient will be in complete darkness. The subject can be monitored from outside the booth by infrared photography. Electrodes are placed in the appropriate positions for monitoring of the induced vestibulo-ocular reflex. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

reflex is, in this case, mechanically generated by a chair in which the patient sits, it can be very precisely and accurately controlled. One advantage of sinusoidal harmonic acceleration is that the stimulus can be determined with much greater precision than can the thermal effects utilized to generate a caloric response in conventional electronystagmography. An additional advantage of slow harmonic acceleration is that the stimulus is physiologic. That is, the sort of rotational movement used to generate a response in the vestibular ocular reflex (VOR) arc is qualitatively and quantitatively like many of the stimuli encountered in everyday movement. Generally speaking, most movements performed during ambulation are a bit quicker, but certainly the stimuli used to generate a response utilizing the motorized chair are basically normal. This same characteristic (of providing a physiologic stimulus) which constitutes a principle advantage of SHA is also responsible for one of its principle disadvantages compared to conventional ENG. By necessity, both labyrinths are stimulated simultaneously and it is not possible to collect data from one side alone.

The patient is tested at five separate rotational speeds measured in cycles per second (Hertz). Typical speeds are one hundredth (0.01 Hz), two hundredths (0.02 Hz), four hundredths (0.04 Hz), eight hundredths (0.08 Hz), and sixteen one hundredths (0.16 Hz) of a rotation per second. Three separate characteristics of the VOR response are determined for each frequency of rotation.[39,44–46]

Phase

It is reasonably appropriate and much easier to understand phase relationships as synonymous with latency. Because the SHA uses a rotational stimulus, it happens that relationships usually characterized as latency can be appropriately described as phase relationships. Suffice it to say that abnormalities of phase (latency) represent changes in how long after the start of the stimulus the compensatory eye movement occurs. It so happens in SHA (as in many other neurodiagnostic tests) that changes in latency are relatively reliable and sensitive indicators of pathological disturbance of function and most peripheral vestibular disorders (i.e., severe viral labyrinthitis, Ménière's disease, traumatic ablation, etc.) have been associated with abnormalities of phase. It is quite typical in these cases for the phase abnormality to be more pronounced at lower frequencies and to return toward normal at the higher frequencies. In fact, if phase abnormalities are the same or worse at higher frequencies, then central dysfunction should be suspected. The data is presented by comparing the patient's response to established norms. As a rule, any response more than two standard deviations from normal is considered pathologic. Once injury has occurred, phase generally remains abnormal indefinitely. Adaptation and compensation do not eliminate phase abnormalities.

Gain

Another parameter of the vestibular ocular reflex evaluated at each frequency during SHA is the magnitude of the induced eye movement compared to the magnitude of the rotational stimulus. This comparison is referred to as *gain*. If the eye movements induced by a given rotation (in degrees per second) were exactly the same as the magnitude of the chair rotation (in degrees per second), the gain would be said to be 1.0. If the induced eye movements were twice as large as the initial movement of the chair, the gain would be 2.0 and, if they were half as large, the gain would be 0.5. Not surprisingly, the amount of gain depends on the velocity of rotation. Very slow rotational movements induce relatively small eye movements and typical gains for 0.01 Hz stimuli are 0.5. As the speed of rotation increases, the amount of eye movement similarly increases. It increases faster than the rotational speed so that, at 0.16 Hz, normal gains are in the 0.7 range.

Patients with bilateral vestibular weakness have abnormal gains and, generally speaking, the abnormality is more pronounced at the lower frequencies. As the frequency of rotation is increased, the amount of gain tends to return toward normal even in patients with bilateral vestibular hypofunction. When gain is very low, there is insufficient vestibular input to provide meaningful data and, with very low gains, one should not interpret abnormalities of phase or symmetry. Low gains will occasionally occur in response to acute labyrinthine lesions when the cerebellum deliberately suppresses output from the vestibular nuclei. However, very low gains are more usually a consequence of chronic bilateral vestibular weakness. Patients with central vertigo will occasionally show increased gain due to the absence of descending inhibition.

Symmetry

Asymmetric responses are a manifestation of directional preponderance or *bias*. That is to say, if there is asymmetry to the right, right-beating nystagmus is always greater than left-beating, regardless of the stimulus. The most obvious examples are situations in which there is spontaneous nystagmus to one side. If the patient, at rest, has 10 degrees of right-beating nystagmus, his right-beating responses to rotational stimuli will be enhanced by 10 degrees per second but his left-beating responses will be reduced by 10 degrees per second. Thus, when examining the response to rotational stimuli, it appears that the

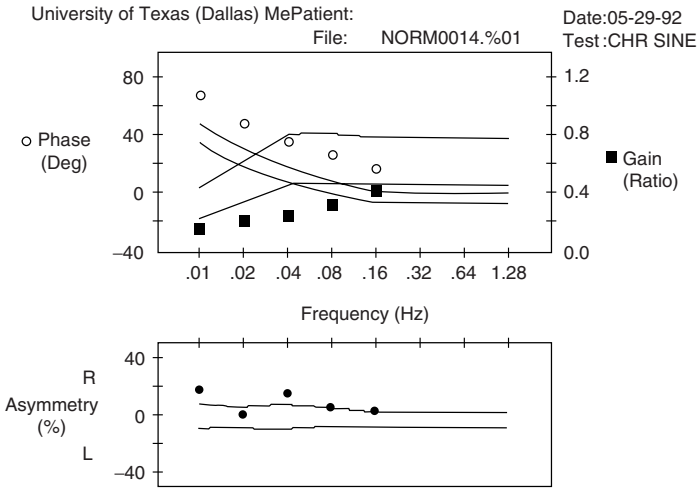


FIGURE 5.14
Summary of diagnostic information obtained from sinusoidal harmonic acceleration. In this patient, there is a significant phase lag. The circles are shown above the lines showing that they are significantly outside the usual standard deviation. In the bottom graph, one can see a mild asymmetry to the right. However, the small squares indicating gain on the upper tracing are below two standard deviations from the norm, indicating a bilateral weakness. In the face of such reduced gain, it is not possible to accurately interpret phase or symmetry changes. This is from a patient after head injury with significant reduced bilateral vestibular function. ENG evaluation showed no response to warm or cold water irrigations bilaterally. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

individual's eyes "prefer" to beat toward the right. Acute peripheral lesions frequently have significant asymmetries associated with them. If the lesion is peripheral, one would expect a phase abnormality to be apparent as well. With classic unilateral vestibular injury, marked phase and symmetry abnormalities are present during the first several weeks or months. With the passage of time and the development of compensation, the asymmetry tends to disappear, but the phase lag will remain. Some types of central disorders will have associated with them variable low level asymmetries (Figure 5.14).

Rotatory chair testing has a number of advantages that make it a useful addition to the armamentarium of vestibular testing:

- The stimulus is precisely controlled and physiologic.
- The test is quite sensitive and very repeatable. Test variability is minimized.
- It produces an objective, quantified assessment of vestibular function.
- In many cases, elimination of asymmetry can document compensation and adaptation.
- Generally speaking, it is well accepted by patients and produces less subjective discomfort than electronystagmography.

There are some disadvantages associated with SHA:

- Both labyrinths are stimulated simultaneously.
- The test is relatively expensive and requires fixed equipment installation.
- It was initially thought that asymmetry data could not be utilized to identify the side of lesion.

Recently, Mohammed Hamid has documented convincingly that asymmetry is reliably toward the side of the lesion when phase abnormalities are present.[47] In the absence of phase abnormalities, asymmetry has no localizing value whatsoever. If additional centers are able to confirm this observation, the role for SHA testing will be considerably enhanced.

Vestibular Autorotation Testing

The vestibulo-ocular reflex (VOR) is the dominant mechanism for gaze stabilization during locomotion. Because other ocular control systems are relatively insensitive above 2 Hz, high-frequency vestibular autorotation testing (VAT) was developed to isolate the VOR for testing. VAT uses high frequency (2 to 6 Hz) active head movements to stimulate the horizontal and vertical VOR to produce measurable eye movements that can be used to calculate gain and phase.[48]

Patients are fitted with a rotational sensor (on a head strap) and conventional electro-oculographic electrodes during testing. They are instructed to move their heads in synchrony with computer-generated auditory tones, with an interval ranging from 0.5 to 6 Hz. Gain and phase data are collected from the last 12 seconds of the test at higher frequencies (2 to 6 Hz).

Advantages of VAT over SHA include the ability to test both horizontal and vertical VOR gains and phases in the most clinically relevant frequency range. Saadat et al.[49] compared the results of VAT to alternate bilateral bithermal calorics and found that many patients with normal caloric test results had abnormal VAT results. This emphasizes the fact that cognitive processes or competing oculomotor systems can influence the VOR at low frequencies but are ineffective at higher frequencies. They recommend VAT as an adjunct to traditional vestibular testing.

In 1994, Murphy evaluated 120 patients with vestibular dysfunction using both ENG and VAT.[50] He noted that ENG continued to demonstrate abnormal vestibular responses in patients with permanent labyrinthine injury even after central compensation. VOR results often normalized after compensation. In this series, ENG was determined to be the most useful initial study in the evaluation of patients with probable peripheral vestibular dysfunction. Certain diagnoses (such as trauma and nondescript dizziness which are not easily determined to be peripheral) were best evaluated initially with VAT.

In short, ENG and VAT provide valuable complimentary information in the evaluation of vertigo. ENG allows localization of peripheral vestibular dysfunction without information about central compensation. VAT examines the VOR in the clinically relevant frequency range and provides information about central compensation, though it does not allow localization of the injury.

Dynamic Platform Posturography

The development of dynamic platform posturography has been an important addition to the armamentarium in evaluating individuals with disorders of balance (Figure 5.15). The use of dynamic platform posturography directly assesses the individual's ability to maintain his balance in a variety of circumstances. It is capable of assessing not only vestibular function but also contributions to balance from the visual and proprioreceptive systems. Dynamic platform posturography assesses changes in the subject's center of gravity (COG) in response to a variety of stimuli in different test conditions. Movement of the center of gravity around a fixed point is termed *sway.* Sway can be measured in both the anterior–posterior and in the lateral planes. Excessive sway can occur at rest in a variety of circumstances, but occurs most frequently in response to deliberate perturbations.[51–53]

FIGURE 5.15
Neurocom® (registered trademark for NeuroCom International, Inc., Clackamas, OR.) dynamic platform posturography. The patient is standing on a moveable platform within the visual surround. Safety straps prevent injury from falling. Sway is monitored in response to a variety of different sensory test conditions. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

Sensory Organization Testing

The amount of sway produced in response to six different situations is recorded. The different test conditions are designed either to eliminate information normally utilized in maintaining equilibrium or to subvert the system by providing inaccurate information. Movement of the patient's center of gravity is assessed in the following situations:

- Sensory Test Condition 1 — the patient stands on the platform with eyes open.
- Sensory Test Condition 2 — the patient stands on the platform, but his eyes are closed. This test condition eliminates vision as a source of information in maintaining balance.
- Sensory Test Condition 3 — the patient stands on the platform with eyes open; however, when the patient sways, the amount of movement he makes is exactly compensated for and mimicked by the movement of the visual surround. He will stay exactly the same distance from the visual surround regardless of what movement his body makes. Thus, vision will provide inaccurate information as to where he is in space relative to his visual surround. In short, in this test condition, the patient's visual system will "lie" to him. This is a more stressful situation than the mere absence of visual information produced in Sensory Test Condition 2. This condition is termed *sway referenced vision* (i.e., the visual surround is "referenced" to the amount of sway the patient has).

- Sensory Test Condition 4 — the patient stands on the platform with eyes open. Each swaying motion the patient produces is now exactly compensated for by a similar movement in the platform on which he is standing. This is a condition analogous to Sensory Test Condition 3 except that, in this condition, it is the patient's lower extremity proprioreceptive system that is "lying" to him. This is referred to as *sway referenced support.*
- Sensory Test Condition 5 — this condition is exactly the same as Sensory Test Condition 4. There is sway referenced support, but the patient is asked to keep his eyes closed. This functionally produces a situation where the patient's lower extremities are "lying" to him and his visual system is providing no helpful information. Theoretically, his balance is now dependent on vestibular function.
- Sensory Test Condition 6 — the patient stands on the platform with eyes open, but both vision and support are sway referenced. That is to say, each sway excursion is matched both by compensatory movement in the platform and in the visual surround. Thus, both the patient's visual and proprio systems are "lying" to him. In this condition, balance is determined solely by the intact vestibular system which must overcome false information from the visual and proprioreceptive systems.

If the patient does not perform well during the first trial, he is allowed two additional chances in which to improve his performance. "Learning" is frequent and many patients will be able to develop a normal response given two or three tries. If, when compared to statistical norms, the patient's center of gravity shows abnormal excursions (i.e., sway), he is considered to have "failed" that test condition.

As it turns out, different types of pathology produce different patterns of dysfunction on dynamic platform posturography. Not surprisingly, vestibular disorders are reliably associated with very poor performance in Conditions 5 and 6 when compensatory mechanisms are crippled by the test conditions. Patients who are overly dependent on vision tend to perform very poorly in Test Conditions 3 and 6. Patients who are visually dependent and also have vestibular abnormalities tend to do poorly on Conditions 3, 5, and 6. If Conditions 4, 5, and 6 are abnormal, it suggests that the patient is quite dependent on somatosensory input to maintain balance. Additional combinations and patterns can be correlated with different sorts of abnormalities. Patients with functional disorders or patients who are malingering frequently produce as bad or worse results on the easier conditions than on the harder ones.

An important contribution of dynamic platform posturography is the ability of this test to determine what sort of "strategy" the patient is utilizing to recover his balance. While standing still, the platform is suddenly "jerked" and the patient response is assessed. Several forward and several backward perturbations (jerks) are evaluated. Well-functioning, normal individuals tend to move their center of gravity around their ankles in response to impending disequilibrium. The use of movement about the hips or "hip strategy" is maladaptive and counterproductive. Fortunately, vestibular rehabilitation may be able to redirect the patient's efforts and reorient his strategy from hip to a more effective ankle strategy.

In addition to assessing the sensory modalities utilized to maintain and correct balance, dynamic platform posturography is able to partially characterize the motor response generated after perturbations. The length of time it takes for the muscle response to occur is measured and called *latency.* In actual clinical situations, it turns out that abnormalities of latency are almost always associated with extravestibular CNS pathology. The strength "symmetry" is measured. This simply assesses the amount of strength utilized in each leg to retain balance. In normal persons, equal amounts of strength will be utilized in each

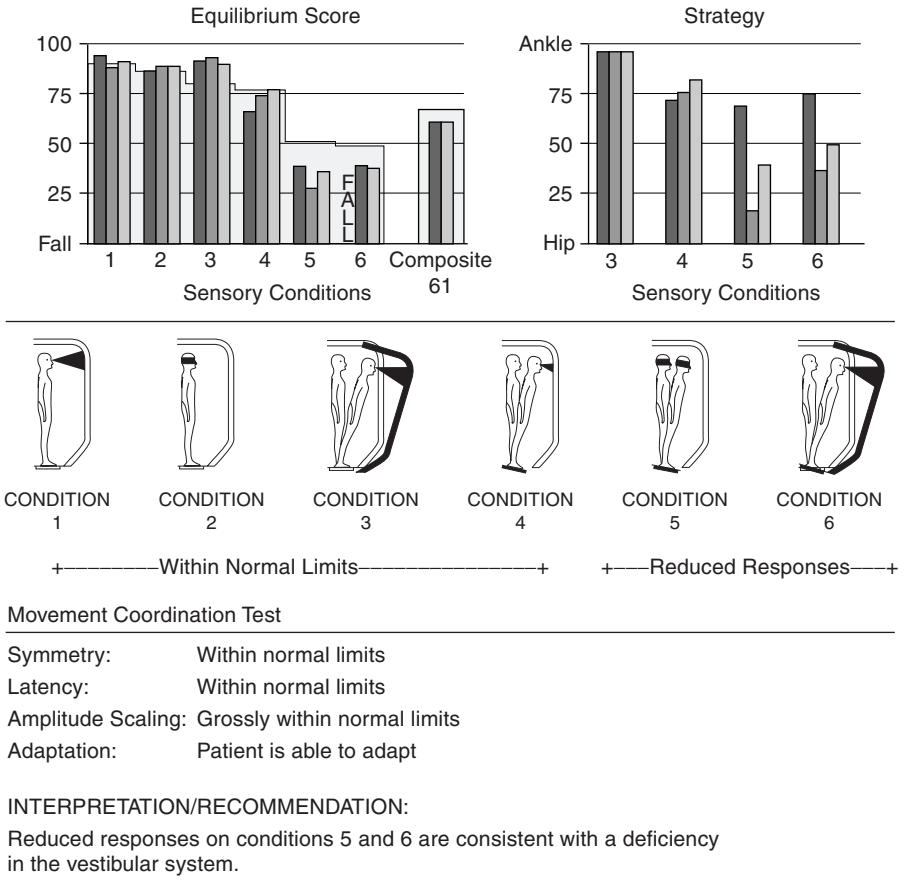


FIGURE 5.16
Six different sensory organization test conditions are monitored and the patient's performance compared with statistically valid norms. A typical summary form is illustrated here. This patient had an acute unilateral vestibular lesion resulting in a very poor performance in sensory organization Test Conditions 5 and 6. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

leg in the process of balance recovery. Once again, in the absence of obvious peripheral or orthopedic problems (i.e., peripheral muscle atrophy, unilateral hip disease, etc.), abnormalities of symmetry also reflect central nervous system disorders. The size of the response is also measured. If minor induced external perturbations produce very large compensatory excursions, large sway oscillations are induced.

Dynamic platform posturography is useful not only in diagnosis but also in the assessment of risk and in rehabilitation. Not surprisingly, patients who perform poorly on platform posturography are at greater risk for falling than patients who perform normally. Specific pattern abnormalities in sensory organization and movement coordination testing correlate even more closely with risk for falling.

An understanding of what sort of compensatory mechanisms the patient is using in response to balance perturbations can be helpful in guiding vestibular rehabilitation therapy. Patients who are overly dependent on vision can be given tasks to enhance their ability to utilize vestibular and proprioreceptive information. Persons utilizing a maladaptive hip strategy, for example, can be redirected to a more appropriate ankle strategy (Figure 5.16).

Platform Fistula Testing

Dynamic platform posturography can be used to generate a sensitive test for perilymphatic fistula. In this test, pressure is applied to the external auditory canal. This increase or decrease (i.e., "negative" pressure) is transmitted to the tympanic membrane, middle ear space, and, if a fistula is present, the inner ear. When perilymph fistula is present, abnormal sway will be generated by these pressure changes. Using the acoustics impedance bridge to quantify changes in external auditory canal pressure and the dynamic platform to quantify anterior–posterior and lateral sway in response to such pressure changes, a sensitive assessment for perilymph fistula can be developed. Several studies have demonstrated that patients with positive platform pressure testing have a high likelihood of suffering from a perilymphatic fistula.

Vestibular Rehabilitation

The clinical rehabilitation process of the brain-injured individual can be much more complicated than the rehabilitation of an individual suffering from vestibular dysfunction only.

Cognitive impairment with decreased attention span, inability to concentrate, and poor frustration tolerance can discourage the patient as well as the therapist.

In addition, patients present with a wide spectrum of central neurological impairments affecting different subsystems of the central nervous system. These impairments demonstrate themselves with symptoms of upper motor neuron lesion (spasticity, weakness), rigidity, and dyscoordination.

Given these complicated circumstances added to the vestibular dysfunction, the task at hand is, to say the least, very difficult. It is necessary to develop a treatment philosophy and to explain this philosophy to the patient each time circumstance dictates the need for more comprehension or motivation.

Vestibular rehabilitation depends on two important characteristics of the vestibular system: redundancy and plasticity.[28] Redundancy occurs principally at the receptor level. That is to say, there are several sensory systems which process information about the body's position in space and relay that information to the central nervous system. These include the vestibular system, the visual system, muscle stretch and position sense receptors in the lower extremity, and muscle stretch and position sense receptors in the cervical area. The last two are generally subsumed under the single heading of the somatosensory or proprioreceptive system, but in fact, they often function quite independently of each other. The visual and vestibular systems are themselves redundant in the sense that the system has two separate sides. When information from one side is eliminated, the system can function using the intact contralateral side alone. Data received from all of the available sensory receptors is initially processed in the brainstem where decisions are made on a reflex basis. Details of this process remain obscure, but it appears that most of the processing is done in or close to the vestibular nuclei with significant input from both the cerebellar nuclei and descending cortical projections. The ability of sensory receptor information to be evaluated, emphasized, de-emphasized, or changed at this level is the principal feature of the vestibular system allowing for progressive modification or *plasticity*.[54]

One way plasticity can be achieved is by the systematic "substitution" of sensory input from one receptor cell system for another. For example, individuals with bilateral vestibular weakness come to utilize visual information more intensively for maintenance of balance and equilibrium. *Habituation* is an additional mechanism for compensation

although its exact physiologic basis remains unclear. Despite its elusive electroneurophysiologic basis, it is clear that constant exposure to situations which produce unpleasant and counterproductive stimulation will reduce or eliminate the unpleasant response.

An instructive example of neuroplasticity is the central nervous system's response to acute unilateral labyrinthine ablation. In the circumstance of abrupt and devastating injury to one inner ear (i.e., temporal bone fracture), the afflicted individual will immediately experience rapid, violent rotation with massive visceral autonomic outflow producing intense diaphoresis, weakness, nausea, and vomiting. This effect is a consequence of asymmetry at the level of the vestibular nuclei. Vestibular nuclei connected to the intact labyrinth are continuing to receive normal sensory input and continue to respond in an appropriate way. Cells in the vestibular nuclei connected to the affected side now no longer receive stimulation from the ablated labyrinth and are "silent." Initial adaptation to this injury occurs within several hours to a couple of days and consists of marked inhibition of those cells still connected to the intact labyrinth. Control of this process occurs in the cerebellum and is accomplished via afferent cerebello bulbar fibers. This response has been termed the *cerebellar clamp* by McCabe because it diminishes activity in normally functioning vestibular cells.[55,56] By reducing function in the normal intact cells, the level of imbalance between the nonfunctioning cells and intact cells is reduced and the symptoms of disequilibrium, nausea, vomiting, and rotational vertigo are reduced. This response has been documented in acute vestibular lesions using sinusoidal harmonic acceleration where occasionally, within a day or two after ablative vestibular procedures, a marked decrease in gain can be documented on SHA testing. Over time, those vestibular nuclei originally connected to the now nonfunctioning labyrinth will develop a spontaneous rate of discharge. As spontaneous activity develops in these neurons, inhibition of the "clamped" normal vestibular nerve cells by the cerebellum is reduced. As the individual regains normal activity and as he is exposed to situations challenging the vestibular system, he will slowly regain normal function. This series of events is an excellent example of neuroplasticity in the vestibular system.[57,58]

Data from patients and animals with acute unilateral vestibular ablation as well as from other types of studies suggest that "relearning" is an important characteristic of vestibular compensation. Stressing the system by having the individual engage in activities which produce disorienting or discomforting symptoms is an important stimulus for compensation and rehabilitation.

Vestibular rehabilitation capitalizes on the natural plasticity of the vestibular system.[59] A good vestibular rehabilitation program should both extend and accelerate the normal process of physiologic adaptation to injury.

Because of the wide variety of possible separate injuries and the almost infinite possible combinations of different sorts of injuries, we believe that each vestibular rehabilitation program needs to be specifically tailored to a particular individual's needs. This is particularly true when dealing with post-head-injury patients because they will almost always have significant concomitant deficits outside the vestibular system. This is best accomplished by a physical or occupational therapist who has made a special study and gained experience in managing vestibular injuries. Such an individual will be best qualified to create programs which take into consideration all of the patient's deficits and all of his potential assets.

Propaedeutic to developing a program for rehabilitation, the vestibular rehabilitation therapist needs to make his own assessment.[54,60] At first glance, this would appear to be redundant, but in fact, it is not. The assessment made by the rehabilitation expert will not only review the history and physical and laboratory findings already obtained by physicians and other healthcare professionals, but will make a detailed assessment of specific situations which induce vertigo (i.e., elevators, crowded stores, driving), assess the severity

on a quantitative scale, and do a detailed assessment of the affect of both position and positioning. As many as 20 separate positions and movements can be separately assessed, and each position or movement can be rated for intensity, duration, and presence of nystagmus and/or dizziness. The patient's history and type of complaint dictate how much positional testing is required. A separate evaluation of eye, head coordination, and gaze stabilization is made as well as a separate and detailed assessment of postural control, both in the sitting and standing positions. Gait is evaluated separately.

Whenever making an assessment for vestibular rehabilitation, it is important to determine whether or not there are other areas of difficulty outside the vestibular system which may affect rehabilitative strategies. This is especially important in the post–head-injury area.

A complete evaluation of the musculoskeletal system needs to be made in order to determine whether there are any coexisting difficulties or deficits. Reduction in strength is common in the post-head-injury patient. Such reduced muscle strength may be secondary to muscle atrophy from coma or inactivity, or may be secondary to direct neural injury. It may, therefore, be generalized or affect only a specific body part. Reduced range of motion should be determined. Range of motion is frequently reduced in the extremities, secondary to orthopedic extremity injuries and may then be limited to a specific body part. Many patients will have associated back injuries. The effects of cervical spine injuries especially need to be taken into consideration. Patients with significant cervical spine injuries will either have had surgery or prolonged periods of neck immobilization. Many, if not all, of these patients will have disordered somatosensory feedback from cervical muscle stretch and joint position sense receptors.

The presence of pain will frequently limit movement. The nature of the pain, its severity, what movements provoke it, and which positions relieve it all need to be detailed as part of the initial assessment.

Some musculoskeletal abnormalities, especially those involving the cervical spine and neck musculature, may actually be secondary to the vestibular disorder itself. Individuals prone to vertigo and disequilibrium will limit head and trunk movements in order to avoid symptoms. Over time, these limitations of movement may cease to be volitional and require specific consideration.

The presence or absence of associated neurological injuries also needs to be addressed. Such injuries may limit or prohibit motor control. These abnormalities may be subtle and manifested only on sophisticated testing as increased response latencies or may be quite blatant in the form of spasticity or paralysis. Such disorders may arise out of injury to either the peripheral or central nervous system. Special note should be made of injuries to the extraocular muscle system. Inability to appropriately move and position the eyes may have a significant effect on balance and equilibrium and certainly can be expected to complicate a proposed program of vestibular rehabilitation.

Additionally, and perhaps particularly, important in post head injuries is injury to the cortical, subcortical, and brainstem areas. Such injuries may produce abnormalities of sensory selection, gaze control, and perceived stability. It is probable that some of the abnormal oculovestibular reflex (production of vertigo secondary to repetitive rapid movement in the visual field) seen in post–head-injury patients also occurs at this level. Oftentimes, sophisticated neuropsychiatric testing will have documented abnormalities of memory, perception, and cognitive processing which are frequently associated with post-head-injury cortical dysfunction.

Any or all of the above associated difficulties may contribute to the patient's symptomatology and require specific and special consideration when a vestibular rehabilitation program is being designed.[61,62] Clearly, individuals with significant associated visual deficits will need management different from those who have associated spastic hemiparesis. Many patients requiring vestibular therapy, and especially the post–head-injury patient,

will have suffered significant deconditioning and require directed programs to improve both muscle strength and general aerobic conditioning.

Vestibular Rehabilitation Process

The process of rehabilitation consists of several parts:

- Vestibular adaptation
- Substitution of other strategies
- Desensitization (habituation)
- Balance retraining
- Cardiorespiratory training or conditioning

Vestibular Adaptation

Adaptation describes the ability of the vestibular system to make long-term changes in the neuronal response to input. The signal that induces adaptation is the movement of a visual image across the retina, referred to as *retinal slip.* The brain adapts by increasing the gain of the vestibular responses. This can be accomplished using two simple exercises that are designed to progressively increase the gain of the vestibular system by inducing retinal slip. In one exercise, the patient is instructed to maintain visual fixation on a stationary object while moving his head back and forth. A second exercise uses a moving target, with the target and the head moving in opposite directions while maintaining fixation.

Substitution

Substitution exercises aim to enhance other strategies for balance (such as postural stability and gaze) in patients with severe bilateral loss of vestibular function. Unfortunately, no other mechanism can completely compensate for the loss of vestibular function, and most patients will continue to have some instability and oscillopsia while pursuing daily activities.

Desensitization (Habituation)

Peripheral lesions produce hypersensitivity to movement with dizziness and nausea as common complaints. Patients are particularly sensitive to specific angular or linear acceleration and deceleration.[63] Desensitization is accomplished by giving the patient a variety of positional exercises designed to reproduce his vertiginous symptoms. These are repeated twice daily for 10 to 15 minutes until the symptoms are ameliorated. The simplest (though often effective) habituation exercises are those first used by Cawthorne (Table 5.3).[64] A variety of more sophisticated techniques are also used.[17,55,65,66] It is important to explain to the patient that, in order to get less sensitive to these complaints, it is necessary to provoke them. With repetition of the prescribed exercise, sensitivity to these movements will subside (Figure 5.9).

Graphs are used to illustrate progress over a period of time. They are good tools for motivation for the patient and give the clinician information regarding the effectiveness of the program.

Balance Retraining

Balance retraining with any vestibular lesion will always start at a level that the patient is independently able to perform. It is very important to stress the issue of independence with rehabilitative exercise, as this will build confidence.

TABLE 5.3

Cawthorne Head Exercises

Begin in a sitting position —
Lie flat on your back
Roll to the left side
Roll to the right side
Back flat
Sit up
Now stand —
Turn to the right
Turn to the left
Sit again —
Put your nose on your left knee
Place your right ear on your right shoulder
Nose to right knee
Left ear on left shoulder
While sitting —
Turn your head counter-clockwise
Now turn it clockwise
Repeat while bending forward
Repeat while going from a sitting to erect standing position
Repeat as you move your head forward
Repeat as you move your head backward
In a sitting position —
Hang your head between your legs, turning to the left
Sit
Hang your head, turning to the right
Sit
Hang your head in the middle, between your legs
Sit

Note: These exercises have been used since the 1940s as effective treatment for vertigo and disequilibrium. The patient is asked to select the six exercises from the above list which provoke the most severe symptoms. He is asked to perform these six selected exercises for 10 minutes twice a day.

Source: From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.

Repetition of the balance exercise, during the session as well as for an agreed period of time after the session, helps build confidence because the exercise will become easier to perform and can be performed quicker. Simplicity of design will enhance both repetition and independence. Obstacle courses are good exercise, but in the beginning of the rehabilitation process, they may increase the patient's sense of frustration rather than his feeling of accomplishment. Functionality of the exercise is important — nothing will frustrate the balance-impaired subject more than exercise that has no bearing in daily life. Realistically, do we improve a person's ability to balance if we teach him to stand on one leg?

The treatment approach with balance retraining is not identical for peripheral or central lesions; however, the philosophy remains the same. The difference is that centrally affected patients are exposed to the same exercise longer during a treatment session and for a longer period of time. (The time necessary until they can move to more complex balance activities.)

Central Vestibular Lesions

Central vestibular lesions are hard to deal with as they do not respond to desensitization exercises as described in the above group. Central vestibular pathology gives rise to

complaints that cannot be specifically provoked by certain movements or positions but form a more steady ingredient in the activities of daily life of a patient.[61,66,67]

A diagnosed central lesion does, therefore, require a somewhat different approach. The diagnosis "central lesion" does not exclude the possibility of adaptation of the central nervous system. The expectation, however, is that rehabilitation will be less complete and usually take a longer period of time.

A program based on angular and linear acceleration and deceleration can be implemented, but with more repetitions per session, usually at a lower speed and maintaining the program for a period of 6 to 12 weeks. Cardiorespiratory endurance training (discussed later in this chapter) is even more crucial to these patients than to the above-described group as physical reconditioning will enhance self-confidence and esteem, which will impart overall motivation.

The effects of such an approach are:

- A decrease in vestibular symptoms
- An increase in self-confidence
- An increase in physical activity

Cervical Vertigo

This is a condition where the complaint of dizziness is related to posterior or lateral cervical myofascial pain dysfunction syndrome, i.e., decreased range of motion of the cervical spine with pain. The proper approach here is to deal with the orthopedic dysfunction first — that is, first treat the pain and impaired motion.

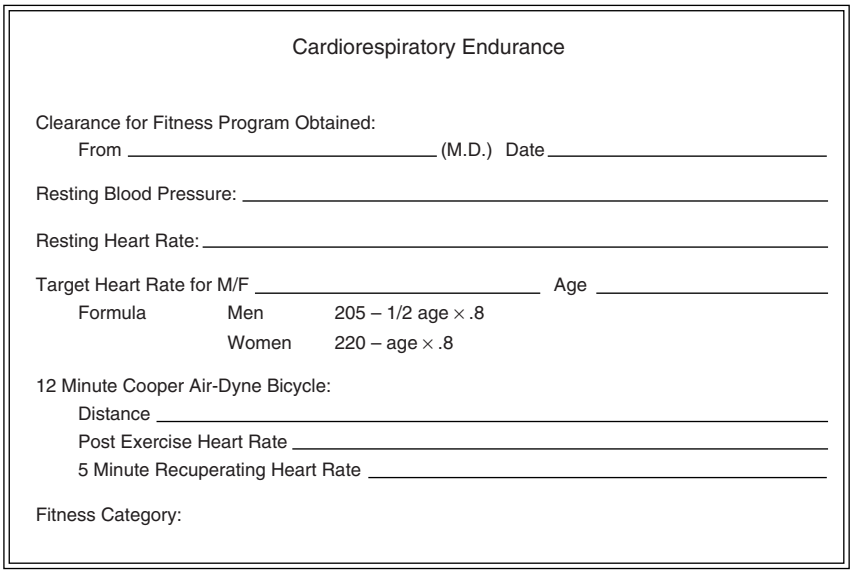
Several recent studies support the benefit of customized vestibular rehabilitation in patients with vestibular deficits. In a 1998 report, Cowand et al.[68] used the Dizziness Handicap Inventory (DHI) to retrospectively study a group of 37 patients undergoing vestibular rehabilitation and found a significant improvement in test scores of 78% of patients posttreatment. This is in agreement with previously published reports of Cohen,[69] Keim,[70] and Telian et al.[71]

Horak et al. studied the relative effectiveness of vestibular rehabilitation, general conditioning exercises, and vestibular suppressant medication on dizziness and imbalance in patients with chronic vestibular symptoms.[72] They found that all methods reduced dizziness but that only vestibular rehabilitation improved postural stability. A 1995 report from Shepard et al. analyzed the benefits of customized vs. generic vestibular rehabilitation therapy programs and found that a superior level of vestibular compensation was achieved in the patients undergoing customized rehabilitation.[73] After 3 months of therapy, only the group performing customized vestibular rehabilitation exercises had a significant reduction in dizziness during daily activities, improvement in postural stability, reduction in motion sensitivity, and a decrease in asymmetry of vestibular function. Patients receiving generic vestibular rehabilitation improved only in static postural stability.

An unsupervised program of Cawthorne–Cooksey[64] exercises is not as effective as a customized, supervised program of vestibular adaptation exercises. Each patient with vestibular dysfunction after traumatic brain injury should, therefore, be independently evaluated in the context of his unique cognitive and vestibular symptoms.

Cardiorespiratory Endurance Training or Conditioning

The vestibularly-impaired patient experiences difficulty with balance, or nausea and dizziness, when moving about and, therefore, becomes less active, no matter what the pre-



Cardiorespiratory Endurance

Clearance for Fitness Program Obtained:
From _____ (M.D.) Date _____

Resting Blood Pressure: _____

Resting Heart Rate: _____

Target Heart Rate for M/F _____ Age _____
Formula Men 205 – 1/2 age × .8
Women 220 – age × .8

12 Minute Cooper Air-Dyne Bicycle:
Distance _____
Post Exercise Heart Rate _____
5 Minute Recuperating Heart Rate _____

Fitness Category:

FIGURE 5.17
The above cardiorespiratory endurance table is used on a weekly basis to evaluate cardiovascular fitness improvements. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, *Traumatic Brain Injury Rehabilitation*, 1st ed., ch. 6, 1995, 131–169. With permission.)

morbid lifestyle. As a consequence, patients experience deconditioning and, sometimes, undesirable weight gain as a result.

Ideally, patients can be started on the Schwinn Air Dyne bicycle with a modified Cooper test to get baseline information on the level of conditioning. This stationary bike provides a gentle form of exercise which rarely triggers vestibular complaints. Patients are encouraged to maintain a pace that will elevate their heart rate to a level appropriate for their sex and age group (target heart rate). Resting heart rate, postexercise heart rates (immediately after stopping and 5 minutes thereafter), and resting blood pressure are monitored (Figure 5.17).

Not all patients can be motivated to participate in such a rigorous exercise routine and they are asked to participate in another form of endurance exercise. Most patients can be motivated to participate in some form of cardiorespiratory training, and it is best to engage the patient in a form of training that has his or her full motivation because it will increase the possibility of overall success of the rehabilitation process. Therefore, in addition to the use of the Schwinn Air Dyne bicycle, treadmills, swimming pools, walking groups, stair climbers, or anything else that will increase the activity level of vestibular patients can be used.

A number of variables will influence the outcome. First and foremost is compliance. The program of vestibular rehabilitation requires the patient to spend 15 minutes twice a day in specifically directed exercises which are advanced on a weekly or biweekly basis. A typical program will require 8 to 12 weeks. Poor compliance is common in individuals with multiple deficits and they generally do less well. Poor compliance may result because the patient has had serious central nervous injury which impairs motivation and cognition, or because associated musculoskeletal or sensory injuries make it impossible to perform the most helpful sorts of exercises. In many of these patients, two to three rehabilitation programs will be in progress simultaneously, which may overwhelm the patient's ability. Individuals with central dysfunction improve at a much slower rate and may never

achieve the same improvement as those who have peripheral receptor-level disorders. Age is another variable which works against rapid recovery.

There is objective evidence to support the usefulness of vestibular rehabilitation. Telian et al. have evaluated the outcome in 98 patients with a variety of different vestibular problems.[66,74] Some patients were excluded because of disease process but all had to meet one of the following criteria: (1) positional or motion provoked vertigo, (2) abnormalities of SOT or abnormal recovery strategies, and (3) abnormal chair/ENG findings. After a 10- to 15-week program performed at home, 87% of patients reported significant subjective improvement and 83% had objective improvement in disability ratings. Of the patients, 31% were completely asymptomatic at the time a follow-up evaluation was performed, and 10% were worse. Half of the latter had unequivocal progressive unilateral vestibular injuries and underwent deafferentation surgical procedures.

Summary

In summary, vestibular rehabilitation is an effective way of utilizing the central nervous system's natural plasticity to compensate for vestibular dysfunction. Specifically, it is useful to improve postural and balance control, eliminate vertigo and disequilibrium, and reduce the effects of visually provoked stimuli. While most patients achieve improvement, only about one third achieve complete elimination of symptomatology. It is useful to present these techniques to the patient as methods for managing and controlling symptoms rather than eliminating them. Vestibular rehabilitation needs to be integrated into an overall plan which takes into consideration all of the patient's deficits as well as his assets and abilities. Those therapists whose priority is improvement in balance and elimination of vertigo need to constantly coordinate with the patient's multidisciplinary team leader to achieve a maximally effective overall rehabilitation strategy for the posttraumatically brain-injured individual.

Acknowledgment

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6

Visual Dysfunction Following Traumatic Brain Injury

Ronald L. Morton

CONTENTS

Introduction

Individuals sustaining traumatic brain injury (TBI) often sustain other injuries in tandem with injury to the brain. Injuries involving the face, neck, back, torso, and extremities are commonly associated with TBI. Frequently, these injuries are readily diagnosed and treated as they are easily evidenced when the person presents at the emergency room.

Less obvious injuries, however, can be overlooked during lifesaving endeavors, in particular, those involving systems which are more difficult to thoroughly evaluate, such as the vestibular or visual systems. This chapter focuses on deficits commonly observed in the visual systems of people with TBI. The purpose of the chapter is to provide a review of the neuroanatomy of vision and illustrate the relationship of commonly observed visual–perceptual and visual–motor deficits following TBI to neuroanatomical structures. Visual system dysfunction following TBI is fairly common and can be quite subtle or relatively frank. Bontke et al. found the overall incidence of cranial nerve injury, for example, in persons hospitalized following traumatic brain injury to be 19%. Cranial Nerve VII was most frequently injured (9%), while Cranial Nerves III (6%) and VI (6%) followed.[1]

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The visual system has not been long regarded as one which can respond to treatments that are other than compensatory (i.e., lenses) or surgical in nature. That the visual system can respond to treatments which impact visual–perceptual and/or visual–motor skills is a relatively recent concept as applied to acquired neurological damage. The visual system functions as a primary sensory receptor for motor, social, cognitive, communicative, and emotive functions. As such, the visual system is highly integrated with many neural functions other than simply sight. Visual system disorders, then, require a fair amount of attention in the person with TBI and should be considered an integral part of the rehabilitation program. Remediation of visual–perceptual and visual–motor disorders can enhance function in all of the aforementioned areas as well as reduce the likelihood of reinjury and enhance maximal functional improvement.

Anatomical Considerations

Retina

In order to fully appreciate the complexities of the visual system, one must recognize that visual integration is not just a cortical process. Rather, visual integration begins peripherally in the visual receptor fields of the retinas.[2]

The fact that visual processing starts in the retina may seem strange until it is recalled that the eye is actually an outpouching of the brain from early in embryological development.[3,4] Figure 6.1 depicts the organization of the photoreceptors, bipolar cells, and ganglion cells. Photoreceptors, when stimulated, pass information to adjacent bipolar cells, which, in turn, differentially affect firing of the ganglion cells. Linear and cross connections

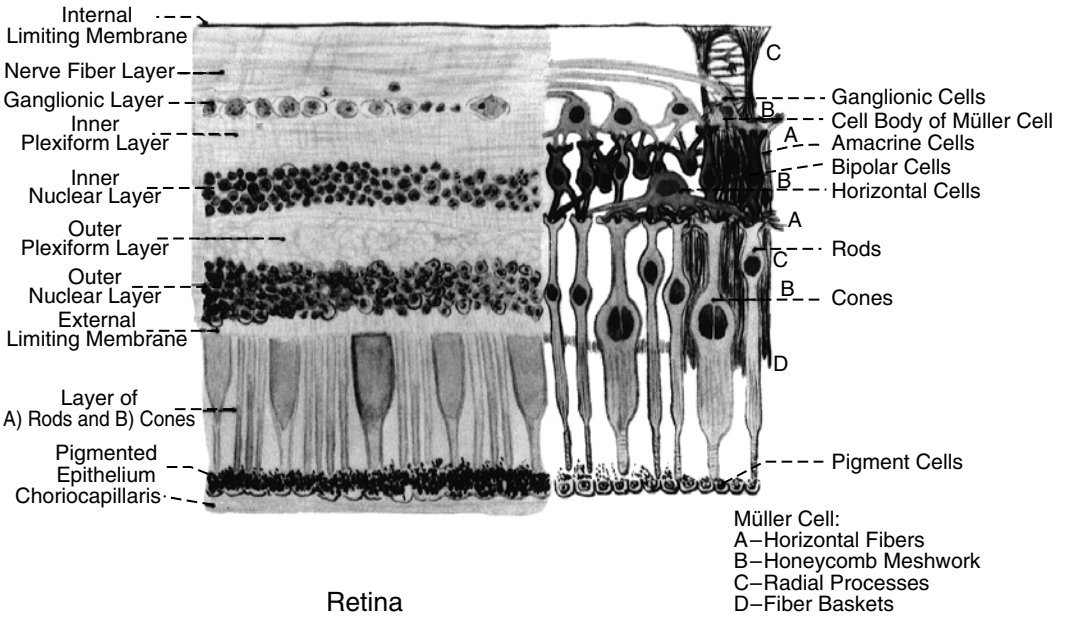

FIGURE 6.1
Eye anatomy. (From *The Eye* (chart), Jacobson, W., Jr., Ed., Anatomical Chart Co., Skokie, IL,1986. With permission.)

of ganglion and adjacent bipolar cells is demonstrated by the fact that the adjacent bipolar cells increase the firing rate of ganglion cells when certain conditions are met.

For example, if a spot of light lands on one photoreceptor while adjacent photoreceptors remain unilluminated, the stimulated photoreceptor will fire at a higher rate compared to the rate at which it will fire when all surrounding photoreceptors are simultaneously illuminated. These patterns of illuminated and nonilluminated photoreceptors were referred to by Werblin and Dowling[5] as on-center and off-surround groups.

On-center and off-surround groups may be joined in such combinations as to form units sensitive to stimuli in the environment of particular spatial orientations. These include, for example, vertical, horizontal, and diagonal lines or edges. Stimuli which are thus organized are relayed to the cortex via the optic tract. The processing of visual stimuli continues, via the optic tract, to be further processed in the lateral geniculate bodies, the occipital cortex, and associated cortices receiving radiations from the primary occipital areas.

As a normal individual gazes upon an object, the image is registered simultaneously in both the right and left retina. Each retina, however, is situated slightly differently in orientation to the object, thus producing a slightly different image to the brain from each retina.[6] This can be demonstrated by gazing at an object and alternately closing one eye, then the other. The object appears to move due to the fact that the image registered is different because of the distance separating the eyes and the slight difference in angular orientation of each eye to the object. Stereopsis, which is the ability to visualize the dimension of depth, arises from the fusing of these two separate images by the sensory system[6] and, consequently, plays a major role in several visual perceptual skills.

Optic Tract Organization and Lesion Characteristics

Knowledge of organization of the optic tract is of great importance in determination of site of lesion from visual deficits presented. Lesions at different points in the optic tract will be demonstrated by pathognomonic visual deficits.[4] In the days prior to CT scanning and magnetic resonance imaging (MRI), the localization of injury was dependent upon knowledge of anatomical relationships. Knowing the proximity of motor and sensory pathways adjacent to the visual pathways allowed determination of site of lesion based upon the constellation of signs and symptoms. Localization of the site of lesion or injury can assist in further diagnosis, determination of etiology, and likely systemic sequelae.

Each retina must direct its information toward the cortex and does so via the optic nerve. The information passes from the ganglion cells, located in each retina, posteriorly via the optic nerve to the optic chiasm. Figure 6.2 illustrates how, at the optic chiasm, right and left visual space are segregated with the contribution of each hemi-retina passed to a single corresponding lateral geniculate body, the specific thalamic relay nucleus for the visual pathway.[7] Right visual space images upon the nasal retina of the right eye and the temporal retina of the left eye. At the chiasm, the optic fibers of the nasal retina of the right eye cross to the left to join the optic fibers of the temporal retina of the left eye. The temporal fibers of the left eye continue uncrossed in the optic tract beyond the chiasm and find their way to the lateral geniculate body on the left. Thus, the left lateral geniculate body receives information from the right visual space from both eyes.

Information from the upper retinal fibers (nasal crossed, temporal uncrossed) passes through the corresponding lateral geniculate body and continues in a portion of the optic tract known as the geniculocalcarine tract until it projects to the primary visual cortex (cuneate gyrus, Area 17) of the occipital lobe.[8] The geniculocalcarine tract courses through the parietal lobe; a lesion involving the geniculocalcarine tract on the right would result in an inferior contralateral quadranopsia (Figure 6.2, Item 9).

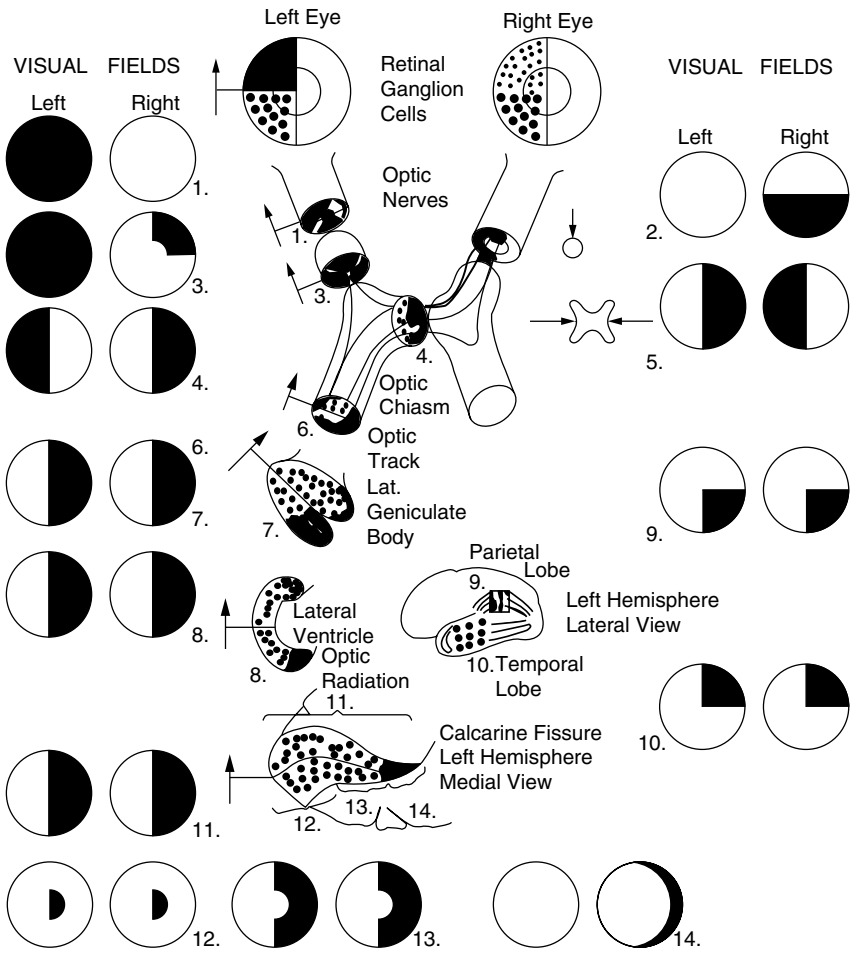

FIGURE 6.2
Visual pathway and resultant field defects. (From Jones, L. T., Reeh, M. J., and Wirtschafter, J. D., *Ophthalmic Anatomy: A Manual With Some Clinical Application*, American Academy of Ophthalmology, San Francisco, 1970, Figure 9, p. 176. With permission.)

Information from the nasal lower retina, however, after crossing over at the optic chiasm to join the temporal lower retinal fibers, leaves the lateral geniculate body and courses into the temporal lobe (Figure 6.3) in a band of fibers known as *Meyer's loop*.[8] These fibers terminate in the lingual gyrus of the occipital lobe. A lesion involving Meyer's loop on the right would cause a contralateral left superior quadranopsia (Figure 6.2, Item 10).

Bitemporal hemianopsia (Figure 6.2, Item 4), for example, results from a lesion which involves the optic chiasm, in particular, the fibers which cross from the nasal field of each retina, serving temporal visual space, to the lateral geniculate body of the contralateral side of the brain. Pituitary hormone dysfunction may be associated with this visual system deficit due to the proximity of the optic chiasm to the pituitary gland. Binasal hemianopsia (Figure 6.2, Item 5), on the other hand, would implicate a lesion of the lateral aspects of the optic chiasm involving the uncrossed temporal fibers from the nasal fields of each retina. In this instance, carotid disease may be involved.

The primary visual cortex is made up of the region of the cortex immediately surrounding the calcarine fissure, extending anteriorly toward the splenium of the corpus callosum.[9] This area is known as the *calcarine cortex*. Lesions involving selective portions of the

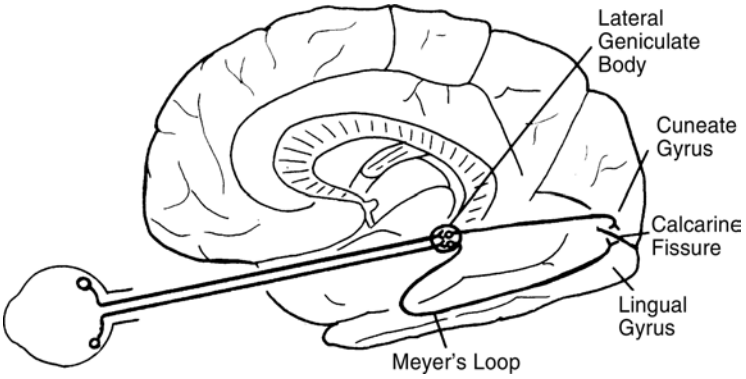

FIGURE 6.3
Meyer's loop. (From Willis, W. D. and Grossman, R. G., *Medical Neurobiology: Neuroanatomical and Neurophysiological Principles Basic to Clinical Neuroscience*, 2nd ed., C.V. Mosby, St. Louis, MO, 1977, p. 287. With permission.)

calcarine fissure and occipital pole can likewise present with specific visual field defects. Figure 6.2, Item 12, depicts an occipital pole lesion induced central scotoma. A lesion at the mid-portion of the calcarine fissure or of fibers to this area would result in a contralateral homonymous hemianopsia with macular sparing (Figure 6.2, Item 13). Lastly, a lesion involving the anterior portion of the calcarine fissure results in a contralateral temporal crescentic field deficit (Figure 6.2, Item 14).

Oculomotor and Brainstem Organization

Discussion of the visual system must include a review of the oculomotor system and its innervation. Oculomotor deficits following brain injury can result in misalignment of the eyes which, in turn, may be reported by the person as double vision, blurred vision, impaired eye/hand coordination, impaired tracking during reading, and so on. Misalignment of the eyes can also lead to cortical image suppression with resultant perceptual deficits which will impact therapeutic performance, balance, coordination, and safety.

Perhaps the most common oculomotor dysfunction seen is that of esophoria. In this condition, the lateral rectus of one eye is weakened, presumably due to injury to the corresponding Cranial Nerve VI nucleus or pathway. These people may report blurred or double vision, though they may also accommodate to misaligned images via cortical suppression of the image from one eye. Careful evaluation may turn up additional subtle impairments of other extrinsic muscle innervations. Suffice it to say that innervational deficits resulting in complete or partial motor paralysis of the corresponding extrinsic muscles are prevalent following TBI and require careful delineation and treatment.

The six extrinsic muscles of the eye[10] are innervated by three cranial nerves as listed in Table 6.1. Cranial Nerve III is responsible for innervation of the superior rectus, medial rectus, inferior rectus, and inferior oblique. The superior rectus rotates the eye upward when the eye is abducted; however, when the eye is adducted, this muscle moves the superior part of the eye toward the medial wall of the orbit (intorsion). The medial rectus rotates the eye nasally. The inferior rectus rotates the eye downward when the eye is in abduction and extorts the eye when in adduction. The inferior oblique elevates the eye when the eye is adducted and extorts the eye during abduction.

Cranial Nerve IV innervates the superior oblique which is responsible for eye depression during eye adduction and intorts the eye during abduction (Figure 6.4). Cranial Nerve VI innervates the lateral rectus which produces temporally directed rotation of the eye.

TABLE 6.1

Cranial Nerve Innervation

Cranial Nerve	Muscle Innervated	Brainstem Nucleus
III	Pupiloconstrictor and Ciliary Muscles	Edinger–Westphal
	Superior, Inferior, and Medial Rectus	Oculomotor
	Inferior Oblique	
	Levator Palpebra	
IV	Superior Oblique	Trochlear
VI	Lateral Rectus	Abducens

The nuclei of Cranial Nerves III, IV, and VI are found in the brainstem, ranging from the midbrain to the pons.[11] Figure 6.5 shows the nuclei of Cranial Nerve III located inferior to the superior colliculus and lateral to midline on either side. The axons innervating the four extrinsic muscles of the eye innervate ipsilateral muscles, except for the superior rectus which may project contralaterally.[2]

The nucleus of Cranial Nerve IV is located below the inferior colliculus. Innervation of the superior oblique muscles is contralateral in nature. Finally, the Cranial Nerve VI nucleus is located in the pons. Its axons remain ipsilateral as they innervate the lateral rectus muscles.

These three cranial nerves are interrelational in function. The medial longitudinal fasciculus (MLF) comprises the major projection system allowing such interrelation (Figure 6.5).[2] Vestibular projections influencing eye movement connect to these cranial nerves via the MLF and account for a good portion of the MLF. The vestibular projections arise mainly from the superior and medial vestibular nuclei. These interconnections between vestibular and ocular nuclei are responsible for coordination of head/eye movements and the production of nystagmus following vestibular over-stimulation.

Cranial Nerves III, IV, and VI receive afferents from the retina, the frontal and occipital lobes, the vestibular nuclei, and the superior colliculus. There may be reticular projections as well.[2]

The nucleus of the oculomotor nerve, Cranial Nerve III, is located dorsally within the midbrain beneath the Aqueduct of Sylvius connecting the third and fourth ventricles. The nuclear complex represents a collection of subnuclei that have specific identifiable

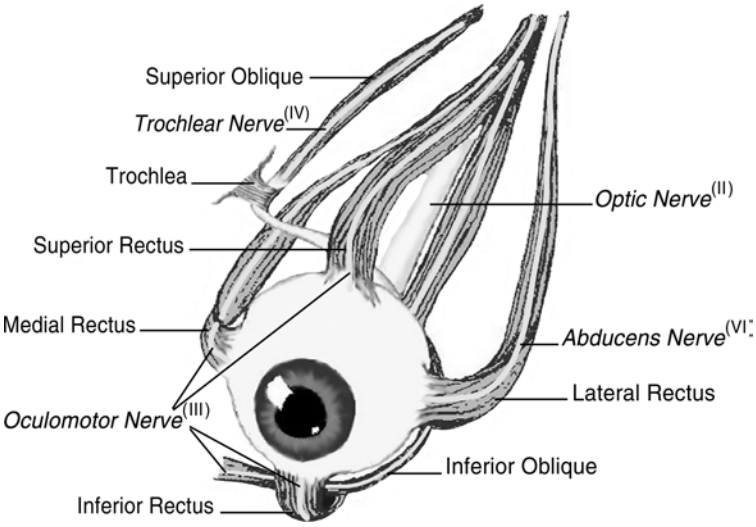

FIGURE 6.4
Musculature of the eye and cranial nerve innervation.

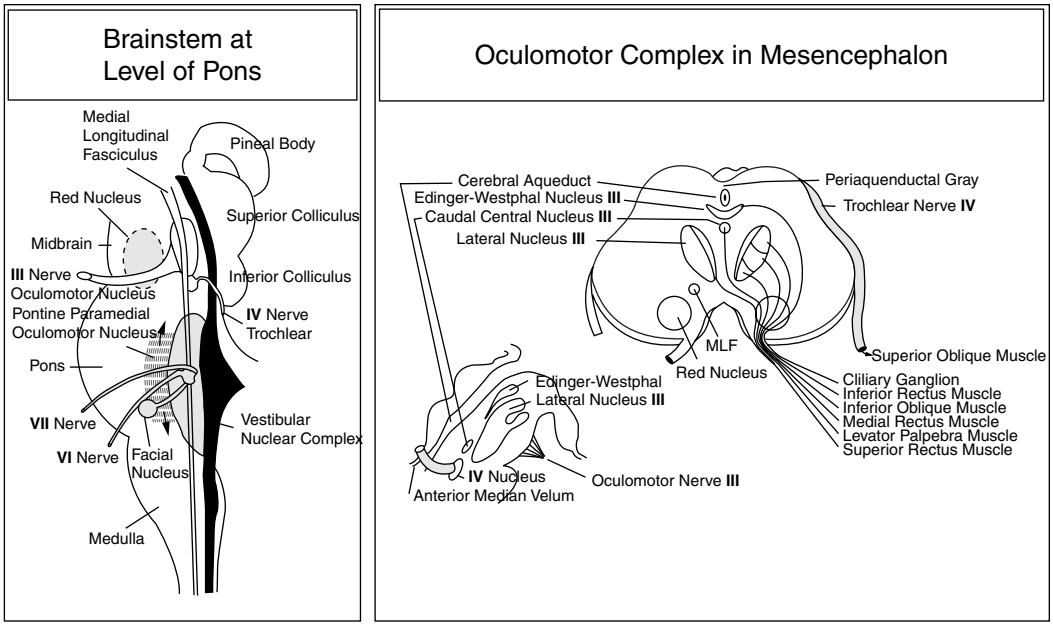

FIGURE 6.5
Brainstem and nuclei and oculomotor complex in mesencephalon cutaneous.

functions. Most dorsally, the levator complex is a midline structure that supplies both third cranial nerves. Rostrally, the Edinger–Westphal nucleus is a paired structure that sends parasympathetic signals to the sphincter muscles of the pupil via the ciliary ganglion and the muscles of accommodation of the ciliary body (Figure 6.6). The medial complex, which lies most ventrally, has been shown to contain three subnuclei that play variable roles in medial rectus functions. One of these subsets may receive input from the mesencephalic reticular formation, firing in response to retinal temporal disparity that indicates a near target. The inferior rectus subnucleus lies dorsally and rostrally. The inferior oblique subnucleus lies laterally between the inferior rectus subnucleus and the more ventral medial rectus subnucleus. Fibers exit ventrally along with the fibers destined to innervate the medial rectus, inferior rectus, and the pupil and ciliary body. The superior subnucleus which lies along the midline is unique in that the fibers cross within it before exiting ventrally with the fibers destined for the levator and superior rectus. Cranial nerve III runs slightly oblique to the tentorial edge parallel to the posterior communicating artery. Pupillary fibers are usually found to run on the medial surface of the nerve where they are particularly sensitive to compression and potential inflammation. The most medial aspect of the temporal lobe, the uncus, which is located just above the tentorium and the subarachnoid third cranial nerve, may be forced through the tentorial notch with a supratentorial mass lesion or hemorrhage and stretch the third cranial nerve against the superior cerebellar artery resulting in abnormality. As can be seen from the relationships in Figure 6.5, with the sixth cranial nerve tethered as it exits the brainstem and prior to entering Dorello's canal, an axial movement of the brainstem can result in stretching or damage to Cranial Nerve VI. The fourth cranial nerve is not pivoted as tightly but is exposed to the tentorium which sweeps around it and so an anterior-posterior movement or swelling of the brain can push on cranial nerve IV and damage that as well during its exposed, long course outside the brainstem.

The fourth cranial nerve lies within the gray matter in the dorsal aspect of the caudal midbrain, just below the Aqueduct of Sylvius, contiguous with the rostral third cranial

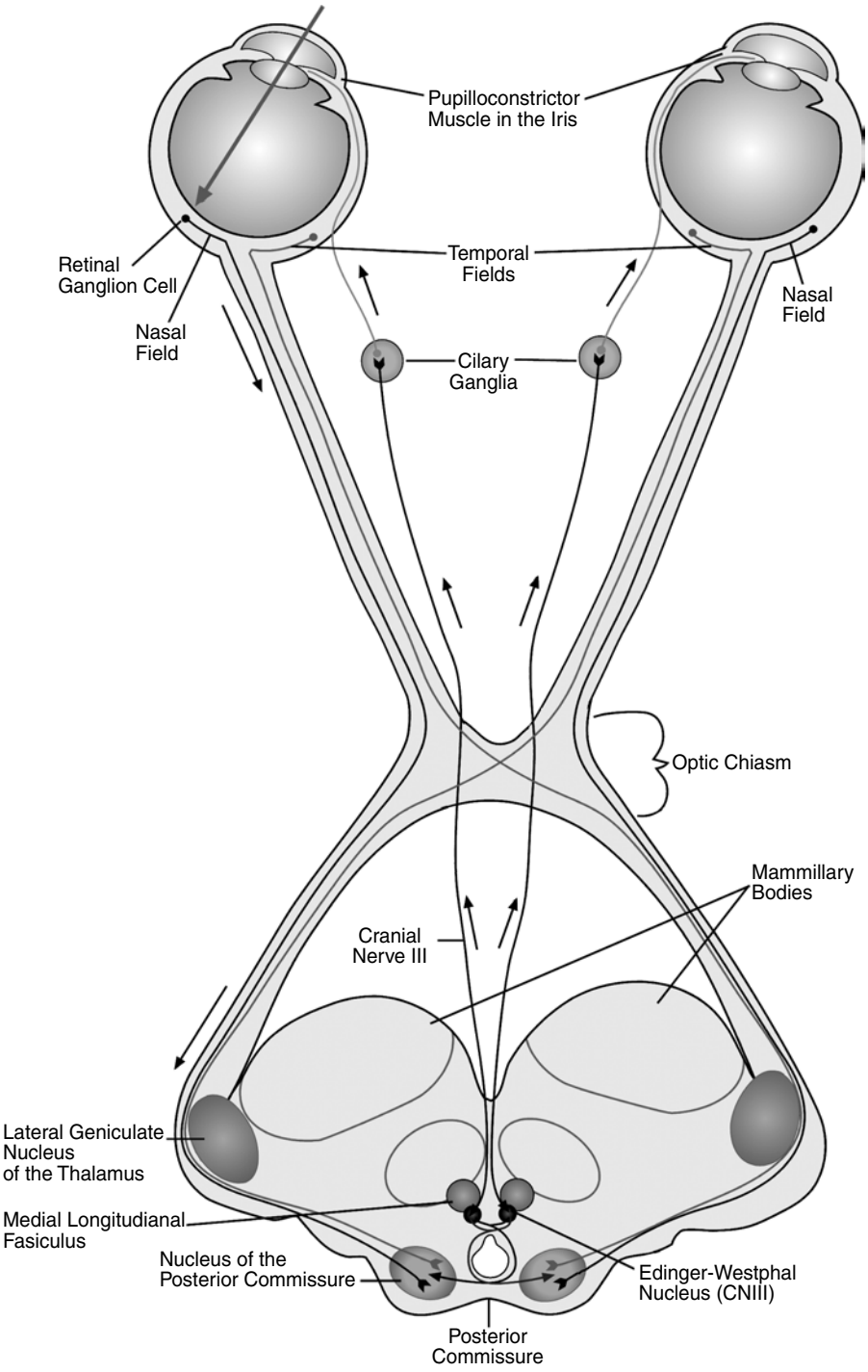

FIGURE 6.6
Edinger-Westphal nucleus and ciliary ganglion.

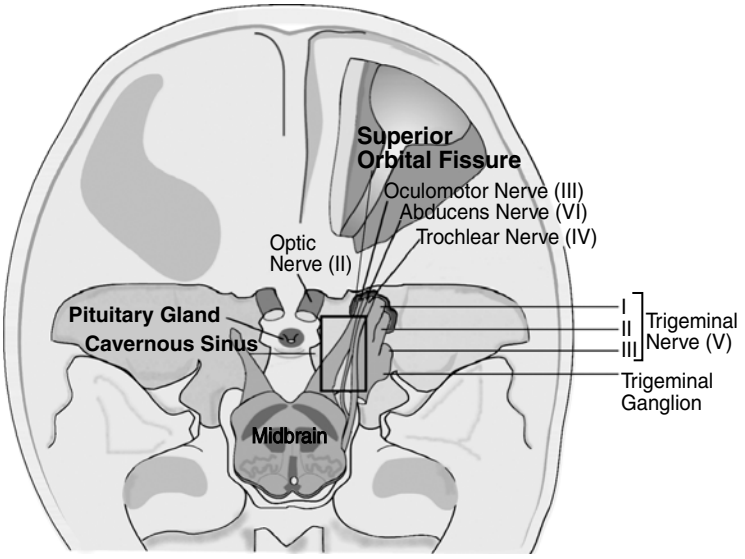

FIGURE 6.7
Course of cranial nerves through the cranial vault.

nerve nucleus (Figure 6.7). The intra-axial portion of cranial nerve IV runs dorsally around the periaqueductal gray to cross within the anterior medullary vellum below the pineal gland. The fourth cranial nerve is the only cranial nerve exiting on the dorsal surface of the brain and brainstem. It has the longest unprotected intracranial course and lies just under the tentorial edge where it is easily damaged by closed head trauma. Just below the anterior tentorial insertion, cranial nerve IV enters the posterior lateral aspect of the cavernous sinus just underneath Cranial Nerve III, runs forward within the lateral wall of the cavernous sinus, then enters the superior orbital fissure just outside the Annulus of Zinn, and crosses over the optic nerve down to the superior oblique muscle.

The sixth cranial nerve originates in the dorsal caudal pons just beneath the fourth ventricle, surrounded by looping fibers of the seventh cranial nerve. The nucleus contains the primary motor neurons and interneurons across from the contralateral medial longitudinal fasciculus to reach the third cranial nerve nucleus for coordination. Pathology affecting the sixth cranial nerve nucleus produces an ipsilateral gaze palsy. The axons exit the nucleus, travel ventrally and slightly laterally, medial to the superior olivary nucleus, to exit on the ventral surface of the caudal pons. After exiting the brainstem, the sixth cranial nerve runs rostrally within the subarachnoid space and over the surface of the clivus from the area of the cerebellopontine angle to the posterior superior portion of the posterior fossa. The nerve pierces the dura and travels forward to lie free within the cavernous sinus but runs parallel to the horizontal segment of the carotid artery within the cavernous sinus (Figure 6.7). It enters the supraorbital fissure through the Annulus of Zinn to enter and innervates the lateral rectus muscle.

Frontal Eye Fields

The frontal lobe contains two regions which are also of importance in oculomotor control. Much of what we know about these fields arises from studies with monkeys. The frontal eye field (FEF), the supplementary eye field (SEF), and the dorsolateral prefrontal cortex are primarily implicated in saccadic control mechanisms (Figurer 6.8). Two specific types

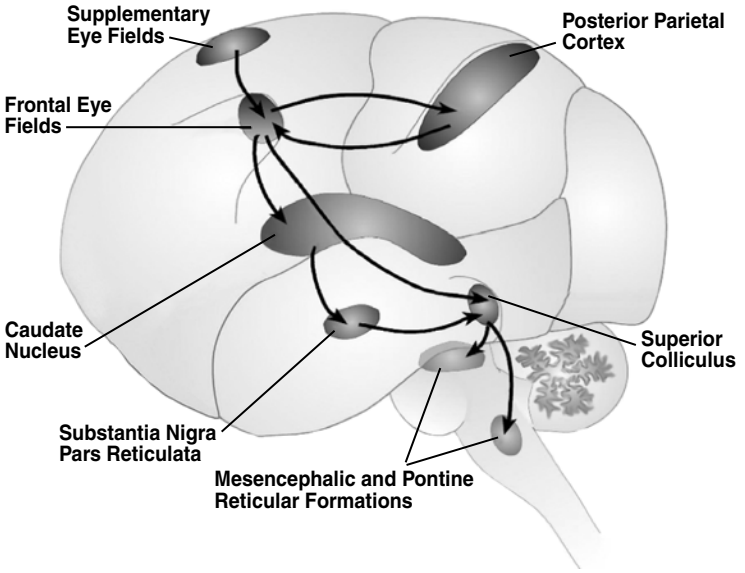

FIGURE 6.8
Frontal and supplementary eye fields of the frontal lobe.

of neurons are found in the FEF — movement-related neurons and visuomovement neurons. Movement-related neurons fire during all saccades regardless of whether the saccade is directed for the purpose of target location. These neurons fire only when the saccades are relevant to the organism's behavior and project to the superior colliculus. Electrical stimulation of a unilateral FEF will cause a saccade to the movement field of the neuron which has been stimulated. Bilateral stimulation to the FEFs causes vertical nystagmus. Visuomovement neurons are implicated in visually-guided saccades. They are active in both visual- and movement-related activity.[12]

Saccadic movements which are involved in cognitive processing appear to be located in the supplemental eye field and the dorsolateral lateral prefrontal cortex. Saccades to a part of a target involve the SEF while saccades to a remembered target involve the dorsolateral lateral prefrontal cortex.[12]

Persons with damage to the FEF may have difficulty suppressing a saccade to a visual target to which they are attending. Parietal neurons implicated in attentional processing send a signal to the superior colliculus, while the signal arising from the FEF which should suppress the saccade by inhibiting the stimulus sent to the superior colliculus fails to do so.[12]

Eye movements in mammals occur largely in coordination with cognitive function. Direction of eye movement involves cortical centers which communicate with the superior colliculus in order to effectuate eye movement.[12]

Pupillary Responses

Pupil size is modulated by both the sympathetic nervous system with its dilator fibers and the parasympathetic system with its constrictor fibers. Pupils are normally of equal size, but differences of less than 1 mm may be present in as much as 20% of the normal population. Pathologic anisocoria is caused by lesions either of the sympathetic or parasympathetic pathways or by local iris disease, such as tumors or scar adhesions.

Sympathetic impulses to the eye originate in the hypothalamus. They are transmitted along the spinal cord, synapsing in the lateral grey columns. They exit the cord via

preganglionic fibers at C8 to T2 and travel upward in the sympathetic chain to synapse in the superior cervical ganglia, lying at the level of C1 and C2. Nonmyelinated, postganglionic fibers form a plexus around the common carotid artery with vaso-motor fibers to the face and the external carotid artery. The internal carotid artery carries sympathetic nerves through the cavernous sinus where the fibers join the nasociliary branch of cranial nerve V. From the nasociliary nerve, they travel into the eye to the radial dilator muscle fibers in the pupils, resulting in dilation.

Parasympathetic pre-ganglionic axons originate in the Edinger–Westphal nucleus of the third cranial nerve (medulla) where they produce a simultaneous and bilateral response in each third nerve through intraneuronal connections. The parasympathetic pre-ganglionic axons run forward in the third nerve and pass through the inferior division of the anterior aspect of the cavernous sinus to the ciliary ganglion for synapse on their way via the short ciliary nerves into the annular constrictor pupillary fibers. The output of the Edinger-Westphal nucleus represents the summation of the input from both the right and left eyes via a certain set of the ganglion cells, some of which cross in the chiasm, along with the other visual fibers through the optic tract and lateral geniculate body on their way to synapse at the Edinger–Westphal nucleus.

This summation, at the Edinger–Westphal nucleus, allows one to elicit a relative afferent pupillary defect — a different pupil size in response to a monocle light stimulus. This reaction is caused by an asymmetry of conduction in the afferent visual system, either at the retina or optic nerve, specifically in the area anterior to the lateral geniculate body. To illustrate, when a traumatic optic atrophy causes the loss of a significant number of ganglion cell axons, the conduction of a light stimulus to the Edinger–Westphal nucleus is diminished and a larger pupil will result (i.e., 5 mm) rather than the small pupil resultant from full stimulation (i.e., 3 mm). Therefore, as a light is swung[13] from the normal side, with 3-mm pupils in both eyes, to the affected side, the pupils will dilate to 5 mm.

Visual Fields

An understanding of visual field integrity is of key importance in accurate diagnosis of visual deficits and their neurological correlates in the person with TBI.[14] Visual field is measured in degrees and the center of fixation is used as a zero referent. Visual field extends to approximately 90 degrees in all directions. Decreasing sensitivity is found the farther out the stimulus is from center. Targets in the less sensitive periphery must be larger and brighter to be seen.

Two types of measurement devices are available for delineation of visual fields. Devices can be categorized as *kinetic* or *static*, depending upon whether the stimulus moves or is stationary. The Goldmann Perimeter is a kinetic device in which the stimulus presented is a spot of light of specific size and intensity which is moved toward the center of fixation until the person reports seeing it. The Humphrey Perimeter is a static device which measures visual field by increasing the brightness of a spot at a fixed location until the person sees it. These two devices have been demonstrated to be fairly accurate and reliable in tests of both a neurologically- and nonneurologically-impaired population. Goldmann fields have been shown to be 97% reliable while Humphrey fields were 91% reliable.[15]

Diplopia fields are evaluated using the Goldmann Perimeter. The person is not patched, as they would be for peripheral field testing. The person is positioned at the machine so that the fixation light is aligned between the person's eyes. A light is introduced. The person follows this light from the center outward and informs the examiner when it breaks into a double image. Thus, a specific map of the person's diplopia is made and can be tracked as treatment progresses. It should be noted that the vast majority of

diplopia can be accounted for as a result of acquired paresis or palsy of one or more of the extraocular muscles.[16]

Visual fields can also be evaluated by "confrontation" which requires no elaborate devices. Confrontation testing is performed by movement of the examiner's finger or a red bottle cap slowly into the person's visual field, with central visual fixation, until the stimulus is viewed. While not a precise system of measurement, confrontation testing can reliably demonstrate certain visual field deficits in the absence of more elaborate testing.[16] Fading of the color red in the field periphery can be an early sign of visual field depression.

Examination

Examination of the person with TBI should first establish best corrected visual acuity, if at all possible. This can be difficult to establish due to problems the person may have in cooperating with the evaluation. Communication problems may be lessened by using the services of a speech pathologist or family member familiar with the communication deficits of a given person.

The face should be examined for lacerations, scars, or foreign bodies. Check the lids for position, remembering that cranial nerve III is responsible for palpebral elevation and cranial nerve VII for closure via the orbicularis muscles.[17] These motor systems should be evaluated for weakness. Skin sensation should be checked in distributions of cranial nerve V (Figure 6.9), possibly manifesting as anesthesia or abnormal sensation, as well as associated motor functions which can manifest as paresis of mastication.[18] Head and neck positioning should be carefully evaluated as compensatory head tilts are quite common due to diplopia and the person's attempt to compensate for same.[6]

Following any facial neuropathy, including a traumatic crush injury, regenerating axons may reinnervate muscles different from those originally served. Such aberrant regeneration can cause synkinetic movements. In this situation, the involved facial muscle may remain weak. Axons originally destined for the orbiculans muscle may reinnervate lower facial muscles and each blink may cause a twitch in the corner of the mouth or dimpling of the chin. Conversely, movement in the lower face, such as pursing the lips or chewing, may invoke involuntary lid closure. Other disorders of aberrant facial innervation include lacrimation invoked by chewing, as in crocodile tears, in which fibers originally supplying the mandibular and sublingual glands reinnervate the lacrimal gland by way of the greater superficial petrosal nerve. This is commonly seen following severe proximal seventh cranial nerve injury and may be accompanied by decreased reflex tearing and decreased taste from the anterior two thirds of the tongue. Another example is a Marcus Gunn jaw-winking syndrome characterized by eyelid elevation with jaw movement caused by an anomalous communication between the trigeminal (pterygoid) and oculomotor (levator) nerves.

The testing of different subsets of the seventh cranial nerve such as salivation, lacrimation, and sensation may help to localize a lesion (e.g., sugar/vinegar on the anterior two thirds of the tongue to test taste). Cutaneous sensation can be evaluated along the posterior aspect of the external auditory canal and tympanic membrane. All functions of cranial nerve VII may be involved if the lesion is relatively proximal from the cerebellar pontine angle to the geniculate ganglia, whereas more distal lesions may affect only certain functions, depending on their location. Testing should include functions of cranial nerves V, VI, and VIII as this may help further localize the cause of seventh cranial nerve palsy.

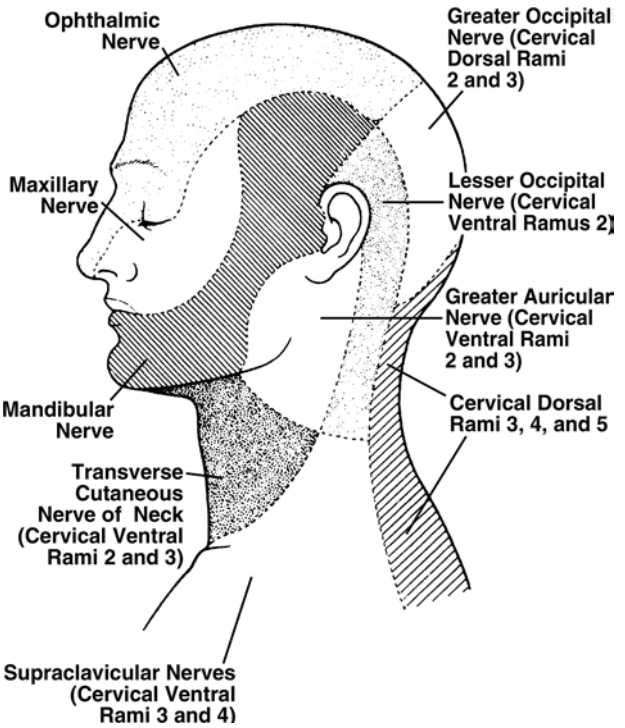

FIGURE 6.9
Distribution of Cranial Nerve V. (From Warwick, R. and Williams, P. L., *Gray's Anatomy*, 35th ed., Churchill Livingstone, London, 1973. With permission.)

Ocular Examination

Examination of the anterior structures of the eye is facilitated by magnification and illumination ranging from penlight and bifocals to slit-lamp examination. Slit-lamp examination allows greater detail to be viewed, as well as better assessment of the depth of any foreign body lodging or scar tissue. The anterior chamber, thus examined, may show blood or inflammatory debris.

Examination of the pupil can provide clues as to the integrity of cranial and optic nerve functions. The responsiveness of a pupil to light and accommodative stimuli can provide information regarding the integrity of the pupillary nerve fibers between the lateral geniculate body, the Edinger–Westphal nucleus (part of the nucleus of cranial nerve III in the medulla of the brainstem), and the sympathetic and parasympathetic nerves which innervate the dilators and constrictors of the pupil. Thus, a relative afferent pupillary defect (APD) may imply optic nerve lesion, traumatic vascular insult, an inflammatory process, or multiple sclerosis.

As shown in Figure 6.10, behind the pupil is the lens.[2] The lens may be affected by trauma in a number of ways. These include penetration by a foreign body, laceration of the globe, blunt trauma to the globe, electrical injury, chemical injury, or concussion. Any of these injuries can result in a loss of lens clarity and result in cataract formation. Cataracts may become dense enough to significantly limit visual acuity and may interfere with the rehabilitative process. In this circumstance, surgical intervention may be required. It is important to note that cataract formation can be accelerated by some tranquilizers or steroids.

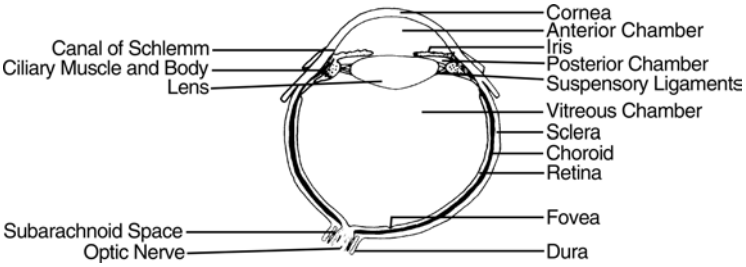

FIGURE 6.10
Major components of the human eye. (From Willis, W. D. and Grossman, R. G., *Medical Neurobiology: Neuroanatomical and Neurophysiological Principles Basic to Clinical Neuroscience*, 2nd ed., C.V. Mosby, St. Louis, MO, 1977, p. 282. With permission.)

Opacities of the ocular media, such as a dense cataract, are usually not sufficient to produce an APD. However, very dense vitreous hemorrhage or dense amblyopia may be sufficient, although it is usually indicative of pathologic lesion in the afferent visual system. This can be correlated with an asymmetric loss of visual field, central acuity, color saturation, or subjective brightness. It should be noted, also, that monocular diplopia can arise from media opacities which cause splitting of the image.[6]

The diagram in Figure 6.11 shows that the intact right eye causes more firings of the central nucleus with light stimulating that side. As the light stimulus is moved to the left side, relatively less stimulus is received at the nucleus, resulting in less tone at the constrictor fibers. The result is a larger pupillary aperture. Thus, as the light stimulus is moved from the intact right eye to the affected left eye, the pupils will dilate as the swinging flashlight crosses to the affected side. This is called a positive swinging flashlight test or a left Marcus Gunn pupil. This is an apparent paradox, with a pupil dilating as it is struck by light, as the light moves from the position determined by the intact right side (i.e., a 3-mm pupil) to the affected left side (i.e., a 5-mm pupil).

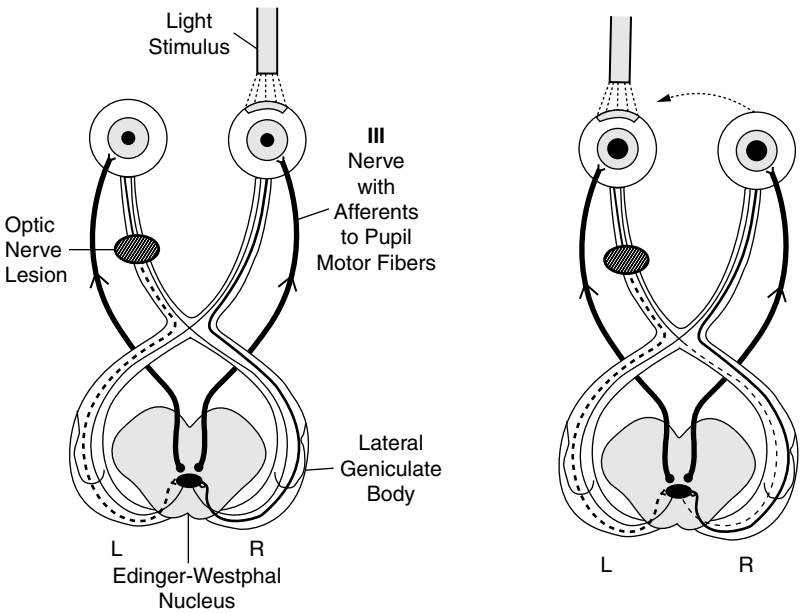

FIGURE 6.11
Anatomy of pupillary defect.

Trauma may extend to the posterior segment of the eye. As such, injuries can include retinal breaks, tears, or detachment in which the retina separates from its underlying supportive tissues, losing function, and ultimately causing wrinkling and scarring. Hemorrhage may occur and it is possible for there to be contusion to the optic nerve itself.

Extraocular Motility: Peripheral and Central Dysfunction

The extraocular muscles of the eye are responsible for aligning the eyes, enabling them to be pointed at the same object, and moving the eyes to different positions of gaze in a manner which allows the continuous perception of a single image. The movement of each eye is managed by six muscles and controlled by three cranial nerves. Therefore, between the two eyes, there are twelve muscles and six cranial nerves involved. Any of these muscles or nerves can be adversely affected following injury, resulting in interference with the alignment and tracking of the eyes. Injuries such as direct contusion to the orbit or fracture of the orbit can cause injury to the muscle or nerve complex. Mechanical entrapment of a muscle can occur or bony fragments from an orbital fracture can impinge cranial nerves.

The course of the cranial nerves from the brainstem to the orbit makes them subject to contusion injuries. In particular, cranial nerve VI exits from the ventral side of the brainstem and ascends the bone along the base of the skull. It enters the superior orbital fissure of the orbit on its way to the lateral rectus muscle. Cranial nerve IV exits from the dorsal side of the brainstem and sweeps around to the sides. It also passes through the superior orbital fissure to innervate the superior oblique. Blunt head trauma, with the associated violent shaking of the brain, can cause the dura along the dorsal aspect of the brain to impinge on the nerve as it exits and crosses the dorsum of the brain. The result is a fourth nerve palsy which manifests in the person as the inability to rotate the eye downward during adduction and a loss of intorsion during abduction.

In addition to lesions which can affect individual cranial nerves and muscles, resulting in misalignment, there is also coordination which occurs between various cranial nerve motor nuclei in a tract in the brainstem known as the *medial longitudinal fasciculus* (MLF). The MLF serves as a coordination and integration center between the third, fourth, and sixth cranial nerve motor nuclei. As an example, when an individual who is looking straight ahead wishes to turn his/her gaze to the right, several things must happen in a coordinated fashion. First, the firing rate of the right lateral rectus muscle via the sixth motor nucleus must increase as must the firing rate for the left medial rectus muscle, mediated by the third motor nucleus on the left side. At the same time, a relative inhibition or decrease in the firing rate of the right medial rectus muscle and the left lateral rectus muscle must occur leading to a deviation of the eyes to the right. A lesion in the brainstem involving the MLF would interfere with the coordination of these four motor nuclei and coordination of eye and/or head movements might subsequently be impaired.

Eye movements must be coordinated with changes in head position or acceleration of the body in any plane which might stimulate the vestibular apparatus. The vestibular apparatus is mediated through the eighth cranial nerve which has projections into the lateral gaze center located adjacent to the sixth motor nucleus on the ipsilateral side. The right horizontal gaze center fires directly into the adjacent right sixth motor nerve nucleus for its contribution to conjugate deviation of the eyes.

This can be contrasted to a request for a volitional turning of the eyes to the right. Compliance with such a request would require involvement of the left frontal premotor area which feeds posteriorly in the white tracts and projects to the right horizontal gaze center. Consequently, an injury to the frontal lobe or its conduction path to the horizontal

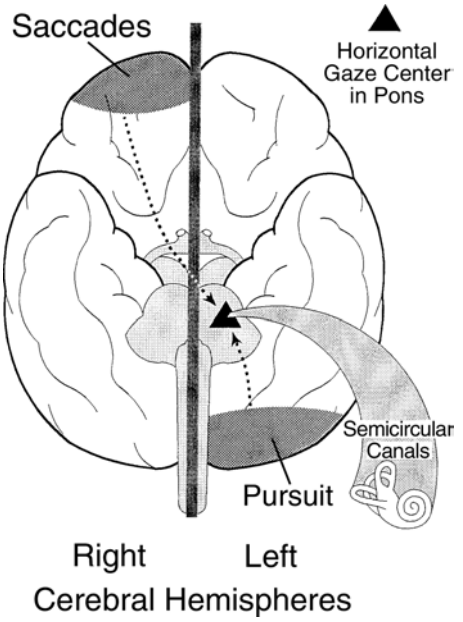

FIGURE 6.12
Inputs to horizontal gaze center.

gaze center could adversely affect the ability of a person to voluntarily turn the eyes from one side to the other. At the same time, vestibular input to the lateral gaze center may remain intact. The Doll's Head maneuver, wherein the head is rotated by the examiner to one side and the normal response is such that the eyes deviate to the opposite side, can be utilized to test the integrity of pathways from the vestibular nuclei to the lateral gaze center.

Horizontal and vertical gaze systems are located in different anatomical locations and tend to function independently of each other (Figure 6.12). Therefore, each should be examined separately to check for impairment. Also, it is important to note if a person can hold steady gaze in the primary or eccentric positions in the presence of any type of nystagmus.

Horizontal gaze palsy with an inability to make a conjugate ocular movement to one side may result from either pontine or supranuclear lesions. Evaluation by the Doll's Head maneuver or caloric stimulation[16] to the external auditory meatus allows differentiation of a lower pontine lesion from one of the supranuclear pathway, which would cause a loss of saccadic gaze in the direction opposite the site of Lesion A (Figure 6.13). Input from the intact hemisphere causes ocular deviation toward the site of the lesion. If the person is unable to look toward that gaze direction by either a voluntary or tracking movement but can deviate the eyes to the involved side during a Doll's Head rotation, this demonstrates that the lower pontine reflexes are intact and that the lesion is in the supranuclear pathway.

The vertical gaze centers are divided above and below the Aqueduct of Sylvius anterior to the motor nuclei of cranial nerve III. The vertical gaze centers can also be selectively injured. Damage to the dorsal vertical nerve nucleus will affect the ability to initiate upgaze beyond midline, allowing horizontal gaze to be preserved with smooth pursuits and saccades intact (Parinaud's Syndrome).

Vertical gaze palsies caused by a lesion of the upper midbrain in the area of the superior colliculus can result in three signs known, collectively, as *Parinaud's Syndrome* or *Dorsal*

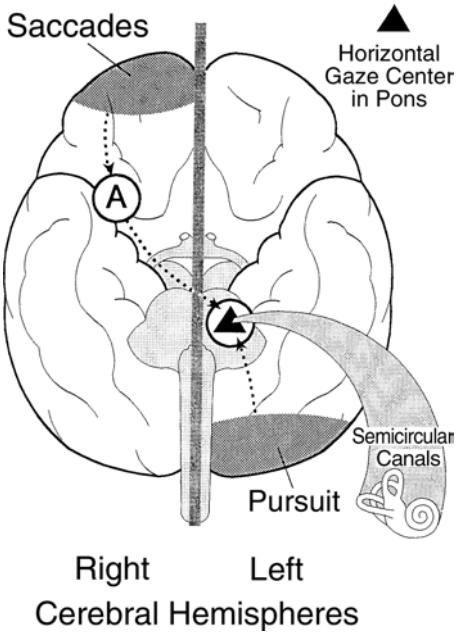

FIGURE 6.13
Supranuclear lesion.

Midbrain Syndrome. This is comprised of a loss of vertical gaze ability and pupillary light reflex, with preservation of near reflex and the presence of an eye movement disorder called *convergence retraction nystagmus.* Convergence retraction nystagmus is triggered by an upward saccade, either voluntary or in response to a downward rotating optokinetic drum, which causes simultaneous firing of both the medial and lateral rectus muscles resulting in convergence and retraction of globes into the orbit. Examination of the pupil shows light/near dissociation with normal-to-mild dilation of pupils and poor or absent light response but, with an accommodative target, the pupil will constrict to a near reaction. A person with this condition has the ability to make rapid horizontal saccades but abilities for voluntary up and down gaze are lost and the person attempts a head posture change to compensate. A Doll's Head rotation may show that vertical movement can be produced with vestibular input when pontine reflexes are intact and only a supranuclear pathway lesion is present.

Early lesions in the region of the posterior commissure can affect upgaze preferentially, particularly vertical saccades. Lesions can press on the midbrain aqueduct leading to hydrocephalus and papilledema. A lateral extension of such a lesion can involve the optic radiation, while a posterior extension of a lesion can produce ataxia from cerebellar compression. Pineal tumors are the most common of such lesions, although emboli, vasculitis, arteriovenous malformations, or arteriosclerosis may also be causal factors. An upper midbrain CVA, by branches from the posterior cerebral artery, can also result in impairment of vertical gaze with retraction of both upper eyelids, called *Collier's sign.* These symptoms usually recover over 2 to 3 weeks.

As has been stated, ocular deviation or misalignment can result from cranial nerve palsies. Deviation is often initially incomitant or variable in different directions of gaze. There is often more deviation in looking to the side of the affected muscle than when looking away from its field of action. This condition may resolve in time with return to normal function or the condition may become more comitant, or even and consistent, in the different fields of gaze. Sequential measurements are used to study the deviation in

nine cardinal positions. Via sequential measurements, the examiner can more readily make determinations about whether function is returning to normal or whether deviation is becoming more comitant.

When ocular deviation is relatively even in primary and reading gaze, prisms can be used to optically move the image to compensate for the mechanical misalignment. Press-on prisms can be applied to the person's glasses resulting in increased comfort and resumption of the ability of the person to see binocularly. Press-on prisms may be changed at will, unlike ground-in prisms. As the person's divergence reduces, the amount of prism can also be diminished to maintain alignment and keep fusional vergence drive active as an aid to further rehabilitation.

Nystagmus

Ocular stability, the maintenance of fixation and alignment on a target, is the result of multiple input paths in a carefully balanced feedback loop. Elements of the feedback loop include a visual stimulus and output from the occipital cortex, vestibular system input, and proprioceptive information arising from head and neck position A decrease or imbalance in any of these systems can lead to spontaneous ocular movements and the failure of the compensatory mechanisms. These spontaneous eye movements may be asymptomatic. However, they can be of sufficient amplitude to result in diminished acuity that people may interpret as blurring or a decrease in vision. Occasionally, people with certain types of nystagmus can complain of oscillopsia or the sensation of the world moving. Because nystagmus may be associated with ocular misalignment, the person should be quizzed with regard to whether he/she does or does not have double vision. Likewise, vestibular dysfunction may be associated with nystagmus so a problem with hearing or tinnitus and trouble with balance and vertigo may be associated. This subject is dealt with further in Chapter 5.

Depending on the degree of movement associated with nystagmus, simple observation may be sufficient or additional magnification and illumination may be needed, either with direct ophthalmoscope or during ophthalmoscopy. It is possible to get very precise oculomotor recordings with an electro-oculogram or other device that will describe the movements and their characteristics with regard to waveforms and velocities. Clinicians should note the amplitude and frequency of the movements, the direction of the gaze that induces nystagmus, and all points where the nystagmus is least evident. The movements are commonly recorded with arrows to designate the fast phase of the eye movement, both in terms of direction and in terms of amplitude. The movement most commonly consists of a slow drift to the eye, followed by a corrective saccade, as in a jerk nystagmus. For instance, a right jerk nystagmus would have a slow movement to the left with a fast movement to the right. Pendular nystagmus is relatively symmetric in that there is not an identifiable slow phase and shows relatively equal amplitude in speed in separate directions. Nystagmus may be horizontal, vertical, or have a torsional or rotatory component.

In the early onset category, congenital nystagmus is usually recognized in the first few months of life. There is often a family history and the acuity may be good. People with congenital nystagmus are not bothered by the eye movements. In young children, it is important to detect any impairment of visual tracking or optic atrophy. The presence of either should encourage neuro-imaging as congenital nystagmus most often occurs in isolation but may be seen in conditions such as albinism, achromatopsia, Leber's congenital amaurosis, and aniridia. The nystagmus is almost always conjugate and horizontal. It may be continuous or intermittent. It may appear as jerk or pendular in character. Null

points are common and the person may adopt a head turn or posture in an attempt to improve vision. Visual fixation often amplifies the nystagmus, which is not the case with peripheral vestibular nystagmus. Two characteristic signs are reversal of the normal pattern of optic kinetic nystagmus in which the slow phase of the eye movement moves in the opposite direction of the rotation of the drum and in electro-nystagmography when a pattern is observed in which the velocity of slow phase movement increases exponentially with distance from fixation. Nystagmus is also associated with 15% of people having a strabismus. It is abolished by sleep and, in addition to being accentuated by fixation, it is diminished by convergence.

Latent nystagmus is another form that appears early in life and is a horizontal jerk nystagmus that is seen in conditions of monocular viewing. The fast phase tends to be toward the viewing eye, away from the occluded eye. The uncovered eye tends to drift toward midline. Its fast phase reverses each time the eye is alternately covered. To obtain the best acuity, one must blur the nontested eye with a plus lens or other filter and not simply occlude the eye which will unleash the nystagmus and result in greater optical blurring. Latent nystagmus is very commonly associated with esotropia. Another variation is manifest latent nystagmus in which the characteristics of latent nystagmus are present even when both eyes are open. Both these forms of nystagmus are typically benign.

An important subset is a monocular nystagmus in childhood. This is typically vertical and relatively small in amplitude. The eye may have an afferent pupillary defect, optic atrophy, or decreased vision and is commonly associated with chiasmal glioma. A spasmus nutans may resemble a monocular nystagmus of childhood. It consists of a nystagmus in both eyes that is intermittent, horizontal, low amplitude, rapid, and often dysconjugate. There may be associated head nodding and/or an abnormal head posture. It can be monocular and, thus, would be confused with the more ominous monocular nystagmus of childhood and, therefore, also warrants neuro imaging. It typically is spontaneously resolved after several years.

In the category of acquired nystagmus, the first is gaze-evoked nystagmus in which people have difficulty in maintaining eccentric gaze. The eye drifts back toward the center and a corrective saccade to reposition the eyes more peripherally is required. Thus, the fast phase is in the direction of the gaze. It is caused by an imbalance in the neural integrator located in the nucleus propositus hypoglossi adjacent to the medial vestibular nucleus in the pontomedullary junction that is responsible for matching neural activity to maintain eyes in the eccentric position. The nystagmus is often symmetrical right to left. Advanced age is the most common cause, although metabolic and toxic etiologies are more common in younger adults, either from ethanol or anticonvulsant drugs. Whenever gaze-evoked nystagmus is asymmetric, it can be presumed that there is a lesion of the brainstem or the cerebellum. Perhaps stroke, demyelination, or tumor has asymmetrically affected the vestibular nuclei. Gaze-evoked nystagmus may occur in normal subjects at the extremes of gaze and this should be assessed by examining the stability of fixation at roughly 40 to 50 degrees from primary position.

Disassociated nystagmus may result from lesions of the medial longitudinal fasiculus (MLF), causing nystagmus of only the abducting eye when the gaze is directed to the side opposite the lesion. The person is often diplopic because of the limited adduction of the ipsilateral eye. It may be associated with demyelinating disease in younger people or vascular insufficiency in more advanced age. Most acquired jerk nystagmus in primary position is due to asymmetric vestibular input which may be related to peripheral pathology affecting the vestibular end organ, semicircular canals, or the vestibular nerves or to the central pathology affecting the vestibulocerebral connection. Because tonic input regarding eye position is mostly vestibular, which feeds directly to the contralateral horizontal gaze center located in the sixth cranial nerve nucleus, asymmetric loss of input

results in a conjugate ocular drift. The correcting fast phase is away from the affected side. Peripheral vestibular lesions are typically not discrete and affect all three semicircular canals in the otolith organs. This results frequently in mixed (horizontal, torsional, and vertical) nystagmus. The horizontal component often dominates. Visual fixation tends to dampen the peripheral nystagmus. This can be seen by observing the fundus with direct ophthalmoscope while the alternate eye is covered and uncovered to see the difference in amplitude that fixation on a distant target has on the nystagmus. A peripheral nystagmus is often accompanied by tinnitus, hearing loss, and vertigo or disequilibrium.

Central nystagmus, in which the fast component is directed toward the side of gaze, is relatively common, often secondary to medications, such as anticonvulsants, sleeping aids, sedatives, and antianxiety medications, or alcohol. Visual fixation has little effect on central vestibular nystagmus. Bruns nystagmus is a characteristic form of vestibular nystagmus associated with cerebellar pontine angle tumors. Initially, the vestibular nerve is affected; the eyes drift toward the side of the lesion with corrective phase in the opposite direction. As the lesion enlarges, the ipsilateral brainstem is compressed, causing problems in maintaining ipsilateral eccentric gaze. As the person looks to the side of the lesion, the fast phase changes direction to ipsilateral, beating more slowly and with a coarser amplitude.

Some forms of nystagmus and nonnystagmus saccadic oscillations are highly correlated with lesions and are useful for localization within the central nervous system. Downbeat nystagmus results from defective vertical gaze holding; the eyes tend to drift up and a corrective downward saccade is generated. The presumed mechanism is asymmetric loss of the tonic input from the anterior semicircular canals resulting in an upward drift of the eyes. Downward nystagmus is almost always present in primary position. People may report difficulty in reading and may report oscillopsia. Structural lesions are present in approximately 50% of people. An Arnold–Chiari malformation, in which the cerebellar tonsils herniate through the foramen magnum and compress the cervical medullary junction, is the most common structural etiology. Differential diagnosis includes angioma, cerebellar hemangiomas in the foramen magnum, and demyelination disease. Stroke, cranial trauma, drugs (alcohol, Lithium, antiseizure medications), syrinx of the brainstem or upper cervical spinal cord, brainstem encephalitis, or nutrition are some of the etiologies to be considered.

Upbeat nystagmus may be present in primary position or only in upgaze. It is commonly associated with lesions of the anterior cerebellar vermis. Common causes include demyelination, stroke, cerebellar degeneration, and tobacco smoking.

Seesaw nystagmus is a variety of vertical nystagmus that is dysconjugate — as one eye moves up, the other eye moves down. The upward moving eye also intorts while the downward moving eye extorts. This occurs with lesions around the diencephalon. Craniopharyngioma is the most common cause. Other parasellar tumors and trauma may produce seesaw nystagmus. There is an associated afferent system pathology, including bitemporal visual field defects.

Periodic alternating nystagmus may be congenital or acquired and is characterized by an oscillation of cycles of horizontal movements of approximately 4 minutes. The nystagmus beats in one direction for 2 minutes, slows, then reverses to the other side for the next 2 minutes. It is most common in posterior fossa disease, especially of the cerebellum. Common causes include multiple sclerosis, cerebellar degeneration, and Arnold–Chiari malformation. Etiology is thought to be in the vestibulocerebellum and is manifest as a shifting in the null point.

Pendular nystagmus of both a vertical and horizontal component may be oblique (if the components are in phase) or circular or elliptical (if they are out of phase). It is not localizing and is usually acquired in association with multiple sclerosis.

Microsaccadic refixation movements are an abnormal eye movement resulting from inappropriate saccade. Most common is square-wave oscillations which is a small movement away from, and then back to, fixation. The smaller movements may be seen in normally aged people. Larger amplitude oscillations may occur in people with progressive supranuclear palsy, cerebellar disease, or multiple sclerosis.

Ocular flutter is a horizontal small amplitude high frequency movement. Opsoclonus or high frequency multiple direction movements (or saccadomania) are associated with a burst of saccades released from the pons without the normal latency between consecutive saccades. Neoplastic etiology must be excluded in these people. In children, neuroblastoma is a primary consideration. In adults, small cell carcinoma of the lung and cancer of the breast or ovaries must be ruled out. These eye movements may be an early sign of cancer.

Convergence retraction nystagmus commonly occurs as part of a dorsal midline syndrome of Parinaud (which includes absent upgaze, light–near dissociation, and Collier's lid retraction). Anomalous eye movements result from a co-contraction of the horizontal extraocular muscles on attempted upgaze. It is best elicited by having the person follow a downward rotating optokinetic nystagmus drum.

Ocular bobbing is a rare sign in which rapid downward movement of both eyes is followed by a slow return of the eye position to midline. The person is usually comatose or has severely compromised mental status, usually from bilateral pontine infarction or hemorrhage. These lesions ablate the paramedian pontine reticular formation on both sides, thus horizontal movements are lost. Severe metabolic disturbances may, in the absence of structural lesions, cause ocular bobbing with possible later recovery.

The last form of nystagmus to consider is *voluntary* nystagmus. It is typically horizontal in direction, appears as a relatively high frequency convergent saccades, and can rarely be maintained for longer than 20 seconds. Although it can be induced volitionally in many normal subjects, it may, occasionally, not be consciously generated and can distress people because of oscillopsia.

Learning and Therapy

One model for learning and memory includes repetition. Repetitive use of a synaptic connection causes a broadening and flattening of the endplates with a decrease in resistance across the synaptic gap and a preference for using that synapse over adjacent pathways that have not been so facilitated.[19] Learning has been shown to affect dendritic spine formation.[20] These concepts are anatomically supportive of many standard teaching methods from repetition of spelling lists and multiplication tables to rehearsing a speech to learn a pattern of words.

Repetition may also serve as a foundation for retraining a person with TBI in whom preferred pathways may have been damaged, resulting in an initial inability to perform an old, remembered task. The inherent complexity of the central nervous system may be advantageous in that there seems to be alternate pathways available for bypass of damaged areas and establishment of new circuits or series of synapses that will allow one to perform old tasks in perhaps new ways. Therapy can be thought of as a means of helping to identify some of these previously unused or little used pathways and, through repetition and building upon prior skills, developing new ways of performing old tasks.

Case History 1

A 32-year-old male sustained postconcussion syndrome after being struck in the head by a falling pallet. Initially, he presented with complaints of diplopia and blurry vision. On evaluation, he was noted to have eight prism diopters of exophoria at near and distance, with some difficulty on upgaze. Cogwheeling of saccades was present. It was noted on screening and confrontation fields testing that temporal constriction in the right eye was present. Recommendation was made for saccadic exercises, such as the vertical swinging ball, and convergence exercises. At the next visit, exophoria was decreased to six prism diopters and saccades had improved with therapy.

Two months later, exophoria remained about the same and saccades had ceased cogwheeling on left to right gaze and had greatly improved on right to left gaze. The individual continues with vision therapy and has graduated to exercises that are more difficult for him, such as the color bead sorting tray.[21]

Case History 2

A 42-year-old male suffered blunt head trauma from metal pipe. Initially, he presented with complaint of decreased vision. On examination, acuity was correctable to 20/25– in the right eye, 20/20 in the left eye. No strabismus was noted. Saccades were slowed, with difficulty moving eyes left to right, and slight exophoria on upgaze. Pursuit was jerky. Worth Four-Dot testing revealed partial suppression with left eye. Visual fields, on confrontation, were constricted bilaterally. Recommendations were for pursuit and saccadic exercises and the individual was started on swinging ball exercise.

Two months later, saccades were greatly improved, with almost no cogwheeling. Approximately 6 months after the initial examination, the individual was started on Ritalin for impaired speed of processing. Immediately, he began to complain of more difficulty with tracking and decreased vision. On examination, smooth pursuit had become very jerky, as were saccades. Best corrected acuity had decreased to 20/30– in the right eye and 20/40– in the left eye. He discontinued Ritalin 3 months later and was evaluated after 2 weeks, noting vision still decreased. Smooth pursuits and saccades were still jerky. Acuity had increased to 20/20– in each eye, with difficulty. Final evaluation was done 4 months later. Acuity was 20/20 in each eye, best corrected. Smooth pursuits were improved, but still jerky, and suppression was noted in the left eye via Worth Four-Dot testing.

Case History 3

A 31-year-old male suffered a closed head injury with intracerebral hemorrhages after a motorcycle vs. car accident. Initially, he presented with 20/20 vision, best corrected, bilaterally. Six prism diopters of exophoria with ten prism diopters of left hyperphoria was noted on primary gaze. There was vertical nystagmus on abduction and large lag on abduction. Smooth pursuits were jerky. Recommendations

were for saccadic and smooth pursuit exercises, such as the Marsden ball, color bead sorting tray, and accommodative flexibility exercises. Four diopters of prism were applied to present glasses via press-on prism.

Six months later, with prism, exophoria was decreased to two prism diopters. Vertical nystagmus had improved, as had saccades. He started the bead sorting tray exercises on a vertical orientation and vertical door jamb reading.[21]

Case History 4

A 31-year-old Hispanic male sustained right cavernous fistula post motor vehicle vs. pedestrian injury. His chief complaint was that he was unable to move his eyes laterally to the right. On examination, visual acuity was 20/70-2 right and 20/60-1 left, without correction. Extraocular motility was with restriction to mid-line with limitation of abduction of the right eye. There was injection and dilation of the vessels, especially temporally on the right eye, similar to venous congestion. Auscultation revealed a bruit that seemed louder on the right side.

The man was sent for MRI of the brain, which was not able to be completed due to movement even after 2 mg of Versed. A "very high flow" clotted cavernous fistula was confirmed upon a second MRI and cerebral/carotid angiogram was performed under general anesthesia. Surgical intervention, by placement of three balloons in the right carotid fistula to close it, was performed. The man showed a 25 to 30 prism diopters right esotropia which did not resolve after the cavernous fistula surgery. He was still only able to just achieve mid-line with maximum effort, but had no abduction. Recommendation was for muscle transposition procedure to obtain alignment in primary gaze. This would require several surgeries to achieve the best result, and even so, would not allow for full range of motion.

Most therapy consists of taking a task, breaking it down into smaller steps, teaching, learning, and repeating each one of the steps, and linking them into larger and larger groups until, finally, a more complex behavior can be performed. Since the goal of therapy is to minimize disabilities and maximize abilities, this retraining process is the key at the heart of the things that we do.

First, the systems or subsystems that have been adversely affected, what things a person is unable to do, and what things the person can do to a limited extent must be determined. Next, a means of working from what the person can do in an additive fashion to allow him/her to regain as much skill as possible must be devised. For example, in treating diplopia, the first temptation might be to simply patch the more severely affected eye to relieve the symptom of diplopia. While this does relieve the immediate symptom, it does very little toward rehabilitation or establishing these alternate pathways that were discussed earlier. Therefore, the act of putting a patch on the eye temporarily blocks the symptom but does not approach a solution to the problem, which is mistracking of the eyes.

A preferred plan would be to determine whether or not there is any position of gaze in which the individual does not see double. Treatment would incorporate prisms in glasses to move the images into alignment so as to allow the person to continue to use both eyes at the same time. The goal would be to enlarge the area of single vision through a series of training exercises. These exercises encourage the movement of the eyes and stimulate the utilization of existing or new pathways to allow smooth tracking of an object or to acquire its fixation and maintain it in good alignment. Treatment may start by using a

large amount of prism in the glasses, perhaps a plastic press-on prism so that it can be easily changed as the individual improves with time under therapy to keep encouraging the person to move ahead. The areas of first concern should be primary gaze (straight ahead gaze) and slightly down gaze in a reading position. These may require two different sets of glasses with two different amounts of prisms.

Programs of visual therapy require coordination of efforts between the physician and the therapist. The physician conducts serial repetitive measurements to determine baseline alignment and provide comparison to previous measurements to monitor progression. The therapist makes suggestions in consultation with the physician regarding what therapies might best improve the individual's condition, keeping in mind tolerance, strengths, and any other concomitant difficulties. As long as progress is being made, it should be encouraged and allowed to proceed.

It may take many months for damaged neural tracts to repair themselves or for compensation to occur within the neurological system. Nerve repair proceeds at a slow pace. At some point, the ophthalmological measurements may plateau and the individual may show no further progress. Depending upon the nature of the deficit at that time, one may consider surgical intervention to realign the eyes in a more central and aligned position. Visual therapy may play a role in stimulating binocular vision, either preoperatively in preparation for surgery or postoperatively in an attempt to stabilize the alignment that has been achieved by mechanical movement of the muscles. Once again, small bits of prism may be utilized to complete the alignment process and then be gradually weaned away as fusional amplitudes increase over time.

A number of people have shown rather dramatic improvement in areas that traditional medicine will tell us should not have improved. Some, who initially could not tolerate things moving near their heads because it gave them a feeling of extreme discomfort, developed a tolerance for having a ball swinging in a circle around their head as they tracked it back and forth. Others needed a program geared specifically to their areas of difficulty, such as working from near to far as they changed their fixation. With time and repeated efforts, they developed an increased facility in this regard. Still other people who had specific difficulties in their saccadic tracking systems were able, with simple repetitive exercises such as door jamb reading, to demonstrate increased facility. This was reported both subjectively, in that they felt they could do the exercises more quickly, more easily, and with less fatigue, and also objectively, in that their examination scores showed improvement over time. It is important to understand that (1) the therapist must realize that the person can get better and (2) the person must be willing to undergo a fairly rigorous and sometimes uncomfortable therapeutic process in order to develop the synaptic relays necessary for improved function.

Summary

Detailed understanding of the visual system is necessary for accurate diagnosis of visual disorders following TBI. It should be understood that surgical and therapeutic interventions exist to ameliorate some visual system dysfunction. Rehabilitation of treatable visual system deficits should be undertaken as a regular component of comprehensive rehabilitation following traumatic brain injury.

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7

Rehabilitation and Management of Visual Dysfunction Following Traumatic Brain Injury

Penelope S. Suter

CONTENTS

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Introduction

This chapter surveys the nonsurgical rehabilitative services available to provide effective treatment of brain-injured patients with visual sequelae. It should be a useful reference for those who deal with these patients in intensive rehabilitative environments, as well as for primary care professionals who sometimes find these patients in their care when a rehabilitative hospital or center is not accessible. It may also be useful to both novice and experienced vision care providers working in the area of traumatic brain injury (TBI) rehabilitation.

The basic structure of this chapter remains the same as in the first edition. However, in addition to updating the scientific and clinical references, a number of topics have been added or expanded upon. Also, the model of vision rehabilitation set forth in the earlier edition has been altered in order to acknowledge visual thinking and memory as part of the visual rehabilitation process.

Many of the therapeutic approaches used with TBI patients were developed for other special needs vision patient populations. For this reason, much of the information provided here is applicable not only to the TBI patient, but also to other patients who have suffered organic insult to the brain. For the same reason, although they may lack specific experience with TBI patients, vision care professionals who practice other forms of visual rehabilitation and vision therapy will often be able to provide appropriate rehabilitation for TBI patients suffering from visual dysfunction — given a few additional concepts which are specific to the brain injured population.[1]

Physical Substrates of Vision

In the rhesus monkey, which provides an excellent model of the human visual system, more than 50% of the neocortex is involved in visual processing.[2] To date, researchers have described approximately 305 intracortical pathways linking 32 different cortical areas implicated in visual function; 25 of these are regarded as either predominantly or exclusively involved in visual function, and seven are considered visual-association areas.[3] The ganglion cells traveling from the retinas represent approximately 70% of all sensory input fibers to the brain. In addition to multiple subcortical areas (see Chapter 6), every lobe of the cortex is involved in visual processing (reviewed by Kaas[4]). The occipital lobe contains primary visual cortex for initial processing of vision as contour, contrast, and depth. The inferior temporal lobe is involved in object identification, the middle temporal area in motion processing, and the parietal lobe in processing for spatial organization and visual attention.[4,5] The frontal eye fields and adjacent areas of the frontal and prefrontal lobes are involved in motor planning and initiation of self-directed eye movements, as well as visual search[6] (Figure 7.1). In addition, simple visual awareness requires interactions between primary visual cortex, posterior parietal cortex, and the frontal eye fields. Input from the limbic system (especially the cingulate gyrus) may mediate motivational

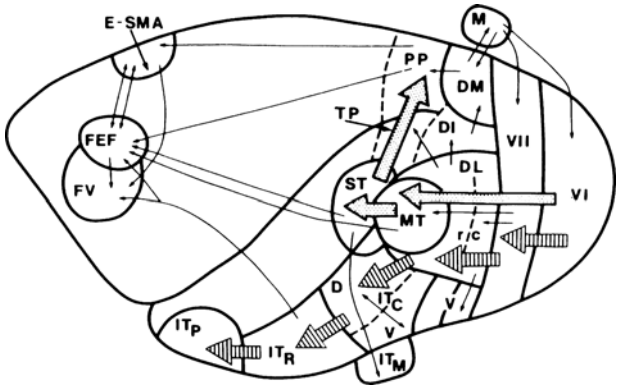

FIGURE 7.1
Areas of visual cortex and some of the ipsilateral cortical connections in visual cortex of the owl monkey. The arrows indicate two major cortical pathways of visual processing. The superior path (dotted arrows) to posterior parietal lobe via the middle temporal area supports "where" processing. The inferior path (hatched arrows) to temporal lobe supports "what" processing. (From Kaas, J. H., Changing concepts of visual cortex organization in primates, in *Neuropsychology of Visual Perception*, Lawrence Erlbaum Associates, Hillsdale, NJ, 1989. With permission.)

relevance of the external stimulus, guiding sustenance of attentional activation in the visual system.[7]

Considering this, visual rehabilitation becomes a sweeping term which ranges from rehabilitation of the eye and surrounding structures, to rehabilitation and management of sensory processing, organization of sensory input from the eye into visual percepts, and use of these percepts to support cognitive or behavioral functions. Visual dysfunction may affect the ability to carry out daily tasks such as reading, driving, walking, and functioning in the workplace. Diagnosis and rehabilitation of the eye, eyelids, extraocular muscles and surrounding bony structure, eye movement and eye teaming disorders, as well as the higher visual functions such as visual perception, spatial organization, visual memory, and the ability to integrate visual information with other modalities, all fall under the umbrella of visual rehabilitation. Multiple professionals may be involved and considerable networking or case management provides for the most effective care.

The Multidisciplinary Approach

Two types of eye doctors are frequently required in management of the visual consequences of TBI — the ophthalmologist and the optometrist. In general, their roles may be considered analogous to the computer equivalents of hardware and software repair persons, respectively. The ophthalmologist will often be needed to provide medical/surgical treatment of the hardware or anatomical and physiological aspects of the visual system before the optometrist can provide rehabilitation of the software or functional aspects of the visual system.

Ophthalmologists are trained to diagnose and manage damage to the eye and surrounding structures as well as to diagnose lesions of the visual pathways and ocular-motor system. They sometimes prescribe exercises for eye movement disorders which are often performed with the assistance of an occupational therapist. Occasionally, an ophthalmologist will work with an orthoptist, an ophthalmologically trained therapist, to remediate eye teaming disorders such as strabismus. However, ordinarily, ophthalmologists are

mostly concerned with providing the medical/surgical support required in early rehabilitation, or for later surgical intervention if spontaneous recovery and therapy fail to produce an acceptable result with a traumatic strabismus.

Neuro-ophthalmologists are ophthalmologists who have specialized in diagnosis and treatment of neurological dysfunction of the visual system. They are more likely to have some experience with rehabilitating the visual software or application of nonsurgical or pharmacological therapies than general ophthalmologists.

Optometrists specializing in vision therapy and/or rehabilitation are trained in diagnosis and nonsurgical treatment of more complex fixation, eye movement, or eye-teaming (i.e., binocular) disorders, as well as perceptual dysfunctions in the visual system. Usually, the treatment of such disorders is performed with the assistance of a vision therapy technician under the doctor's supervision. In an inpatient or rehabilitation center outpatient situation, occupational therapists working under a doctor's supervision or prescription will sometimes assist the patient with vision therapy for perceptual and sensorimotor dysfunctions, or less complex eye movement and eye teaming dysfunctions. They may also assist with teaching new living skills to compensate for residual vision deficits.

Optometrists specializing in low vision assessment are trained in prescription of low vision aids for patients with reduced visual acuity, and "field expanders" which may be required for patients with visual field defects. These doctors will often work with, or refer to, a low vision rehabilitation specialist who can assist in teaching the patient new living and mobility skills to cope with their acquired visual deficit.

Vestibular system damage may cause nystagmus and/or obstruct normal fixation and pursuit. In such a case, referral for vestibular workup to a professional equipped to perform eye movement recordings for diagnosis and to make rehabilitative recommendations may be helpful. Neuropsychological examination may help to give a broader perspective on visual perceptual dysfunctions. Finally, as with other types of rehabilitation following a TBI, visual rehabilitation may be significantly enhanced by the assistance of a counselor or psychotherapist to assist patients in understanding their new limitations and the need to rehabilitate, as well as managing emotional sequelae which can interfere with effective rehabilitation.

Prevalence and Impact of Visual Dysfunction in TBI Patients

Because of the multifaceted nature of visual dysfunction and the broad distribution of visual functional areas in the brain, many, if not most, TBI patients suffer from some sort of visual dysfunction. Transient changes in refractive error which may last for months or years are common after TBI.[8,9] Accommodative (i.e., focusing) dysfunctions are also common[10] and may interfere with reading, fine depth discriminations, and rehabilitative therapies which are performed at nearpoint. Nearpoint tasks, as well as balance, orientation, mobility, and daily living skills, may be affected by visual field defects and binocular disorders, as well as by dysfunctions in visual perception and spatial organization.[9,11] Binocular disorders can cause postural changes as the patient finds ways to either maintain fusion or enhance suppression of one eye by tilting or turning the head or torso.

It is often the case with TBI patients that eye-care professionals, untrained in diagnosing more subtle visual and ocular-motor dysfunctions, may dismiss patient complaints of headache, dizziness, inability to concentrate, blurred vision, fatigue, light sensitivity, or inability to read as due to emotional or other nonvisual etiologies. While many of these symptoms may have nonvisual causes, a careful assessment of the visual system will often

reveal the physiological or perceptual difficulty underlying the patient's complaint.[12] Gaetz and Weinberg have demonstrated deficits in visual event-related cortical potentials in patients with persistent symptoms from traumatic brain injuries classified as mild head injuries or concussions.[13] They conclude that patients with postconcussive symptoms frequently have persistent brain damage which cannot be visualized using CT or MRI techniques, but can be elucidated using visual and auditory event-related potential techniques. Schlageter et al.[14] found that 59% of TBI patients admitted to an acute rehabilitation center had eye movement or eye teaming dysfunctions. *Therefore, it is important that the TBI patient be examined by an eye/vision care provider who has a special interest in the area of neuro-, rehabilitative, or therapeutic vision care.* (See Appendix 7A for a partial list of organizations that can provide educational materials or lists of member doctors who practice in this area.)

A literature survey shows some of the types of visual problems encountered. Cohen et al.[15] found convergence insufficiency (i.e., difficulty pulling the eyes inward as is necessary for binocular fixation on near targets) in approximately 40% of both TBI inpatients with recent injuries and follow-up patients 3 years postinjury. In the follow-up group, convergence insufficiency was positively correlated with duration of coma, dysphasia, cognitive disturbances, and failure to find placement in nonsupported work situations. Lepore[16] examined 60 patients with TBI and resultant strabismus. Among the 51 patients with nuclear or infranuclear findings, fourth cranial nerve palsies were the most common (39%), followed by third nerve palsies (33%), sixth nerve palsies (14%), combined palsies (10%), and restrictive ophthalmopathy (4%). Convergence insufficiency was the most common supranuclear dysfunction. Similarly, in 114 patients referred to an ocular motor clinic for visual disturbances following motor vehicle accidents, Fitzsimons and Fells[17] noted fourth nerve palsy in 36%, third nerve palsy in 25%, and multiple diagnoses in 25%. Aberrant regeneration was noted in 78% of third nerve palsies. Padula and Argyris[18] have identified a constellation of visual deficits which they have termed posttrauma vision syndrome. These deficits may include high exophoria or exotropia, convergence insufficiency, accommodative insufficiency, and ocular-motor dysfunction. Common symptoms include double vision or a perception of motion in stationary objects or printed material, blurred near vision, photophobia, eyestrain, and headache. Further, clinicians and researchers have described visual–motor dysfunctions related to judgments of egocentric visual midline shifts following brain injury. These shifts create symptoms including dizziness and balance problems similar to those created by vestibular dysfunction.

Groswasser et al.[19] reported bilateral visual field defects in 14% of severe TBI patients. Ocular-motor defects in these patients were associated with poor recovery as defined by return to work or school. Bilateral visual field defects were more common in the poor recovery group, but this finding was not significant. A 15-year follow-up study of United States' Vietnam veterans with penetrating head injuries showed that visual field loss and visual memory loss were negatively correlated with return to work.[20] In an assessment of successful vs. unsuccessful TBI clients in a supported employment program, Wehman et al.[21] evaluated the functional limitations of those clients rated most difficult and least difficult to maintain in employment. The two areas of functional limitations which were significantly different between these groups were visual impairment and fine motor impairment. Najenson et al.[22] found that performance on The Raven Matrices Test — which is heavily loaded for visuospatial performance — was highly correlated with successful performance in the rehabilitated TBI patient's working life.

Lastly, as reviewed by Murray et al.,[23] attentional deficits in TBI patients have recently been considered in terms of information processing models rather than in terms of constructs such as sustained attention or distractibility. Shum et al.[24] provide evidence for a four-step sequential information processing model where attentional processes are considered as the sequential stages of: (1) feature extraction, (2) identification, (3) response

selection, and (4) motor adjustment. Children who had suffered severe TBI showed significant impairment on complex choice reaction time tasks designed to test each of these processing stages, as compared to age- and gender-matched controls. Based on these findings, diagnosis and treatment of these primary processing disorders may be the most direct approach to treating attention disorders in TBI patients.

Therapeutic Intervention: What and Why?

Flexibility in the Adult Visual System

The amazing flexibility in modification of the vestibulo-ocular reflex, as well as the visual perceptual apparatus, has been demonstrated in normal adults by application of inverting prisms.[25] Initially, when wearing these prisms, the world appears upside down and backwards, but with continued prism wear, the vestibulo-ocular reflex reverses and the visual perception reverts to normality. Substantial neural plasticity is present in other areas of the adult visual system as demonstrated by orthoptic therapy remediation of amblyopia and strabismus in adults.[26–28] Freed and Hellerstein have demonstrated that the visually evoked potentials (VEPs) of adults with mild TBI frequently normalize following application of vision rehabilitation techniques, in contrast to VEPs of matched participants who do not receive vision rehabilitation.[29] In the non-TBI population, vision therapy has proven effective for treatment of many visual disorders such as accommodative dysfunctions, eye movement disorders, nonstrabismic binocular dysfunctions such as convergence insufficiency, strabismus, nystagmus, amblyopia, and some visual-perceptual disorders in both adults and children.[30–32] Most of these visual disorders may be suddenly acquired with a brain injury.

Remediation of Ocular-Motor and Binocular Disorders Following TBI

Vision therapy has also been applied successfully to remediation of vision disorders secondary to brain injury.[33–38] Ron[39] studied six patients with ocular-motor dysfunctions resulting from TBI such as saccadic dysmetria and decreased optokinetic nystagmus gain. Both saccades and optokinetic nystagmus normalized more rapidly with training, as compared to control patients, and gains were maintained after cessation of treatment. Convergence insufficiency and strabismus have also been successfully remediated with vision therapy in brain trauma patients.[34,36,40] In an experiment to test the practicality of applying therapy to vision deficits in a short-term acute care rehabilitation setting, Schlageter et al.[14] failed to show statistically-significant improvements from repeated baseline measures on pursuits and saccades in six TBI patients who received between 2 and 6 hours of therapy. However, when quality of eye movements was graphed against treatment, the slope increased (showing faster improvement) during therapy for both saccades and pursuits, as compared to the baseline period. Although the occupational therapists and speech pathologists who administered the therapy were trained in a number of therapy techniques for saccades and pursuits, it became apparent during the study that *"establishing a hierarchy of progressively more difficult exercises required a significant amount of training"* (p. 447), and they may have found even better results had they used staff trained in orthoptic or vision therapy. Because of multiple demands on patient time in the acute care setting, treatment for visual disorders will generally not be completed in this setting. However, progress can be made, and visual dysfunction should be considered when making recommendations for the patient at discharge from acute care.

When surgical intervention is required for remediation of a residual posttraumatic strabismus, patterns of eye movement and teaming must be relearned. Fitzsimons and Fells[17] report that among 92 TBI patients who had extraocular muscle surgery, 50% required more than one surgery, and 30% more than two. Of these patients, 52% had satisfactory outcomes as defined by a satisfactory field of single binocular vision with tolerable diplopia (i.e., double vision) when shifting gaze to the sides. Another 27% had moderate outcomes defined as suppression or diplopia with the ability to comfortably ignore one image. Finally, 22% had persistent troublesome diplopia necessitating occlusion. Their success rates may have been even better had they used functional therapy in conjunction with surgery. Pre- or postsurgical application of therapy can be a useful adjunct to surgery in encouraging fusion, expanding the range of binocular gaze, and eliminating diplopia. *Unfortunately, it is common that the professionals who treat strabismus are dichotomized into those practitioners who apply surgery and those who apply functional therapies, rather than having the two work as a team.* Those who apply surgery, alone, rely on the existing visual system to relearn binocular fusion without any guidance. Often, this does not occur. Those who apply therapy, alone, risk not offering their patients the full range of services to assist in the best possible outcome. As more eye/vision care professionals begin to treat TBI patients, hopefully, an integrated approach will become more widely accepted.

Management of Other Visual Dysfunctions Following TBI

In patients with visual loss as measured by decreased visual acuity or visual field, low vision devices such as magnifiers, special telescopes (some of which may be spectacle-mounted) or "field expanding" devices can be applied. As our population has aged, more research and development has gone into rehabilitation for these types of visual loss which are frequent sequelae of stroke and age-related eye disease. Therapy for homonymous hemianopia has been shown to increase speed and breadth of visual search and improve both objective and subjective measures of visual abilities on activities of daily living, including, in some cases, partial recovery of visual field loss.[41,42] Therapy for visual hemifield neglect can be similarly effective.[43] Researchers at the Massachusetts Eye and Ear Infirmary have documented the effectiveness of using a multidisciplinary team including ophthalmologists, optometrists, occupational therapists, and social workers in increasing patients' functional ability during visual rehabilitation.[44]

Therapies for perceptual dysfunctions other than spatial neglect have been previously applied in non-TBI populations by some educators, optometrists, psychologists, and neuropsychologists. Development of computerized therapies for perceptual deficits have made perceptual rehabilitation more accessible and applicable by other therapists, including occupational therapists. As perception is dependent on reception, it is advisable to test for and remediate or manage any sensory visual deficits prior to testing for perceptual dysfunction other than neglect. Present evidence (reviewed by Gianutsos and Matheson[45]) generally supports the efficacy of perceptual therapy following brain injury, although one must be aware that substantial spontaneous recovery occurs during the first 6 months following the injury.

When to Treat

The timing of therapeutic intervention has been a controversial issue. Some practitioners argue that patients who are diplopic should have vision examinations as soon as possible after they are medically stabilized. Appropriate application of prism, cling patches, or partial patching (discussed later) in the early weeks postinjury can give the patient some

relief of symptoms as well as preventing maladaptations which must be trained away later. However, application of either specialized patches or prisms during these early weeks requires frequent reevaluation and adjustment to keep pace with spontaneous resolution of visual defects.

While there is evidence that some visual defects, such as muscle palsies and pareses, may spontaneously recover up to 12 months postinjury,[46] other evidence shows that, in general, untreated brain-injured persons do not spontaneously recover from binocular disorders such as convergence insufficiency.[15] The decision about when to intervene is most appropriately determined by factors other than the hope of spontaneous recovery.

During the initial 3 months postinjury, a rapid resolution may occur in many visual defects as edema in the brain diminishes. After this time, although spontaneous resolution may still be ongoing, it is likely to be slower and unwanted compensatory mechanisms, such as suppression, set in. Further, in patients who are struggling with such deficits as orientation problems or diplopia, failure to address these difficulties in a timely manner may lead to depression and a poor attitude toward rehabilitation when it is finally offered. Patients who are left to their own devices after the acute phase of medical rehabilitation is completed will find ways to survive with remaining deficits — often in ways which are not positive adaptations. Follow-up studies in untreated TBI patients show that they generally do not make continued functional progress and they may even decline in function over the long run.[45]

Even with the most careful diagnosis, one cannot always tell which patients are going to respond to treatment. In the areas of ocular-motor and binocular dysfunction following TBI, reevaluation on a monthly basis can be used to determine whether the patient is making progress. If therapy has been consistent and intensive and no progress is being made, then compensatory measures should be prescribed. Gianutsos[47] suggests that, in cognitive rehabilitation, intensive rehabilitation with an initial goal of restoration of function should be applied for 6 months. If no progress is made, then a different approach should be tried. This seems to be a good rule for visual perceptual and visual memory rehabilitation, with the modification that some compensatory strategies are often applied immediately to help the patient function while pursuing therapy.

A Useful Model for Organizing Visual Rehabilitation

Moore[48] has emphasized the importance of considering functional units in the brain, taking into account contemporary metabolic maps that show brain function, rather than thinking of the brain as it has been mapped in the last century into discrete compartments associated with individual functions. While it is necessary to have an understanding of the neuroanatomy of the visual system in order to help formulate an appropriate diagnosis, knowing the neurons does not provide an adequate basis for guiding therapy. It is equally important to have a working model of visual performance to guide rehabilitation efforts and higher-order visual testing. Neuropsychological models of information processing or even of reading will often begin with a box labeled visual input or sensory input. Exposure to such models may give the nonvision specialist the impression that visual input and its involvement in information processing is discrete and simple enough to fit into such a box. Working without a model of visual processing may encourage attempts to rehabilitate splinter skills such as convergence in cases where a more holistic approach is necessary to get the patient reading again or reoriented in space. Many therapy oriented optometrists

use a model of visual processing similar to that developed by Cohen and Rein[49] and shown in Figure 7.2. Figure 7.3 represents a simplified model which may help the practitioner keep the big picture in mind during testing and treatment.

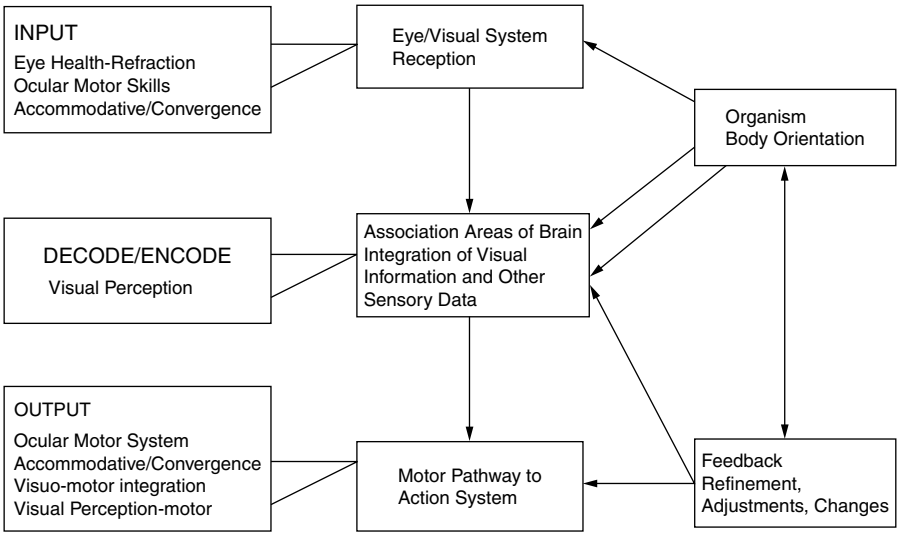

FIGURE 7.2
A model of visual function developed by Cohen and Rein, similar to that used by many optometrists to help guide vision therapy. (From Cohen, A. H. and Rein, L. D., *J. Am. Optom. Assoc.*, 63, 534, 1992. With permission).

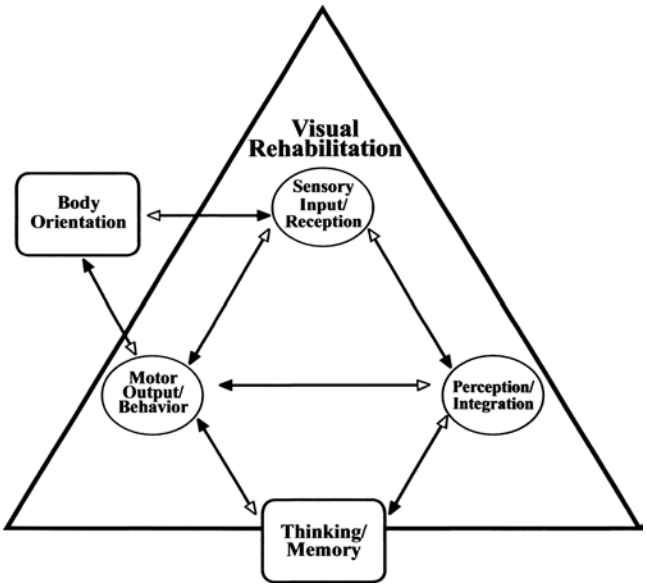

FIGURE 7.3
A modified model for guiding rehabilitation of the visual system. Functions within each processing area are as delineated in the original model by Cohen and Rein.[49] Visual processes fall within the triangle. Closed head arrows indicate the major direction of information flow. Note that all arrows are bidirectional — information flow is bidirectional in most known pathways in the visual system[2] and other bidirectional influences are explained in text.

Sensory Input/Reception

Visual system input, or reception, is dependent on formation of a focused optical image on the retina, healthy eyes, and healthy, intact pathways to primary visual cortex. Accommodation (the internal focusing of the eye mediated by the ciliary muscle) and vergence (the ability to make disjunctive or inward and outward movements of the eyes) are also an important part of getting visual input to the visual cortex without confusion. These two functions are tied together by neural feedback loops. As one expends accommodative effort (trying to focus closer), the accommodative effort drives convergence, pulling the eyes inward. As accommodation is relaxed, the eyes diverge, or relax outward, as for viewing distant targets. There is a similar, but lower, amplification loop from convergence to accommodation; as one exerts convergence effort, it drives accommodation. It should be obvious that a disruption in the balance between these two interacting systems — accommodative-convergence and convergence-accommodation — can cause serious dysfunction in eye teaming and focusing. There are useful models of such disturbances[50] reviewed by Ciuffreda.[51]

Visual reception is also dependent on the ocular-motor skills, that is, full range of motion of the extraocular muscles, the ability to fixate the target of regard, track it if desired, or saccade to another target efficiently and accurately. These abilities are dependent on feedback from areas that monitor head and body orientation and movement, as well as those areas that monitor feedback from the ocular-motor drivers. Reception ends at primary visual cortex where the initial binocular combination of input from the two eyes occurs to allow for fusion and stereopsis. The input is processed as color, contour, contrast, and depth.

Perception/Integration

Visual perception and integration are dependent on intact neural communication within visual processing areas and pathways between these processing areas, as well as intact reception. Current trends in cognitive neuroscience implicate recurrent processing in primary visual cortex (i.e., feedback from higher cortical processing areas to primary processing areas) as critical in awareness of visual input or visual perception.[52,53] Not only does damage to lower visual processing areas decrease activity in higher processing areas through loss of feedforward (e.g., occipital to parietal and parietal to frontal areas), but damage to higher processing areas decreases activity in lower level processing areas through loss of feedback connections.[7]

Integration of visual information is also dependent on pathways to and from processing areas mediating other sensory and motor functions. Much of the cerebral cortex is involved in visual processing, with close to 300 intracortical pathways between the visual areas. Therefore, it is important to maintain a holistic model of the functions of this stage of processing so that one can test for and address functional loss with some guidance from available topographic details of the injury.

The major functions of this stage in the model are organization of space and motion, form perception, and object recognition,[49,54] as well as integration of vision with the other senses and motor system input. Visual awareness is also included here. Interfaces with thinking and memory processes are not in the original model (Figure 7.2), but should be added at this stage in a bidirectional manner as in the modified model in Figure 7.3. Our percepts feed into our memories and influence how we think and our thinking and memories influence our perceptions and behaviors.

Two major concurrent vision processing pathways proceed forward from the occipital cortex — the "where" pathway to the parietal lobe and the "what" pathway to the temporal

lobe (Figure 7.1). The "where" pathway is first identified, anatomically, at the lateral geniculate nucleus where large magnocellular ganglion cells are segregated from the smaller parvocellular ganglion cells. Magno-cells are, in general, sensitive to large contours, lower contrast, faster temporal frequencies, and are retinotopically distributed more peripherally than parvo-cells (reviewed by Bassi and Lemkuhle[55]). Some magno-cells are color-sensitive, but at least half have broad-band spectral sensitivity (i.e., are insensitive to wavelength information).[56] The magno-system is preserved, in a relatively segregated manner, through primary visual cortex to the middle temporal area for motion processing, and ultimately ends in posterior parietal cortex for cortical processing of object localization and visual attention. Parvo-cells generally subserve focal color vision; they transmit more slowly and are more sensitive to high contrast, detailed stimuli. The parvo-pathway ultimately traverses to inferior temporal cortex and is involved in object perception (discussed later). The cortical magno- and parvo-processing streams maintain both separate and interactive functions. "Where" the object is and "what" the object is must be integrated in order to make sense of the world. However, it is possible to selectively interfere with memory for either "what" or "where."[57] Also, it can be demonstrated, electrophysiologically, that spatial attention has a different effect on each of these two pathways.[58]

In addition to the cortical magno-pathway, an extrageniculate, midbrain visual system[59,60] processes information both directly from the retina and from striate cortex to organize orientation in ambient space. Organization of space and motion by both the cortical magno-system and the midbrain ambient system requires interpretation of reception from visual sensory substrates, ocular-motor drivers, and from substrates reporting body orientation and motion in order to ascertain the spatial location of objects in relation to ourselves. This analysis allows us to determine whether we are moving, the external stimulus is moving, or some combination of both. The midbrain system is faster than the cortical magno-system and mediates much of our survival level orienting, head, and saccadic eye movement.

Feedback from both accommodation and convergence help localize objects in depth.[61] Form perception and object recognition require figure–ground segregation, form constancy, visual closure, and some processing of spatial relationships. These functions interact with visual reception in that the ability to perform these functions may be limited by visual field loss or degraded visual acuity, contrast sensitivity, or fixation.

Cross modality integration is dependent on intact pathways to and from the neural substrates mediating the other senses, as well as cortical processing to make matches between them. Object perception includes integration with the visual input of information about the object from our other sensory modalities.

Visual awareness, while most often taken for granted by rehabilitation professionals, is surprisingly often disrupted in TBI and other pathology of the visual system. Patients with neural damage to the visual system are often unaware that there has been any change in their function. It is only when one demonstrates to them, on a visual field printout, a line bisection or crossout test for visual neglect or a processing speed test that their performance is grossly subnormal that they begin to understand that there is a visual deficit.

Considering the covert nature of many visual deficits following brain injury, it becomes clear how such a pervasive system as the visual system can be so frequently ignored in the rehabilitation setting, as neither patients nor practioners may be aware that the patient's symptoms are visual in origin. Those systems which traditionally receive the most rehabilitation effort tend to be those that are overt in nature (e.g., language reception and expression, vestibular dysfunction, and motor dysfunction) even though the representation in the brain (and, therefore, the impact of TBI) is often considerably less for these systems than for the visual system.

Motor Output/Behavior

Organization of body movements in relation to visual targets is mediated, most directly, by the posterior parietal areas and angular gyrus. Three major pathways connect these areas with the motor areas — one via intracortical connections, one via the basal ganglia, and one via the cerebellum.[62] Individual functions of these three pathways are not well understood.

The percepts of our visual world that we construct during reception and perception are used to guide further motor activity, both within the visual system and in visually-guided motor activity such as mobility or eye–hand coordination. These percepts direct our ocular-motor activity and eye pointing. They influence the frontal lobe areas which generate executive commands for voluntary eye movements so that we may regard objects at will rather than in a purely stimulus-driven manner. They are involved in direction of the next movement, whether for perception or for action. In short, these visual percepts and the resultant thought processes dependent on them are the foundations for much of the everyday behavior of a sighted person.

Visual Thinking/Memory

Much of our thinking and memory is processed as part of the visual processing stream. Visualization of complex problems or forms is one method of problem solving and organizing which does not require language. While visual thinking, in general, is typically addressed by education in the rehabilitation setting, the skill of visualization — the ability to generate and manipulate endogenous images — is typically addressed by visual rehabilitation providers. Memory is a concept with which every person is familiar, and yet it is poorly understood. Memory has both short-term and long-term components. In neuropsychology, long-term memory is often subdivided into procedural, perceptual representation, semantic memory, and episodic memory.[63] Short-term, or working, visual memory is encoded and stored separately from auditory and haptic memories[64] and can be broken down into spatial memory (thought to be processed by the magno-stream) and object memory (thought to be processed by the parvo-stream).[58] Rehabilitation of visual memory most often involves rehabilitation of visual aspects of working memory as well as the ability to transfer this information to long-term perceptual representations.

Assessment and Rehabilitation of the Visual System

Assessment and Rehabilitation of Sensory Input/Reception

In the rehabilitation setting, testing and treatment of visual dysfunction has traditionally centered on the higher-order perceptual disorders, tending to ignore reception.[65] It is important to keep in mind that many of the higher-order visual abilities are dependent on sensory input and ocular-motor functions involved in reception.

Eye Movements

Eye movements can be classified into those which shift the direction of gaze (i.e., saccades, smooth pursuits, and vergences) and those which hold the direction of gaze steady (i.e., the vestibular driven, optokinetic, and fixation mechanisms).[66] Vergences are discussed below under binocular disorders. Optokinetic nystagmus (OKN) may be used in testing

and therapy for other visual dysfunctions, but deficits in OKN are not generally considered and rehabilitated in the TBI population as visual deficits. This may be because detection of deficits in OKN requires more sophisticated eye-movement monitoring than is available in most vision practices.

Saccades

Saccades are the fast eye movements one makes to change the object of fixation; the eyes seem to jump from one target to another. They are the movements that take us from word to word in reading and from object to object in driving. Saccades, during reading, may be affected in a bottom up manner, that is, the eye movement controllers have been damaged (see Chapter 6), or in a top-down manner, that is, the ability to comprehend text has been damaged causing more regressions and less accurate fixations due to poor guesses about what is coming next.[67] Patients with acquired primary saccadic dysmetria (i.e., saccades that overshoot or undershoot the target) will often complain of slow and inaccurate reading.

Voluntary saccades, which allow us to change our gaze at will, and stimulus-generated or reflexive saccades, where we correct our gaze or saccade to a target that has attracted our gaze, are controlled, in part, by separate brain centers and should be addressed separately. It is also important to assess the ability to inhibit saccades to peripheral targets. This may be a function of the fixation mechanism discussed below. Simple observation while the patient makes voluntary saccades between two targets or reflexive saccades to alternately lit targets gives a qualitative measure of latency, speed, and accuracy of the saccades. This procedure should be done at least for lateral saccades in right and left gaze orientation. Each eye should be observed independently. Scoring systems for these observations are reviewed by Griffin.[68]

A more quantitative approach, which can provide additional data, is provided by the Developmental Eye Movement Test (DEM).* This is a timed test in which the patient must saccade to numbers which are arrayed on a page and name them as quickly as possible. The DEM is a substantial improvement over earlier saccadic tests of this genre in that timed baseline measurements are taken with the patient reading columns of evenly spaced vertical numbers so that difficulties with decoding or verbal expression can be differentiated from difficulty with the ocular-motor task. Next, a series of horizontal rows of digits are read. The number of errors and the time required to read all of the digits are combined into separate scores for the vertical and horizontal tasks, with a higher score being slower or less accurate performance. A high ratio of horizontal score/vertical score indicates a saccadic problem. The DEM does not differentiate between difficulties in speed, latency, or accuracy, although error scores give some indication of the latter. Normative data by age is provided for times and error scores on both the vertical and horizontal tasks, as well as the ratio between them.

A variety of instruments have been designed to objectively monitor and record eye movements. These eye movement monitors give the most easily interpreted data, but are less frequently used in the clinical setting due to issues of availability and expense.

Ordinarily, when training saccades, latency, speed, and accuracy are lumped into the same scores; one trains for accuracy and then for speed, which improves as any one of the three parameters improves. Therapy may start with something as simple as saccading from one penlight to another as they are alternately lit in a dim room and progress to complex search tasks, such as finding the next in a series of letters or numbers scrambled on a page. Instruments, such as the Wayne Saccadic Fixator** or the

* Developmental Eye Movement Test: Available from Bernell Corporation, Mishawaka, IN, www.bernell.com.
** Wayne Saccadic Fixator: Available from Wayne Engineering, Skokie, IL.

Dynavision2000,* with various programs for training saccades in combination with eye–hand coordination, are both useful and motivational. A number of computer-based programs have also been developed for orthoptic treatment of ocular-motor and binocular disorders. If difficulty inhibiting saccades or sustaining fixation is noted, one can apply therapies such as making saccades only on a designated command to each in a series of targets. The ultimate goal of therapy is to develop fast accurate saccades, both large and small, which can be sustained and performed with a high degree of automaticity. The latter is tested by adding a cognitive load, such as addition or spelling, while the patient does a saccadic task. This is an important concept in much of the visual therapy of eye movements. When a cognitive load is added, performance of the ocular-motor task will break down in patients *who are allocating excessive resources to what should be, for the most part, an automatic task.* Griffin[68] and Press[69] have written excellent texts for vision care providers interested in learning about vision therapy programming and specific therapeutic techniques. Many of these therapy techniques may be prescribed by vision care practitioners for application by occupational therapists in the rehabilitation setting.

Pursuits

Pursuits are the smooth eye movements used to follow a moving object and hold a clear image of it stationary on the retina. They are complementary to the vestibulo-ocular reflex in holding images stationary on the retina when we are moving. Pursuits are limited in speed to about 30° per second. Attempts to track a faster target cause saccadic intrusions and "cogwheeling" of the movement. Pursuits are usually tested at the same time that the range of extraocular muscle motion in each eye is tested. Simple observation gives qualitative information about the ability to track a target to the full range of motion of each of the extraocular muscles monocularly, and then binocularly. The ability to track should be judged on smoothness, accuracy, stamina, and the ability to track without head movement. As with saccades, a cognitive load should be applied to judge automaticity. Griffin[68] outlines systems for scoring pursuits.

Therapy for pursuits is often combined with extraocular stretching exercises relieving restrictions or contractures of the extraocular muscles by following targets to the farthest peripheral directions of gaze possible. These exercises are also important in the initial stages of therapy for binocular disorders. If there is any deficit on monocular testing, extraocular movements are trained monocularly prior to training binocularly so that equal facility is gained with each eye before adding a fusional load to the task.

For most vision therapy, one goal is to make the patient self-monitoring. Pursuit therapy is most effective when patients can be made aware of jerkiness or saccadic intrusions in their pursuits so that they can try to correct them. Many patients will be able to feel their eyes jump when their attention is directed to noticing interruptions in their smooth pursuit. However, in many TBI patients, proprioception from the extraocular muscles seems to be diminished or absent so that they are unable to feel when their eyes jump. In such cases, cues can be added to assist the patient. One technique is to use afterimages to tag the fovea by using a camera flash which has been masked off except for a small central target which the patient fixates while the flash is triggered. The patient tries to maintain this afterimage on the pursuit target without interruption. A simpler technique which is sometimes effective is to have the therapist tell patients every time their eyes jump until the patients can begin to feel it for themselves.

Various instruments, from rotating discs with targets on them to computer-generated pursuit games, have been designed for facilitating pursuit therapy under both monocular

* Dynavision2000: Available from Dynavision2000, Markham, Ontario, Canada. www.info@dynavision2000.com.

and fused conditions. The ultimate goal of therapy is to be able to sustain smooth pursuits with either or both eyes in all fields of gaze with a high degree of automaticity, initially without moving one's head, and then, adding head, and later, body movement.

Vestibular-Driven Eye Movements

Vestibular-driven eye movements, in particular, the vestibular-ocular reflex (VOR), help hold the visual world steady as we move within it. Patients who do not spontaneously adapt to damage affecting the VOR may complain of oscillopsia, or rhythmic movement of stationary objects. One way to test for a VOR problem is to have patients read a nearpoint acuity card while shaking their head side to side and, then, up and down. In the case of a VOR dysfunction, the visual acuity will be severely degraded as compared to an acuity taken with the stationary target.[70] While therapy techniques have not been specifically developed for VOR dysfunction, applying the after-image techniques discussed above with the patient attempting to stabilize the afterimage, initially, while sitting still and, later, with head movements, may give enough extra feedback to assist in recovery. Whether the patient recovers or learns to adjust to the movement, oscillopsia should be taken into consideration in driving rehabilitation.

Fixation

Fixation, or the act of holding gaze steady on a target, was once thought to be a function of the pursuit system at zero velocity. This may be why fixation, itself, is seldom evaluated except in relation to strabismic amblyopia. However, recent evidence implicates an independent visual fixation system, perhaps located in the parietal lobe.[66] Disturbances in fixation may be considered in terms of inability to sustain fixation, as well as inability to fixate centrically and steadily. The former can be easily observed by having the patient hold fixation on a target for a minute. The ability to fixate steadily and centrically is only observable with special techniques. The easiest, most objective measure is with a visuoscope or, similarly, an ophthalmoscope with a central target. The examiner looks into the patient's eye with the scope which projects a target onto the retina. The anatomy of the posterior pole of the eye and the projected target are viewed simultaneously. The patient is instructed to fixate the target while covering the other eye. The stability of the foveal reflex and centricity with regard to the target are easily observed in this manner. Other methods require reliable subjective feedback. For instance, the Haidinger brush, an entoptic phenomenon that marks the fovea, may be elicited with an instrument such as the Macular Integrity Tester* in which the patient fixates a target and reports the location and stability of the Haidinger brush in relation to the fixated target.

In the case of inadequate ability to sustain fixation, the first step is to rule out refractive, binocular, accommodative, or other ocular-motor dysfunctions that may lead to asthenopia (i.e., eyestrain and/or headache) or discomfort. Such dysfunctions may make extended viewing aversive. They are also remediable, where a primary attention or fixation mechanism dysfunction might not be.

Unsteady or eccentric fixation is most typically encountered as a developmental phenomenon associated with strabismic amblyopia. In this manifestation, they cause decreased visual acuity but are seldom accompanied by asthenopic symptoms. There is an effective arsenal of therapeutic techniques to routinely remediate developmental eccentric fixation.[28,68] Unfortunately, unsteady fixation which is acquired following TBI may cause asthenopic symptoms as it may be bilateral rather than unilateral and it may be more resistant to treatment.

* Macula Integrity Tester: Available from Bernell Corporation, Mishawaka, IN, www.bernell.com.

Binocular Dysfunction

Accommodation

Accommodative dysfunctions are common in the TBI population.[9] They can cause blur or asthenopic symptoms at nearpoint, as well as slow focus change from distance to near and back. *A simple nearpoint acuity test does not rule out an accommodative problem* because it only indicates whether the patient can momentarily hold focus at near. It does not indicate either that patients can sustain that focus or that they have any focusing flexibility. Objective techniques, such as nearpoint retinoscopy performed while the patient processes visual information (e.g., reading or active involvement in viewing a picture), give an accurate assessment of the patient's lag of accommodation and ability to sustain accommodation on a nearpoint task. Use of such tools as convex to concave lens flippers (i.e., devices with two pairs of lenses for viewing — one pair of convex lenses which requires that accommodation relax to clear the target and one pair of concave lenses which requires accommodative effort to clear the target — set into a holder so that one can flip between the pairs of lenses) of various powers can give measurements of facility. These can be used as a subjective test with patients reading small print as they are able to clear it or as an objective test during retinoscopy. As discussed above, accommodative difficulties can cause convergence dysfunction, and convergence difficulties can cause accommodative dysfunction. In many cases, it is impossible to tell which problem is primary.

Typical treatments for accommodative dysfunctions are vision therapy or convex lenses worn either as single vision reading glasses or bifocals. In a prepresbyopic patient, vision therapy is an effective way to improve the amplitude and facility of accommodation, provided that the innervation subserving the function is sufficiently intact. Near-to-far focusing jumps and concave-to-convex lens jumps with nearpoint targets may increase both amplitude and facility. Associated vergence difficulties must be treated in conjunction with the accommodative problem for effective remediation. If rehabilitation of accommodative function is not possible in the young patient, compensatory convex reading lenses should be prescribed, generally in a bifocal format. Treatment of convergence insufficiency due to the sudden loss of the accommodative-convergence mechanism may be necessary in these patients.

Nonstrabismic Binocular Disorders

Nonstrabismic binocular disorders are those eye-teaming difficulties which do not result in a frank strabismus (eyeturn). Convergence insufficiency — difficulty pulling the eyes inward for near work — may be the most common nonstrabismic binocular finding in TBI patients. *Convergence insufficiency will often be missed by the simple pushup or near point of convergence test.* Krohel et al.[40] found that 6 of 23 TBI patients with convergence insufficiency had a normal near point of convergence but showed abnormal convergence reserves on prism testing. Prism vergence ranges should be mandatory in the visual evaluation of the TBI patient. Convergence insufficiency can lead to fatigue, headache, tearing, blurred vision, and eyestrain.[40] Often, it will cause skipping of words while reading, or transpositions when reading digits in numbers, as the eyes struggle to converge after each saccade. High exophoria (i.e., nonstrabismic outward resting posture of the eyes) is also a common finding in TBI patients. Padula[9] hypothesizes that exo- deviations of the eyes following TBI are caused by damage to the midbrain structures which integrate ambient vision and spatial orientation.[60] This would be anatomically consistent with simultaneous damage to the mesencephalic structures involved in convergence control.[15] Padula et al. have described posttrauma vision syndrome,[18,71,72] a cluster of common posttraumatic visual deficits which may include high exophoria, convergence insufficiency, and accommodative dysfunction. Using brain response testing (VEPs), Padula et

al. demonstrated visual processing abnormalities in posttrauma vision syndrome, as well as improvement in the brain response to visual stimuli with application of low amounts of base-in prism and binasal patching.[71] Their work also provides a clinical protocol for diagnosing posttrauma vision syndrome using the VEP. If posttrauma vision syndrome is diagnosed or suspected, early application of base-in prism and/or binasal patches may be profitable in treatment.

Prior to treating other binocular disorders, monocular eye movement and accommodative dysfunctions should be treated insofar as possible. Treatment of exo- binocular disorders may include prism in reading or distance lenses, binasal patches, or therapy. One difficulty with putting base-in prism in lenses is that patients may prism-adapt over a matter of days or weeks, developing the same phoria through the prisms as they had prior to introduction of the prisms. In such cases, the prescription of base-in prism increases the tonic error in binocular posture — leading some optometrists to argue that prism is poison. However, in a significant number of patients, base-in prisms provide an immediate reduction of symptoms and the patients do not prism adapt. The difficulty is in determining for which patients this will be the case. In-office, short-term trials may help in this decision. In any case, patients wearing base-in prism in their habitual spectacles should be followed carefully. If they prism-adapt, additional prism should not be prescribed.

Besides use of base-in prism, Padula and Shapiro[10] recommend use of bitemporal or binasal occluders (i.e., occluders covering only the temporal portion of both lenses or nasal portion of both lenses, respectively) applied to the patient's habitual spectacles for nonstrabismic visual dysfunctions. They suggest that bitemporal patches may reduce confusion by reducing input from the midbrain ambient vision system when the patient is attempting focal tasks such as reading. Binasal patches may be used in an effort to increase patients' awareness of their ambient vision while eliminating physiological diplopia (i.e., the normal diplopia for objects in front of or behind the plane of fixation), which may initially cause confusion in the post-TBI patient. They also argue that this encourages reorganization of the midbrain-based ambient visual system which is critical for visuospatial organization and vision during movement.

Vision therapy for poorly compensated exophoria or convergence insufficiency should include fusional exercises to improve the amplitude of, and the ability to sustain, convergence, as well as the speed of reflex fusion. Convex lenses may be used to work fusional convergence through the accommodative-convergence loop. Viewing through the convex lens relaxes accommodative-convergence so that the patient must exert more fusional convergence to avoid diplopia. Prisms can be used for manipulating images, causing the fusional vergence system to respond to the displaced image. Polarized or anaglyphic materials may be used in order to create second- or third-degree fusion targets (i.e., flat fusion or stereoscopic fusion, respectively) which can be manipulated to expand vergence ranges. At the same time, matches are developed between the ocular-motor feedback and position-in-space interpretation. Many specialized instruments have been developed for treatment of such binocular disorders. Some of these techniques may be prescribed for application by occupational therapists. Many of these techniques require more experience in vision therapy or more extensive instrumentation for effective application and, therefore, need to be performed in the vision care setting.

Esophoric (i.e., nonstrabismic inward resting posture of the eyes) deviations of binocular vision are less common. This may be due to anatomical considerations or because esophorias are more difficult to compensate for and are more likely to break down into a strabismus. Poorly compensated esophoria will often cause eyestrain or headache around the eyes or temples. Treatment may include use of convex lenses for near work, base-out prism, and vision therapy similar to that described for exo- deviations. The same cautions

regarding use of prisms apply here — perhaps even more so, as base-out prism is more difficult to remove once the patient has become dependent on it.

Strabismus

In strabismic deviations secondary to TBI, diplopia causes disorientation, as well as difficulty with spatial judgments, eye–hand coordination, mobility, and reading. Patients will often squint, close one eye, or assume head turns or tilts in order to try to block one eye or to keep objects in a field of gaze where they are able to fuse. In children, suppression and amblyopia may result. Patients who are diplopic should have a visual examination early in their rehabilitative program. Assessment of refractive status, binocularity, and ocular health do not require verbal communication from the patient. The same objective techniques that one would use to determine these conditions in a 4-month-old infant can be applied in the TBI population, when necessary. Prisms or partial patching (as discussed below) can be prescribed to eliminate diplopia so that other ongoing therapies can be more effective. Any time that prisms or patches are prescribed, frequent follow-up is required to keep pace with spontaneous and therapy-related recovery.

Fresnel (flat stick-on) prisms may be applied in an effort to reestablish fusion at the angle of the deviation. Lenses may also be applied in a therapeutic manner, using the accommodative-convergence relationship to mediate the angle of the deviation. For patients who are able, therapy is then applied, as described above for nonstrabismic errors, creating equal, efficient monocular skills, followed by vergence exercises combined with fusion, depth, and spatial localization training. Initial attempts at reestablishing fusion in adjustable instruments or with variable prisms may be met with horror fusionis-like responses where the images from the two eyes will approach each other and then jump to the other side, or may be superimposed, but not fuse into one object with the percept of depth.[73] The prognosis for recovery is best for patients with horizontal strabismus, uncomplicated by vertical deviations. However, vertical deviations will often resolve with therapy or as therapy is applied to the horizontal component of the strabismus. Residual vertical deviations can often be managed with prism ground into the patient's lenses. Patients who are not able to perform vision therapy for remediation of their strabismus are generally managed over the long term with patches and prism. They may also be managed surgically beyond the time period when spontaneous recovery might continue to lessen the angle of deviation.

Traditionally, TBI patients have been advised to use constant patching of one eye to resolve diplopia. However, this has undesirable consequences, such as loss of peripheral vision on the patched side while patched and disuse of the patched eye which may lead to suppression and/or diminish the chances of spontaneous recovery of fusion. *Partial* patching to eliminate diplopia or *patching for limited time periods* to facilitate other therapies is more desirable. If patients are unable to access rehabilitative vision care in a timely manner and diplopia is a major problem, patching the eyes on a daily alternating schedule may minimize the detrimental effects of patching until they can access such care.

Partial patches are tailored to the patient's particular deficit and should encourage recovery. As discussed above, binasal patches applied to the patient's spectacles allow for a full field of vision while eliminating diplopia. They are a particularly good patching method for treatment of esotropia and may enhance peripheral awareness while encouraging abduction. If the esotropia is unilateral, a single patch may be applied to the nasal portion of the patient's spectacles over the nondeviating eye. This technique encourages abduction of the esotropic eye, as patients must either abduct that eye or turn their head to view in the visual field ipsilateral to the deviating eye. Exotropic deviations may sometimes be treated with translucent bitemporal patches. Thus, each eye must adduct to view in the contralateral field. However, bitemporal patches limit peripheral vision and

are not recommended for long-term application or during ambulation. For patients who fuse in some fields of gaze but have noncomitant strabismic deviations, partial patches may be applied to a portion of one spectacle lens to occlude only the diplopic field of gaze, allowing for fusion, most of the time. At the same time, vision therapy should be applied to expand the field of comfortable binocular vision.

Partial patches may be as inexpensive as a piece of translucent tape applied to the patient's spectacle lenses. Cling patches* are also available commercially. These patches, which stick to the lenses electrostatically, may be easily removed for therapy and reapplied. These also come in varying densities to degrade visual acuity to approximately 20/100, 20/200, or 20/400. The less dense patches enhance patient acceptance since they are, cosmetically, quite good and can hardly be discerned on the spectacle lenses by outside observers. Binasal, bitemporal, and partial patching may not work well for persons with various types of field defects.

Because most TBI patients with secondary strabismus had normal fusion prior to their injury, their prognosis is good for recovering fusion, even if one or more muscles are palsied. Even in apparent paresis of the muscle, recovery can occur, although the prognosis is more guarded. If a horror fusionis-like response is elicited on initial testing, peripheral fusion techniques emphasizing depth and SILO (see text below) may be used until the patient is able to fuse more central targets. Antisuppression therapy should not be used on these patients until there is evidence of their ability to attain central fusion.

Suppression

Suppression is the ability to diminish or eliminate the central vision originating from one eye to avoid diplopia. In children, it may lead to development of amblyopia in a unilaterally-suppressed eye. Once suppression develops, antisuppression therapies must be applied in order to continue with fusional training.

Suppression may be considered either a blessing or a curse, depending on the goal of rehabilitation. If the goal is to restore central fusion with all of the fine motor and stereoscopic advantages that come with it, then suppression is to be avoided through proper application of prisms, patching, or early application of vision therapy. If spontaneous resolution and 3 months of intensive vision therapy show no progress at all toward fusion, then perhaps encouraging suppression to develop may be the most effective way of avoiding diplopia.

If the patient cannot learn to successfully fuse or suppress, then a monovision refractive correction may be prescribed in which the spectacle or contact lens for one eye is set for near work and the other lens is set for distance clarity. This creates one clear image at each distance so that, with practice, the patient learns to easily attend to the clear image, giving a stable referent at each distance.

Decreased Visual Acuity

TBI patients with decreased visual acuity which cannot be improved by refractive means or by increased contrast will generally profit from standard low vision rehabilitation techniques. Unfortunately, the prospect of accepting their limitations and working hard to learn to use the remaining vision in the most efficient manner possible is not as motivating as the prospect of performing other types of therapy to recover lost visual function. This makes low vision rehabilitation a less positive experience for many patients.

Numerous small telescopes have been developed for magnification of distant objects. These may be hand held for stationary viewing or for spotting and identification. Increased magnification results in reduced visual field. Therefore, telescopes used only for spotting

* Cling Patch: Available from Bernell Corporation, Mishawaka, IN, www.bernell.com.

and identification will generally have higher magnification than telescopes used for distance viewing. Telescopes may also be mounted in the top portion of a spectacle lens for frequent spot reference during such tasks as driving and note taking. A slight downward tilt of the head allows access to the telescope.

For nearpoint tasks, aids range from high powered convex lenses for nearpoint work, allowing the patient to hold reading material closer, to video enhancement of images via closed circuit television. Bar magnifiers may assist low visual acuity patients in keeping their place during reading. Magnifiers that are handheld or stand-mounted for stability are also frequently used.

One of the difficulties in prescribing for the patient with moderately reduced acuity (20/60 to 20/120) is that many magnifying techniques will slow the process of reading. One must judge whether the patient can be rehabilitated with convex lenses and proper training or whether a magnifier will be of greater assistance. Trial and error to find the correction with which the patient is most comfortable will be a large part of the decision.

Decreased Contrast Sensitivity

Contrast sensitivity is the ability to discriminate differences in luminance between adjacent areas. Low contrast situations occur in fog, darkness, and when viewing through media opacities in the eye such as cataracts. Reduced contrast sensitivity should be suspected when patients with good visual acuity complain of not seeing well. Neural damage in the visual system may also cause poor contrast sensitivity.[74] Damage to the magno-system results in a reduction of contrast sensitivity for middle to low spatial frequency (larger contours). Damage to the parvo-system results in loss of contrast sensitivity in detailed targets and may result in decreased visual acuity. Patients with diminished contrast sensitivity in the high frequency range resulting in decreased visual acuity may find magnifying low vision aids helpful. Those with diminished contrast sensitivity for middle to low spatial frequencies are not helped by magnification. Printed material for these patients should be good quality and high contrast. In well lit conditions, contrast enhancing tints (usually yellow to amber tints that screen out blue light) or overlays may be used. The selection of tint is usually based on the patient's subjective assessment of the quality of their vision. Working with special lighting for specific tasks may be helpful.

Visual Field Loss

Many patients with TBI have resultant visual field loss. Knowledge of visual field defects is important in helping patients adjust their behavior. It is also important for other rehabilitative therapists working with the patient to adjust their therapy, taking the field defect into account. Field defects may be either absolute, where there is no sensation of light or movement from within the scotoma, or relative, where brighter, larger, or moving stimuli may still be sensed within the scotoma. Assessment may range from simple confrontation testing, to tangent screen, to automated perimetry with a fixation monitor. Each has advantages and drawbacks. Confrontation testing can be done with no special equipment on patients who are unable to sit as required for the other tests. It gives a gross assessment of the extent of the visual field in each direction with each eye. However, it will not reveal scotomas within those boundaries. Tangent screen testing allows the examiner to very closely map small scotomas and islands of vision within the field which may not be mapped well on an automated perimeter that presents test points in a predetermined pattern. Automated perimeters with fixation monitoring give a relatively reliable measurement against which one may chart change in the visual field through repeated measures across time. However, the testing is often lengthy, taxing both posture and attention.

Probably the most common visual field defect necessitating rehabilitative services is homonymous hemianopia. Rehabilitation has mainly been concentrated on recognizing the field defect and working on compensatory scanning patterns, as well as mirror or prism devices to allow more peripheral areas of the scotoma to be viewed with smaller excursions of the head or eyes. Patients with hemianopia may also have mild balance difficulties (with their center of gravity shifted toward the blind field).[75] Yoked prism (discussed below) may be helpful in reestablishing balance.

Compensatory visual search into the scotomatous field is found to expand as a result of training and these gains remain stable over time. Patients with hemianopic field defects who do not receive training do not tend to use adaptive search strategies.[76]

Mirrors can be mounted on spectacle lenses[77,78] or Fresnel prisms with their apices toward the pupil can be added in the peripheral portion of the lens in the scotomatous field(s).[79] These devices move the images that fall in the periphery of the scotomatous field closer to the center of vision. Both of these techniques enhance peripheral awareness because it is easier to view farther into the scotomatous field without head movement and having the device applied to the spectacles serves as a reminder to do so. Considerable training and motivation are required for successful application of these devices as, when one scans into binocularly applied peripheral prism, the visual world jumps. If the prism is applied monocularly, then patients are diplopic while scanning into the prism and must turn their head to fixate the object of interest singly after locating it. Rather than using Fresnel prisms, the prism may be ground with patients' spectacle prescription and mounted into their spectacle lens, reducing the optical blur induced by the Fresnel type prism. Limited visual field recovery has been reported in some patients with this type of peripheral prism system applied monocularly,[42] perhaps from reallocation of cortical receptive fields. For patients with severe visual field constriction, the prism technique may be used in all affected fields.[80] Peli[81] recommends application of horizontal strips of Fresnel prism placed (base toward the visual field defect) superiorly and inferiorly across the extent of the patient's lens on the side of the field defect; for a left hemianopia, one would place the prism strips on the left lens. Peli argues that this creates peripheral diplopia, which is easier to adapt to than a peripheral prism that one scans into, and it cues attention to the unsighted visual field without regard to the lateral position of the eyes. Field expanders or reverse telescopes may be helpful in occasional sighting for orientation, as when entering a room or locating objects on a table. Distortion and minification when viewing through field expanders make them difficult to use and, again, considerable training and motivation are required.[82]

Perceptual speed and perceptual span, often trained with tachistoscopic techniques, are also important. During mobility, the patient with visual field loss must make more fixations to cover the necessary visual expanse. Perceptual speed and span are also important for reading as any visual field loss that approaches the midline will tend to slow the reading process. Patients with left field loss may not see the beginnings of longer words and misread them as similar words. They also have difficulty returning to the beginning of the next line. The simplest technique for remediating this problem is to keep a finger at the beginning of the next line down, or use an L-shaped marker that marks the line being read and has a bright flag at the beginning of the line to indicate the position of the beginning of the line. Typoscopes or rulers may also be helpful. A contrasting strip of ribbon placed vertically along the left margin is a simple, effective technique. Patients with right hemianopias lose the preview information that allows them to judge the placement of the next saccade and guess at the content of the next word. They also have difficulty judging where to return at the end of a line of print and will often return to the next line too early. A finger, hand, or strip of ribbon held at the end of the line serves as an easy marker. These patients may do better reading upside down or rotating the text

90 degrees and reading vertically so that they can preview the text coming up in their sound visual field.[83]

Lastly, there have been reports in the literature of some partial resolution of hemianopia through training with lit targets moving from the scotoma toward the intact visual field and scanning into the scotoma.[84,41] These findings have been questioned by Balliet et al.[85] who were unable to replicate findings of recovery by training with lit targets. They bring up valid concerns regarding this controversial issue. However, Balliet et al. used smaller targets in their training than were used in the original studies because the smaller target led to less intrasubject variability. In therapy, variable responses may be the hallmark of recovery. In their desire for scientific reproducibility, Balliet et al. may have thrown away the therapeutic effect. Kerkhoff et al.,[41] in a study which had positive results, used a three-step training procedure which included: (1) performing large saccades into the blind field, (2) improving visual search on projected slides, and (3) transfer of both to activities of daily living. With this procedure, they were training skills that the patient needed to acquire, and partial resolution of the scotoma seemed to be an additional gift for some of their patients.

Photophobia

Photophobia (i.e., extreme light sensitivity) is a common after-effect of head trauma.[86] Jackowski,[87] using dark adaptation studies, has demonstrated damage to rod mediated visual mechanisms in brain injury patients with significant photophobia, even though they seldom complain of their night vision being reduced. The rods (i.e., dim light vision receptors) mainly feed into the magno-visual subsystem. Cone mediated visual mechanisms were also damaged in these patients, but these deficits were small in comparison to the rod mediated visual loss. The cones (i.e., daylight vision receptors) mainly feed into the parvo-pathway. The magno- and parvo-pathways are mutually inhibitory. Jackowski has hypothesized from her findings that damage to the rod system, or magno-pathway, disinhibits the cone or parvo-pathway, causing this bright light sensing pathway to be overly responsive; this mechanism may be the cause of posttraumatic photophobia in many patients.

Patients who have posttraumatic binocular disorders or pupil dilation of one or both eyes may also complain of photophobia. Successful treatment of the binocular dysfunction will lessen the photophobia in cases where this is the primary cause. Otherwise, photophobia may be handled with any number of tints in the patient's spectacle lenses — the color and density of which are mainly prescribed for subjective comfort. Photochromic lenses, which darken in sunlight and lighten indoors, may be helpful, although they do not darken well for driving applications. While eye protection from ultraviolet radiation should be a consideration for everyone, it is even more important to incorporate ultraviolet protection into tinted lenses for patients with mydriatic pupils. In extreme cases of mydriasis, it is sometimes possible to prescribe an opaque custom contact lens with a small transparent pupil to decrease the light entering the eye. However, often, patients with mydriatic pupils have dry eyes and contact lenses would be contraindicated.

Assessment and Rehabilitation of Perception/Integration

Localization and Spatial Vision

There is little information on effects of brain injury on the magno-pathway until it reaches cortex. However, it is known that the large axon diameter of the magno-cells makes them

more vulnerable to various types of damage as in glaucoma and Alzheimer's disease.[55] Disorders of motion perception are rare.[88] Indeed, studies in monkeys show that a lesion in the middle temporal area produces disorders of motion perception but that most of these disappear within a few days, presumably because the function is taken over by redundant pathways. Damage to the posterior cerebral cortex (usually, right posterior parietal) often results in spatial inattention to the contralateral visual field known as *unilateral spatial neglect* (USN) discussed below.

A number of reception dysfunctions affect perception of spatial localization and orientation. For instance, we use the feedback from our vergence system to assist us in judging distance. If our eyes are more converged, then the target we are fixating is seen as closer. In persons with good binocularity, this effect, called *smaller in, larger out* (SILO),[89] can be demonstrated by the use of prisms. If one fixates a target and places base-out prism in front of the eyes, the images of the target are moved in a convergent direction and the eyes must converge in order to avoid diplopia. The target will be perceived as having moved *in* toward the observer and will appear smaller than before. Size constancy dictates that objects get larger as they come closer but, since the target has not really moved, the image size on the retina remains unchanged. Therefore, since the vergence system says the object is closer but the image size remains unchanged, the interpretation must be that the object is now smaller. Base-in prism produces the opposite effect, where the eyes diverge, the object appears to move out, away from the observer, and appears larger. Due to the roles of accommodation and convergence in depth perception,[61] sudden onset of dysfunctions in accommodation or convergence secondary to TBI can make objects appear closer or farther away than they actually are, effectively collapsing or expanding visual space.

Conversely, feedback from the cortical and subcortical spatial processors affects the vergence system. For example, one type of convergence is driven strictly by proximity to an object; targets close to the face make us converge even though we may be viewing through an optical system set at infinity. The TBI patient with a primary visuospatial disturbance will often have inaccurate eye pointing.

Feedback in visuospatial processing runs both ways, from the binocular system to visuospatial processors and from visuospatial processors to the binocular system. Therefore, the most effective therapy for disorders of spatial perception in depth must take into account the binocular response. Similarly, the most effective treatment for eye teaming will often concentrate not only on achieving the correct motor response but also on creating correct spatial judgments which can be used to guide the motor response.

Other difficulties in spatial organization may be reflected in inability to properly localize objects in relation to oneself. Egocentric "midline shifts" of varied etiologies have been noted in patients following brain injury. These shifts in midline perception can cause shifts in posture and weight distribution which may cause difficulty with balance and gait. They may also affect eye–hand coordination. Tests used to detect egocentric visual midline shifts include line bisection tasks[90,91] and, more commonly, subjective judgment by the patient of when a wand or pencil, held in a vertical orientation and moved laterally, is directly on the horizontal midline (i.e., in front of nose).[10] Visual field defects, hemifield visual neglect, disruption of the midbrain ambient visual system, tonic ocular-motor imbalance, and imbalances in extraocular proprioception, or efferent copy commands to the extraocular muscles, are all possible causes of midline shift. As described by DeRenzi,[92] tonic ocular-motor imbalance is an increased tone in the muscles turning the eyes to the side contralateral to the lesion. During routine testing, it is masked by the fixation mechanism, but it can be elicited by having the patient attempt to look straight ahead in darkness. During development, we learn to maintain position constancy of objects in spite of eye movements by comparing the efferent copy (commands going out to the eye muscles) and

proprioceptive information received from the eye muscles, with the movement of the retinal image.[66] As the eyes, extraocular muscles, and separation between the eyes grow and change, slow adjustments in these systems take place. However, in TBI, a sudden change in any one of these systems may occur, changing the perceived location of objects in relation to ourselves.

Therapy for spatial distortions may include therapy for accommodative and convergence disorders as described above, with special emphasis on development of SILO and spatial localization. Lenses and prisms may be applied in either a compensatory manner or for therapy purposes. Spatial and postural effects of these optical devices are thoroughly reviewed by Press.[93] Padula[9] advocates use of small amounts of base-in prism in order to facilitate reorganization of the ambient system by reducing stress on the peripheral fusional system in cases of exophoria. Yoked prisms (i.e., equal amounts of prism in front of each eye with both bases in the same direction — up, down, right, or left) are an effective intervention for many cases of egocentric midline shift. These prisms move images of the surrounds in the direction of the apex of the prism for both eyes. Low amounts of yoked prism may be used in a compensatory manner[18,94] to shift images of objects that belong on the visual midline to the recently misplaced perceived visual center; this relieves the perceptual mismatch between what actually *is* and what is perceived — often restoring balance, normal gait, and the ability to move about easily in the world. More often, large amounts, such as 15 prism diopters, will be used in therapy to force problem solving and increase flexibility in the sensorimotor system. Activities such as walking or tapping a swinging ball while wearing these prisms involve recalibration and integration of vestibular, proprioceptive, kinesthetic, and extraocular efferent copy systems. This is an extremely effective technique for disrupting habitual patterns in patients who have been unresponsive to more instrument-based therapies so that, with guidance, they can reorganize their visual-motor system in a more adaptive manner. It is important to note that, in an observer with a normal visual system, prism adaptation would be expected to occur with long-term wear. Therapeutically, yoked prisms are only worn for periods extending from a few minutes to a few hours. Presumably, those individuals who experience a long-term compensatory effect wearing yoked prism full time have visual dysfunction which precludes prism adaptation to this prescription. This reasoning makes sense in that, if these patients had been able to do the sort of reorganization that prism adaptation requires, they would probably not have sustained an egocentric visual midline shift.

Unilateral Spatial Neglect

Unilateral spatial neglect (USN) is a phenomenon where an entire hemifield (usually the left) is simply unattended, as if a hemianopia existed there. Worse, patients are unaware of the defect. This makes them more prone to accident and more difficult to rehabilitate than the hemianope without neglect. When neglect affects only the visual system, it may easily be mistaken for hemianopia and, indeed, often coexists with true hemianopia. Recently, split-brain research[95] has provided evidence that the right hemisphere allocates attention to both visual fields, where the left hemisphere allocates attention to only the contralateral field (Figure 7.4). This finding in split-brain patients suggests that the right hemisphere allocation of attention to right visual field is probably mediated through subcortical mechanisms. It may also help explain why most cases of neglect are secondary to right brain damage. Although USN is easily mistaken for hemianopia, the mechanisms and damaged brain substrates underlying USN are quite different from hemianopia. Hemianopia is a sensory loss, where the damaged neural substrates are in the postchiasmal visual pathway up to and including primary visual cortex. USN is a perceptual deficit, where the neural substrates necessary for sight are intact, but the visual substrates or

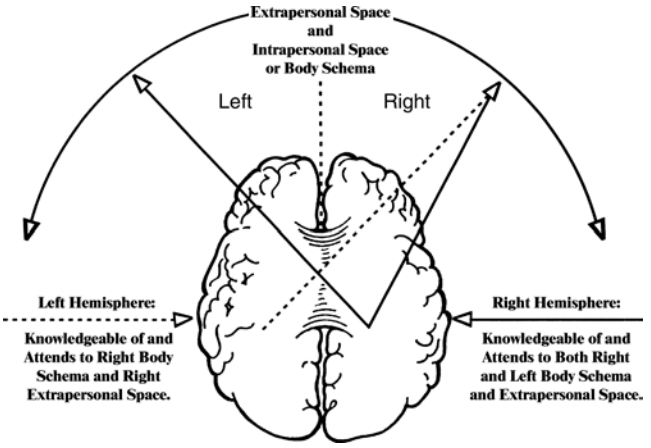

FIGURE 7.4
Allocation of spatial attention by the cortical hemispheres. The right hemisphere allocates spatial attention to both right and left visual fields, while the left hemisphere allocates attention to only the right visual field. Thus, USN of the left visual field (following right brain damage) is considerably more common than USN of the right visual field. (Adapted from Moore, J. C. and Warren, M., Effect of visual impairment on postural and motor control following adult brain injury, Continuing education workbook by visABILITIES Rehab Services, Inc. [www.visabilities.com].)

pathways necessary to attend to or perceive the sensory input are not. These neural substrates probably lie in two major centers of the brain — the posterior parietal lobes, which are involved in allocation of visual attention, and the frontal lobes, which are involved in generating eye movements.[7]

Various tests, including drawing, line cancellation, pointing to objects scattered around the room, reading a newspaper article, and line bisection, have been developed to determine the presence of USN. USN may vary in degree and appear on some tests but not others.[96] Inattention may also be differentially distributed along the vertical meridian of the neglected field.[91,97] As reviewed by Kerkhoff et al.[41] during line bisection tasks, patients with neglect typically transect the line off to the side contralateral to the field defect. Patients with hemianopia generally do the opposite, deviating in the direction of the scotoma. Patients with both are more likely to bisect the line. Compared to patients with hemianopia without USN, patients with USN have even more abnormal scan paths when viewing simple figures and with fewer excursions into the blind field.[98]

Clinically, three considerations are important during therapy for USN (N. W. Margolis, personal communication). First, the patient must be made aware of the condition. Second, compensatory strategies such as scanning and reading strategies should be taught. Last, these strategies must be generalized to both static, predictable stimuli, such as those encountered in reading or walking down a familiar corridor, and to dynamic, nonpredictable stimuli, as encountered in new environments. Gordon et al.[99] present a three-step program for remediation of perceptual deficits in patients with right brain damage. Step 1 is basic scanning training. Step 2 is somatosensory awareness and horizontal size estimation, and Step 3 is complex visual perception training combined with left to right visual scanning within these tasks. They present evidence that, with extensive training, these functions generalize to daily living. Gianutsos[45] reviews the literature on perceptual rehabilitation in USN and concludes that, overall, the efficacy of therapeutic intervention is supported. However, studies of solely microcomputer-based scanning therapy have not been shown to generalize.[100,101] For an excellent review of diagnostic and therapeutic activities, see Margolis.[102]

Object Perception

The visual percept we construct from sensory signals supercedes even the concrete sensation of touch. For instance, if an object, such as a square of plastic, is viewed through a minifying lens and is simultaneously manipulated by the hand (with the hand covered so that it cannot be used as a visual cue), the observer reports the square as being smaller than the real square. This is true whether the method of report is visual (i.e., picking a matching square out of a range of squares of various sizes), visual and tactile (i.e., drawing the square to size), or, surprisingly, tactile (i.e., picking a matching square by touch alone).[103]

It has been suggested that, visually, we construct perceptual objects via a two-step process.[104] First, preattentive data-driven filtering produces shapes and registers their features, as in reception. Then, focal attention is used to select a spatial location and integrate the features registered there into a perceptual object. This is analogous to figure-ground organization and should be concept-driven processing rather than data- or sensation-driven. Evidence arguing for this feature integration theory comes from the way that stabilized retinal images fade feature by feature rather than in small random parts. Principles at work during the second integration stage may be the Gestalt principles of proximity, good continuation, similarity, closure, and pragnanz (i.e., simplicity, regularity, or symmetry) or local vs. global processing. In addition to integrating visual features, object perception includes cross-modality integration (i.e., integrating auditory, tactile, and olfactory sensations with visual information to complete the perceptual object). Spatial orientation, both the ability to process the orientation of external objects (extrapersonal orientation) and the ability to process the orientation of ourselves with regard to other objects (personal orientation), is discussed here because the treatment modalities are generally more similar to those used with object perception, rather than other spatial dysfunctions. Personal orientation may be supported by the frontal lobe (particularly in the left hemisphere); extrapersonal orientation may be supported by the "where" pathway, particularly the right posterior parietal area.

Assessment and treatment of perceptual/integrative vision must take into account dysfunctions in reception. Multiple tests, with some redundancy, are necessary to differentially diagnose perceptual dysfunction of the visual system. For instance, copy-form tests are useful and may tell you something about spatial organization, but if the forms are poorly reproduced, you do not know whether this is due to difficulties in reception, perception, visual–motor integration, or fine motor coordination. One must have a battery of tests that probe perceptual functions such as figure-ground discrimination, closure, and spatial organization, as well as cross-modality and visual–motor integrative functions from different perspectives using different modalities. Gianutsos[45] reviews most of the available perceptual tests in the literature. For a sample test battery, see Aksionoff and Falk.[105] The perceptual workup will generally take 2 to 3 hours to administer and may need to be broken up into multiple sessions for TBI patients who fatigue easily.

During therapy, the patient and therapist must constantly keep in mind that it is the process, not the final answer, that is important. Where possible, the strategies patients are using to solve a particular problem in therapy should be discussed. This creates awareness of the process, insight for the therapist, and provides the opportunity for the therapist to suggest modifications in the patient's problem-solving strategy. As reviewed by Groffman,[106] perceptual therapies may be considered as falling into a number of treatment modalities: (1) motor activities, (2) manipulatives, (3) instruments, (4) vision therapy, (5) lens therapy, (6) auditory therapy, (7) workbooks, toys, and games, and (8) computers. The modality is tailored to fit the level and perceptual deficit of the patient.

While gross motor activities applied in vision therapy have often been criticized by those not involved in therapy, they are sometimes necessary to create more optimal support for the visual system. The eyes and visual system do not exist in isolation; the

eyes are horizontally displaced from each other in the head and the biomechanics are such that they are intended to work with a horizontal disparity in relation to gravity. Tilting the head induces ocular torsion. Gross motor activities are also used for creating visual–proprioceptive and visual–kinesthetic matches in ambient space. Vision is dominant over touch in the normal visual system. However, in therapy, proprioceptive and kinesthetic feedback can help teach veridical visual perception. In the rehabilitation setting, many therapeutic activities with these two goals can be taken over by physical or occupational therapists.

Manipulatives are objects that can be used on the table top so that they can be handled, rotated, rearranged, and examined in a very concrete way. They allow for learning higher-order visual concepts such as visual discrimination, form perception, and spatial orientation and organization with very concrete tools. These include blocks and puzzles specifically designed to teach perceptual skills. Other common examples of manipulatives are flannel boards (used with felt shapes of varied sizes and colors), geo boards (i.e., boards with evenly spaced pegs on which designs are made by stretching rubber bands between the pegs), or Peg-Boards™ which can be used for reproducing patterns with or without rotations in orientation. Manipulatives also provide excellent eye–hand coordination activity.

A variety of instruments have been developed for visual–perceptual training. Instrument techniques are varied and seem to provide additional motivation to many patients. An example would be adjustable speed tachistoscopes which are used to increase visual perceptual speed and span, as well as visual attention and short-term memory. Tachistoscope targets may vary from abstract geometric forms to be copied, to digit strings, or words. They are also useful to demonstrate USN or hemifield loss to the patient as, without time to scan, they will only see the portion of the word presented in the intact field.

Application of vision therapy to remediate receptive dysfunction often involves visual perception — both in spatial organization as discussed above and in that many fusion tasks require figure-ground discrimination. Lens and prism therapy have already been discussed in terms of shifts in the localization and orientation of local surrounds.

Use of the auditory modality can enhance integration of visual and auditory senses. A number of tape and record programs are available for development of various perceptual and perceptual-motor skills including spatial relations, directionality, and visual–motor integration.[107]

Many workbooks, toys, and games are available in educational supply stores, including popular activities with hidden pictures or words for figure–ground discrimination and form perception. Worksheets with simple, incomplete figures to be completed by the patient may be used for development of closure, as well as form perception. These tools also help develop eye–hand coordination. They are generally two-dimensional representations, but have the advantage that, once they understand the process, patients may practice unsupervised with worksheets.

With most of the above activities, the understanding of the visual goals, experience, and creativity of the therapist are key to the success of therapy. However, through development of computer programs, perceptual therapy has become more accessible and more easily administered by other rehabilitation disciplines such as occupational therapy. A number of perceptual programs which combine the challenge and motivation of a video game with good perceptual therapy are commercially available. Such programs were reviewed by Press[108] in 1987. Although more programs have been marketed since then, many of the same companies are developing them, and Press' review is a good resource for those interested in applying these techniques. Computer therapy generally requires the ability to manipulate a joystick or press a limited number of response keys. For patients having motor control problems, this may be easier than using workbooks or manipulatives.

Visual Agnosias

Agnosia is the inability to recognize objects visually. Object recognition may be apperceptive, where the perception of the object is faulty, or associative, where the object is perceived correctly but cannot be associated with prior memories or past experience.[109] In apperceptive agnosia, patients might not be able to match similar objects, draw or copy objects or shapes, or name objects by sight. However, if allowed to use tactile input, they could both name and match the object, as well as describe its function. Apperceptive agnosia is rare and is associated with diffuse cerebral damage of the occipital lobes and surrounding areas.

In associative agnosia, objects and shapes can be matched but the patients are unable to associate them with past experience or function. For instance, they may be able to draw a key that is placed before them but be unable to name it or describe its function. When allowed to handle the key, they could both name it and relate that it is used to unlock doors. Associative agnosias can be surprisingly specific. The more common types of agnosia include object agnosia, prosopagnosia (i.e., inability to recognize familiar faces), and color agnosia.

Diagnosis of visual agnosias is important in deciding the proper course of treatment — therapy or compensation. Associative agnosias may be due to lesions in the pathway that connect the visual "what" pathway with memory areas. De Haan, Young, and Newcombe[110] have shown that covert recognition of objects and faces may exist in the absence of overt recognition. They suggest that this may provide a foundation for rehabilitation. Sergent and Poncet[111] report some restoration of overt face recognition under specific circumstances in one patient. While, in some cases, restoration of function may be possible, therapy to directly address the agnosia is likely to be a long process and success is not guaranteed. Compensatory strategies, as for low vision/blind patients, may be the best alternative for immediate management of agnosia.

Alexia

An important part of text recognition is the decoding of visual percepts into language. Interruption of visual pathways at the left angular gyrus[112] or splenium[113] prevent this decoding process from occurring, resulting in acquired alexia or inability to read. Most case reports of this dysfunction show some residual reading function. Treatment of alexia using integration strategies and based on the patient's residual reading skills has been successful. Often, a letter-by-letter reading strategy can be employed by these patients, although it severely slows reading. Motor rehearsal, in terms of copying or tracing letters and words, as well as flash card techniques pairing the written with the spoken word have been applied with some success.

A successful strategy employed with one patient is described by Daniel et al.[112] Initially, the patient spelled words aloud from flashcards and then said the word (as he recognized the word from auditory spelling). With practice, the patient was able to substitute covert spelling. Continued practice in this manner significantly increased his ability in reading and naming so that he was able to return to work within 4 months postinjury. At the 1 year follow-up, reading was still laborious but the patient was able to read sufficiently to function in his job.

Assessment and Rehabilitation of Motor Output/Behavior

Visually-directed motor output includes not only the planning and execution of eye–hand coordination and visually-guided movement through space, but also the planning and

execution of the next eye movement. As in the model (Figure 7.3), reception affects perception which affects cognition — and both of the latter affect programming of the next eye movement, feeding back into reception (control of binocularity, eye movements, and fixation). This is a flexible, but closed, loop.

The Eyes

Most aspects of assessment and rehabilitation of motor output to the eyes have been discussed in the Assessment and Rehabilitation of Sensory Input/Reception section in this chapter. The rehabilitation already discussed is generally performed in the vision care setting. Some specific exercises may be prescribed for application by occupational therapists in either inpatient or outpatient rehabilitation settings.

In addition to the aspects of ocular-motor and binocular control which have already been discussed, ocular-motor planning and integration with the output controllers to the eyes are involved. Ocular-motor gaze apraxia is the inability to execute purposeful eye movements (reviewed by Roberts[109]). Patients with ocular-motor gaze apraxia may be differentially affected for various stimuli, e.g., unable to change fixation in response to verbal commands or peripheral visual, auditory, or touch stimuli. This may be exploitable in that one may be able to practice saccades to a multimodality stimulus and wean out the intact modality. An activity such as Letter Tracking* where one underlines rows of letters until a target letter is reached and then circles the target letter, may allow tactile-proprioceptive feedback to help guide eye movements. Treatment here falls into the realms of neuropsychology, occupational therapy, and vision therapy.

Compensatory strategies should be trained at the same time that remediation is attempted. Many compensatory strategies developed for low vision or the blind may be useful. Other strategies that lessen the necessity of looking in a particular location or reduce the need to scan can also be taught. For instance, moving the television away or using a small screen lessens the need to scan the scene in an organized fashion.

The Hands

Eye–hand coordination will be affected by receptive and perceptual problems, as well as by motor planning and integration of percepts with motor output controllers. Mild difficulties that occur developmentally in these areas will often result in clumsiness or difficulty with such tasks as producing clear handwriting. More severe dysfunction is described by two terms — *optic ataxia* and *constructional apraxia*.

Optic ataxia is an inability to visually guide the hand toward an object. Differentiating optic ataxia from primary dysfunctions in motor control can be achieved by having patients touch their index finger on one hand with the index finger on the other. Usually, in optic ataxia, the misreaching occurs for objects in the peripheral field. However, in more severe cases, misreaching will occur for visually fixated objects.[109] For milder cases, training the patient to visually fixate manipulated objects may be all that is required.

Constructional apraxia generally results from lesions of the posterior parietal lobe or the junction between occipital, parietal, and temporal lobes. It may be due to perceptual deficits, more frequently associated with right hemisphere lesions, or motor function deficits, more frequently associated with left hemisphere lesions. Walsh[114] lists differential effects on drawing which may be used to discriminate between perceptual and motor etiologies. For instance, right hemisphere lesions will tend to result in energetic, scattered, or fragmented drawings with a loss of spatial relations and orientation; left hemisphere

* Letter Tracking: Available from Academic Therapy Publications, Novato, CA.

involvement tends to result in drawings which are spatially intact and coherent but simplified and laborious, lacking in detail.

Again, treatment here falls into the realms of neuropsychology, occupational therapy, and vision therapy. A multitude of hand–eye coordination activities exists in the literature. For constructional apraxia, the differentiation should be made as to whether it is primarily perceptual or primarily motor and treatment should emphasize that modality.

The Body

As discussed above, receptive and perceptual dysfunctions can lead to adoption of head tilts or turns and shifts in posture, creating or complicating problems in balance during standing and walking. Patients are often unaware of these postural adjustments and, when asked, will deny any distortion in their percept and usually in their posture, even though something as easily noticed as a pronounced head tilt may be present. Testing for binocular dysfunctions and conditions that may contribute to egocentric midline shifts in the vertical and horizontal directions has been discussed. The vision practitioner must take a careful history and specifically ask about difficulty with balance, instability, mobility, etc., as most patients with these symptoms will often not bother to tell an eye doctor about these difficulties, as they assume the symptoms are unrelated to their eyes.

If a binocular dysfunction exists, the associated postural problems generally resolve as the binocular problem is remediated or when appropriate patching is applied. Treating the binocular difficulty not only relieves the diplopia or intermittent loss of fusion which can cause patients to adopt compensatory head and body postures, it may also involve teaching patients to reorganize their visual space in which the binocular problem has created distortions.

In the case of an egocentric midline shift, the specific etiology is often not diagnosed. Tests for midline shift or observing immediate responses to large amounts of yoked prism may be the extent of the diagnostic procedures. The effects of yoked prism on spatial organization and resultant shifts in posture with a normal visual system are well documented (reviewed by Press[93]). Yoked prisms move the images of the ambient surrounds in the direction of the apex of the prism for both eyes. In the normal visual system, this gives a funhouse effect. It is, initially, rather disturbing during head movements and walking to have the world shifted to the right or left or, seemingly, stretched upward or squashed downward before you. Base-up prism will generally cause wearers to shift their weight backward onto their heels; base-down prism generally has the opposite effect, causing the wearer to shift weight forward onto the toes. Sometimes, these prisms may be prescribed to assist the physical therapist in rehabilitation of standing and walking. Often, with TBI patients, yoked prism applied in one lateral direction will create no noticeable difference and application in the opposite direction will make them unable to walk as they try to balance against the shift in surrounds. This type of behavior is a good indication that yoked prism therapy or compensatory yoked prism in patients' spectacle lenses can help normalize their posture and balance, either by reorienting their egocentric visual midline or by moving the image of the outside world to match their new internal visual midline. Patients who veer in one direction while walking may also benefit. Even without a visual midline shift, yoked prisms used for short therapy periods may be useful in breaking down maladaptive habitual postures which are resistant to treatment.

Similarly, visual interventions may be useful in patients with upper limb hemiparesis, although there is not a visual cause. Practicing visual imagery of movement of the paralyzed limb in conjunction with physical and occupational therapy can improve outcomes over therapy alone.[115]

Assessment and Rehabilitation of Visual Thinking/Memory

Visual images may be stored in either analog or verbal storage. Therefore, when attempting to rehabilitate visual thinking and memory, it is important to be sure that the patient is not merely encoding the information verbally but actually forming the mental image. Unlike visual perception, which is largely a bottom-up process, visual imagery is largely a top-down process. Visual imagery uses visual information that has been previously organized and stored; therefore, it is often possible to use visual imagery even though, after a TBI, visual input and perception may be disordered. Thus, sometimes, it may be trained in parallel with, or even in the absence of, organized visual perception.

Visualization, or use of visual imagery, has long been considered a useful high-end visual task by therapy-oriented optometrists. Visualization can be used for visual memory enhancement, such as visualizing the spelling of a word, or for spatial relations and spatial organization, for instance, visualizing object rotations or visualizing a map of how to get home from the grocery store. Numerous studies using various biological indices (e.g., electrophysiology, cerebral blood flow, and other types of brain activity imaging) as well as studies of adults with brain damage show that, when internally constructing visual imagery, we may use many of the same visual representations as in constructing visual percepts from sensory input (reviewed by Farah[116] and Kosslyn and Thompson[117]). Techniques based on visual imagery may be used effectively for perceptual therapy for those patients who do not have manipulative abilities, provided that they are effective at using imagery. Problem solving with visual imagery occurs both by using visual imagery from memory and from imagination. These are separate skills and are used differently in problem solving.[118]

Visual memory, particularly visual sequential memory, is frequently impaired following TBI. Often, when there is post-TBI memory loss, verbal compensatory strategies are employed, such as list making and writing in a calendar or log. These techniques rely heavily on left hemisphere mechanisms. Rehabilitation of visual memory, which can be built on visual imagery, a heavily right-hemisphere function,[119] can provide supportive memory function and help organize incoming visual information, reducing general confusion.

There are many well-standardized tests that tap visual memory. One such test, which taps short-term visual memory and visual sequential memory, is the Test of Visual Perceptual Skills[120] (also available in Upper Level[121]). An advantage of the Test of Visual Perceptual Skills is that it allows the patient to simply point to the correct answer, minimizing the need to generate complex motor or verbal responses. It also provides separate assessments of visual memory for figures and visual sequential memory, the latter being critical in reading comprehension and in creating order from the visual information received.

One representative technique for practicing visual imagery from memory and improving visual memory is to use flannel boards. The therapist and patient have matching felt forms such as squares, circles, rectangles, and triangles of varying sizes and colors; each of them also has a flannel board on which to place the forms. The therapist places some of the forms on a flannel board in a spatial or sequential pattern. The patient is instructed to form a mental image of the pattern presented without using words to describe it. Then, the therapist's board is covered and the patient reproduces the pattern on his/her flannel board. As the performance improves, the number of forms is increased, the exposure time is reduced, and the delay between exposure and reproduction is increased in order to encourage transfer to long-term memory. Distracters may be interposed during the delay between exposure and reproduction. Flat, three-dimensional blocks, available commercially in foam or wood, can be used for patients who have difficulty manipulating felt forms.

Using visual imagery from imagination is a separate skill and is used in problem solving. Activities that emphasize this skill would include solving constructional or rotational problems.

Summary

The term *visual rehabilitation* is so broad that it often encompasses the services of neuropsychologists, occupational therapists, and psychotherapists, in addition to ophthalmologists and optometrists, and specially trained orthoptists or vision therapists. Besides damage to the receptive structures such as the eye and optic nerve, visual dysfunction may be caused by damage to any lobe of the brain, as well as midbrain structures and cranial nerves. Functional deficits include photophobia, decreased visual acuity or contrast sensitivity, ocular-motor disorders, binocular dysfunction (including strabismus), visual field loss, spatial disorientation, imbalance, unilateral spatial neglect, other visual perceptual disorders, integration disorders, and problems with visually-guided motor planning and motor output.

Visual sequelae are quite commonplace in the TBI patient, but often overlooked. Therefore, once the medical/surgical rehabilitation of the visual system is complete, the issue of functional recovery or compensation must be examined. Vision care specialists who provide other patient populations with orthoptic or vision therapy or low vision services will generally be able to adapt many of their techniques to working with the TBI patient. Treatments often must be innovative and coordinated among the various professionals providing rehabilitative services. Visual sequelae to TBI can affect the patient's ability to perform such varied tasks as reading, walking, and driving. Unrehabilitated functional visual deficits can interfere with other therapies and with the patient's ability to perform activities of daily living, as well as return to work or school. They may also be a source of emotional turmoil as the patient may experience unexplained feelings of imbalance, spatial distortion, or visual confusion, and may be unjustly suspected of malingering.

The neuroanatomy of the visual system is so complex that, in order to provide effective therapy, one must have a working model with which to organize rehabilitation. Such a model is described in Figure 7.3. The major components of the model to be considered in diagnosis and therapy are: (1) sensory input/reception, (2) perception/integration, (3) motor output/behavior, and (4) visual thinking/memory. In this model, each component affects the other. Our receptive functions affect perception and survival motor outputs. Our percepts affect our motor planning/output, as well as our thinking and memories. Our thinking and memories mediate our perceptions, as well as affecting our motor planning/output; motor planning and output determine where our bodies are and how we are going to use our eyes next — mediating receptive function. Carefully planned vision therapy or use of lenses and prisms can intervene in any of these areas in a constructive way, or disruptively to break down bad adaptations.

The redundancy of the visual system as well as the flexibility of the visual system — demonstrated by experiments such as adaptation to inverting prisms, together with clinical experience such as therapeutic remediation of strabismus and amblyopia in adults — makes recovery of function a reasonable goal for many visual dysfunctions following TBI. While one cannot always predict which patients will respond to such therapy, it seems inappropriate to offer less if there is a chance of recovery. Where therapy is ineffective at restoring function within a reasonable time frame, there are many compensatory devices and strategies that can be applied, for instance, partial patching, prisms, or low vision devices and techniques. Even these

should be prescribed with an eye toward maximizing function within the limits set by the patient's condition. The area of visual rehabilitation for TBI patients is still in its infancy. However, many visual dysfunctions encountered in TBI patients have been addressed for other special-needs populations. The multiple deficits in sensation, speech and language, cognition, and motor control encountered in TBI patients add to the challenge of providing effective vision care.

Illustrative Visual Case Studies

Patient J.G.

Patient J.G. was seen for vision evaluation 4 years after sustaining a mild TBI when she slipped and hit her head. Since then, she had been unable to read, sew, or do any near work for more than 10 minutes without getting a headache. She also complained of dizziness and photophobia. She had been through vision therapy previously but on an intermittent basis due to geographic constraints. She was admitted to a postacute inpatient rehabilitation setting for treatment.

J.G. was diagnosed with accommodative and convergence insufficiencies, as well as a saccadic dysfunction. Based on her symptoms and these findings, a working diagnosis of posttrauma vision syndrome was indicated. Glasses were prescribed for full-time wear. As J.G. was orthophoric at distance, base-in prism was not prescribed. However, she received a bifocal (in order to compensate for her accommodative insufficiency) with binasal patches (to help reduce her visual confusion and reorient her in space). J.G. reported immediate relief of many symptoms, with decreased photophobia and increased ability to do near work while wearing this prescription. Because her stay would be limited and her visual complaints were central to her rehabilitation, J.G. was seen weekly in the optometrist's office for vision therapy. Exercises were prescribed for convergence, accommodation, and saccadic dysfunction, which were administered by occupational therapists daily at the rehabilitation center. J.G. responded well to her prescription, binasal patching, and vision therapy. She simultaneously underwent vestibular therapy with the physical therapists. Within 3 months, the binasal patches were removed from her glasses and she was able to read and sew as long as she liked (which turned out to be for hours at a time). She continued to wear the glasses full time. The rehabilitation center arranged for her to spend an evening waitressing in a local restaurant (this was her former occupation) and she performed so well that the owner offered her a job. She returned to her home feeling fully rehabilitated and ready to return to her preinjury work and home life.

Two factors may have contributed to J.G.'s dramatic recovery in this case. She was in a rehabilitation setting where she was able to take advantage of coordinated rehabilitation services on a constant, rather than intermittent, basis. Also, placing her in a full-time prescription with binasal patches provided her with consistent, organized, visual input so that she could create a stable visual environment.

Patient J.R.

J.R. was seen for vision analysis 2 years post-TBI. He suffered a severe TBI in a motor vehicle accident. His chief complaint was double vision. He was referred

by a local optometrist for treatment of large constant exotropia. His case is notable because, although he had seen at least two ophthalmologists and an optometrist since his injury, no one had diagnosed him with a right hemianopia with visual neglect. He was unaware that he had a visual field defect. He and his family assumed that his spatial disorientation was simply part of his brain injury. When advised of the diagnosis, his mother asked if that was why he always veered to the left when driving. Fortunately, he had only been driving on their property. J. R. also suffered significant memory loss.

J.R. was seen on an outpatient basis, intermittently, for several years. Because he had no previous rehabilitation, working in a half day at the rehabilitation center several times a week and a vision therapy office visit once weekly proved to be a challenge for the family, and J.R. was inconsistent in his attendance and his homework. Nonetheless, over a period of approximately 18 months, the exotropia for which J.R. had been wearing a pirate patch for over 2 years resolved with vision therapy. Therapeutic techniques included both orthoptic visual therapy and spatial organization. Scanning and visual memory therapy activities were prescribed and administered by occupational therapists and his parents. J.R. learned to scan effectively in familiar environments but had residual difficulty in busy, unfamiliar environments, such as the shopping mall. Unfortunately, while his memory improved, it remained significantly impaired.

Although his rehabilitation was extended due to less than ideal compliance, J.R. was happy to be rid of his patch and to have better ability to move about in his space world. He continued to live with his parents and young son. Although he required cueing for many tasks, he was able to help raise his son, participate in sports, and maintain a part-time job as a dishwasher in a restaurant.

Patient C.L.

Patient C.L. was seen for visual evaluation 13 years after TBI sustained in a motor vehicle accident. Her chief complaints at the time of the vision examination were that her eyes rolled back in her head during seizures and she experienced some eyestrain, although her occupational therapist had noted that C.L. complained of headaches and blurred vision after near work.

Examination revealed a convergence insufficiency exotropia (i.e., strabismus when viewing at nearpoint due to inability to converge her eyes). She was diplopic almost constantly when doing tasks within arm's length. When queried about the diplopia, she said that the doctor she saw just after her accident had told her it would go away in time, so she just waited.

Although her phorias were not large (9 prism diopters of exophoria at near), she had almost no elicitable base-out reflex fusion and abnormal convergence ranges on prism vergence testing with a negative recovery (i.e., once fusion was broken with base-out prism, it required base-in prism to reestablish fusion). Her nearpoint of convergence on push-up testing was 16 inches. Because she had so little fusion response, we were unable to prescribe any out-patient therapy.

C.L. was treated on a daily basis for 2 weeks, 45 minutes per day, using large fusion targets projected on a wall to attain peripheral fusion and SILO. Instrument (amblyoscope) convergence techniques were also applied. After 2 weeks, she was fusing well enough at nearpoint that we were able to prescribe convergence exercises for practice with her occupational therapist at the rehabilitation facility. She continued in-office therapy once weekly and made continued progress with this regimen.

Patient L.R.

Patient L.R. was seen 4 months postinjury with chief complaints of poor depth perception and difficulty keeping things level. Examination revealed a mild (approximately 10 prism diopters) right esotropia and a mild left superior rectus palsy which resulted in a noncomitant vertical component to the eyeturn (6 prism diopters in primary gaze, increasing on left gaze). The superior rectus also intorts the eye. Her complaint of difficulty keeping things level probably resulted from a combination of extorsion of the eye and the noncomitancy of the vertical component. Pursuits were jerky. Ductions were full with the right eye and showed a superior temporal restriction with the left eye. Although she appeared to fixate with her left eye during the entire examination, she showed alternating suppression on her stereopsis testing. She also had reduced accommodative amplitude and facility.

Therapy progressed from monocular and biocular (i.e., two eyes open, without fusion) skills to antisuppression activities and in-instrument fusion with vertical and base-in vergences. After 12 weekly sessions in office with an hour of home therapy daily, her extraocular range of motion was full with each eye, with smooth pursuits. She showed no vertical or horizontal phoria, at distance or near, and she was comfortable with her vision. Therapy was continued for six additional sessions to improve fusional and accommodative flexibility. At her one year progress check, she had maintained all of her visual gains.

Patient B.B.

Patient B.B. was seen for examination 4 months postinjury. He had no light perception from his right eye, due to optic nerve atrophy following his injury. His left eye was healthy and intact. He presented with decreased acuity (20/80 when reading a vertical column and 20/30 when reading horizontally). He had reduced contrast sensitivity for medium spatial frequencies. He also had a left hemianopia with macular sparing. He had difficulty reading. He watched his feet when walking and tended to veer leftward. Saccades were slow and pursuits were jerky. He had a reduced amplitude of accommodation and was already wearing a bifocal correction, which he found useful. He read at approximately 8 inches from his eyes for the additional magnification.

B.B. was aware that he had a field defect but did little to compensate for it. The physical therapists had already taught him to use a walking stick on the blind side, both for physical support and to protect that side. However, like most hemianopes, he did not scan toward the affected side. During tachistoscopic procedures, he generally missed the first few letters or digits and he, initially, had poor perceptual speed and span. On line bisection tasks, he transected the line at the center or contralateral to the blind field. This is the expected performance for a patient with hemianopia combined with USN, rather than just a hemianopic defect. On some other tasks, his performance was consistent with a mild case of neglect. For instance, when instructed to scan a wall for target figures, he would scan from right (his intact field) to left. When asked to scan again from left to right, he would become argumentative, stating that he always scanned left to right and then would proceed to scan from right to left again. He showed few other indications of neglect. Copied forms were complete. On crossing-out tasks, he generally covered the entire page, always starting from right to left, but was careful to reach the left margin of the page.

Therapy began with monocular skills and tachistoscopic procedures for perceptual speed and span. These skills improved rapidly with therapy. Peripheral awareness techniques for expanding awareness within his intact field were applied with good success. B.B.'s overall reading speed improved along with his saccadic speed, perceptual span, and perceptual speed.

A number of techniques were applied for making B.B. more aware of space within his blind field. Some of these met with more success than others. He rejected application of Fresnel prism, saying he would rather move his eyes farther without the prism. He actively participated in both table-top and wall projected scanning activities, trying to adopt an efficient scanning pattern, moving from far left in his blind field, rightward. However, initially, these activities did not seem to generalize outside of the therapy room. He was able to adopt a scanning pattern while walking. He looked left on every fourth step, which helped him walk without deviating leftward. His mobility and reading improved enough through his course of therapy that he was able to return to his life as a student at a junior college.

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Appendix 7A

Organizations to contact for information regarding orthoptic or vision therapy, or referral to member doctors who may provide or prescribe therapy:

College of Optometrists in Vision Development
243 North Lindbergh Blvd., #310
St. Louis, MO 63141
(888) 268-3770
www.covd.org

Neuro-Optometric Rehabilitation Association
P. O. Box 1408
Guilford, CT 06437
(866) 222-3887
www.nora.cc

Optometric Extension Program Foundation, Inc.
1921 East Carnegie Ave. Ste. 3-L
Santa Ana, CA 92705
(949) 250-8070
www.oep@oep.org

8

Auditory Function Assessment in Posttraumatic Brain Injury Rehabilitation

Juan J. Bermejo

CONTENTS

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Introduction

The ability to effectively communicate with fellow human beings assumes great importance in a rehabilitative setting. With the focus of various therapies directed toward advancing a disabled individual's recovery, we must ensure that communication among therapists and patients is unencumbered. For this reason, audition is critical to the rehabilitation of people with brain injury because it is a vital component of the communication process. As we shall discover, hearing loss is a frequent sequela of traumatic brain injury (TBI), and its potential impact on peoples' quality of life, as well as their rehabilitation, is well recognized.

The role of the sense of hearing in daily living is no less important than any of the other human senses, contrary to popular thought that vision supersedes all others in importance. Awareness of sound in diverse environments can be critical to survival and the ability to detect and recognize sound patterns that comprise speech is central to human communication. TBI can alter human performance by disrupting a person's awareness and recognition of, and attention to, sound. At a higher level, processing and comprehension of speech and execution of other cognitive functions that involve memory, ability to communicate knowledge, and judgment can be affected by hearing loss. Therefore, the status of a person's hearing sensitivity should be known to all clinicians, even before the rehabilitative process is begun. As with all disabilities, early identification and assessment provide valuable information useful to rehabilitation.

The following section explores the magnitude of auditory problems in the TBI population. The discussion of the anatomy and physiology of the auditory system will help clarify how this sensory system can become impaired. An important role of audiologists is in helping to evaluate auditory function using conventional and newer audiologic techniques described below. This information should prove useful to therapists formulating their clinical interventions.

Demographics

Using national data from 1995 to 1996, the Center for Disease Control (CDC)[1] estimates that more than 80,000 persons in the United States are discharged annually from hospitals with disabilities secondary to TBI. Approximately 5.3 million Americans suffer from TBI-related disabilities.[1] Estimating how many Americans suffer TBI-related hearing loss is much more difficult because of the unavailability of premorbid audiologic information about many of them and the lack of a national survey seeking this information. A Medline search for data from 1978 to 2002 regarding the incidence of TBI-related hearing loss yielded little national data. Instead, many reports appear to be regionalized, based on small numbers of patients seen at a specific medical center. From these studies, it is clear that hearing defects are common in people with mild to severe TBI. Abd Al-Hady et al.[2] found that 20% of their subjects with minor head injury had varying degrees of hearing loss. In a study of 130 individuals with minor head injury, five were found to have temporal bone fractures that caused greater high-frequency hearing loss than found in those with no temporal bone fracture.[3] Out of 123 people with temporal bone fractures, Ghorayeb and Rafie[4] reported varying degrees of hearing loss in all of them. Zimmerman et al.[5] analyzed audiologic data from 50 children suffering from head trauma and noted the occurrence of hearing loss in 48% of the cases.

Overseas, several similar findings have been reported. Vartiainen, Karjalainen, and Karja[6] concluded that their head-injured patients with neurosensory hearing loss suffered

cochlear lesions. They based this conclusion on their analysis of audiologic data from 199 Finnish children with blunt head injury. Dorman and Morton[7] studied 40 New Zealand children treated for minor head injury. Audiologic data from 25% of them revealed mild hearing loss. A more recent study by Jury and Flynn,[8] also conducted in New Zealand, found that, in 30 people affected by TBI for 19 months to 27 years, persistent hearing loss occurred in 33%. In 1989, Wennmo and Svensson[9] found that 75% of their 20 Swedish subjects with temporal bone fractures suffered hearing loss. Bergemalm and Borg[10] studied audiologic data from 25 TBI patients admitted to two Swedish hospitals. They concluded that changes in auditory function are common in TBI, vary in site of lesion, and can become progressively worse.

From these studies, it is clear that even mild TBI can affect auditory function. For this reason, hearing loss should always be suspected in a person with TBI until clinically proven otherwise. That hearing impairment impedes sound awareness and recognition, as well as effective comprehension of speech, is well known.

In order to understand the potential effects of TBI on auditory structures and, therefore, the onset of hearing loss, it is essential to discuss and appreciate the anatomy involved.

The Human Auditory System

The conventional approach to a discussion of human auditory anatomy, physiology, and neurophysiology is the division of the auditory system into external, middle ear, inner ear, and retrocochlear sections. This compartmentalization will aid in understanding pathophysiology as well as site-of-lesion testing.

A good starting point is a brief description of the skull. There are four sections of bone that comprise the skull: the frontal, temporal, parietal, and occipital. Of principal importance to this discussion is the temporal bone. The temporal bone has four sections, the most important of these being the petrous portion because it houses the sensory organs for audition and balance. Other bony sections (the tympanic, mastoid, and squamous) help form the ear canal and middle ear cavity.

External Ear

The external ear consists of the auricle or pinna and the osseous and cartilaginous portions of the ear canal (Figure 8.1). The auricle is cartilaginous, quite flexible, and helps to collect sound and direct it inward to the ear canal. The concha, the helix, the antihelix, the tragus, and the antitragus are principal features of the auricle. Of these, the concha, a large bowl-shaped depression near the middle of the auricle, is important because it helps funnel sound into the ear canal and is involved in providing slight amplification of high frequency sounds. Yost and Nielsen[11] point to the auricle's role in helping to localize high-pitched sounds and to identify sound sources occurring behind or in front of the head. A more passive function is to protect the middle and inner ears by maintaining constant temperature and humidity and to help in keeping out foreign bodies.

The human external auditory meatus (EAM) averages 28 mm in length and 7 mm in diameter.[12] The orifice of the EAM is generally oval in shape and is situated slightly lower than the medial portion near the eardrum; this may help keep water from lodging there.[13] The EAM is divided into cartilaginous and osseous portions. The cartilaginous portion occupies the lateral $^1/_3$ to $^1/_2$ while the medial $^1/_2$ to $^2/_3$ section is osseous. Sebaceous and ceruminous glands located in the cartilaginous portion produce cerumen or earwax.

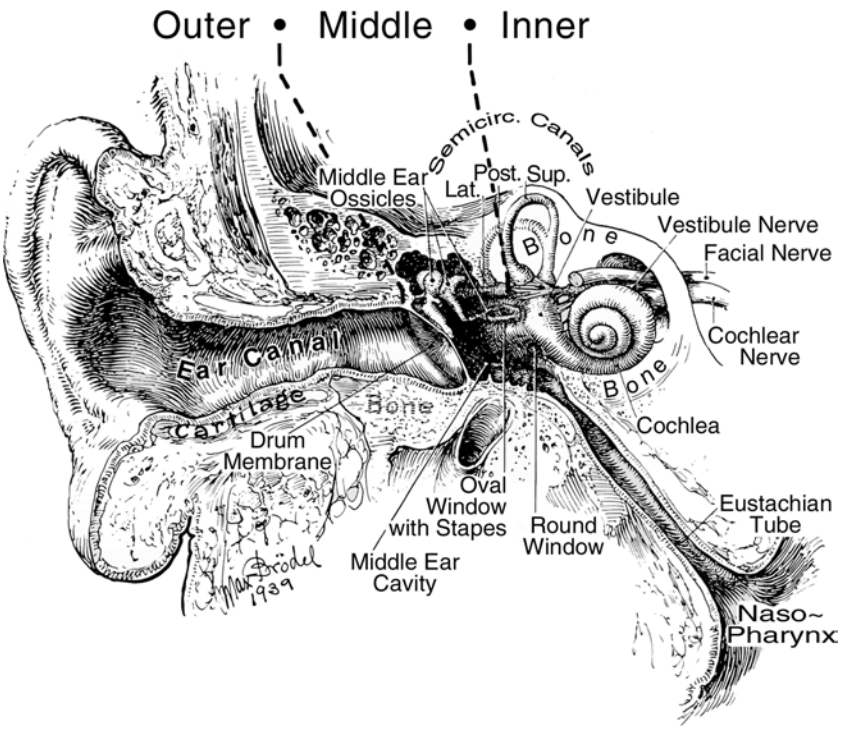

FIGURE 8.1
Drawing of the outer, middle, and inner ear. (From Durrant, J. and Lovrinic, J., *Bases of Hearing Science*, 2nd ed., Williams & Wilkins, Baltimore, 1984. With permission.)

Functionally, the EAM appears to respond best (resonate) to sounds whose frequencies approximate 3800 Hz.[13] Together, the EAM and concha provide increased amplification in the 3000 to 5000 Hz range. This fact is important to consider in patients with EAM blockages caused by cerumen, dried or oozing blood, or foreign debris.

Middle Ear

The human tympanic membrane (TM) is the medial terminus for the ear canal, anchored fast to the annulus and measuring about 55 to 90 mm^2 in area.[11] The stiffness of the eardrum is provided by the pars tens; a portion of the TM, the pars flaccida or Schrapnell's membrane, lacks stiff fibers and is, therefore, very flexible. As such, it may allow for some small degree of pressure equalization between external and middle parts of the ear.[13] On direct observation, the appearance of tympanic membranes may vary from translucent to opaque. In most individuals, the manubrium of the malleus in its attachment to the tympanic membrane can be easily observed during otoscopic examination.

The role of the TM is to propagate sound energy from air to the inner ear. Sound transmission is accomplished by air-conduction, by bone-conduction, and through resonation of the air in the middle ear cavity.[11] Recently, Freeman, Sichel, and Sohmer,[14] studying small mammals, described another mode of sound transmission. They were able to record auditory neural responses by directly applying a bone conduction stimulus to exposed brains. They postulated that cerebrospinal fluid may transmit sound pressure through to the inner ear fluids during bone conduction stimulation.

The air-filled middle ear space or tympanic cavity has a volume of approximately 2 cm^3 and communicates, anteriorly, with the nasopharynx via the eustachian tube and, posteriorly, with the air cells of the mastoid bone. Suspended in the middle ear space are the ossicles or middle ear bones: the malleus, incus, and stapes. These are the smallest bones in the body. Also found in the middle ear space are the stapedius and tensor tympani muscles, the chorda tympani, and ligaments supporting the ossicles.

The malleus has its manubrium attached to the tympanic membrane. A middle ear muscle, the tensor tympani, has its insertion on the manubrium and neck of the malleus. The incus and malleus articulate via a "saddle-type" joint. The incus attaches to the head of the stapes, forming the incudostapedial joint. Medially, the stapes footplate is fastened to the oval window. The malleus is supported by the anterior, lateral, and superior ligaments. Support for the incus is provided by the posterior ligament. The stapes is lodged in the oval window recess, held in place, but not fixated, by the annular ligament.

The stapedius and tensor tympani muscles are the auditory muscles and have an important role in stiffening the ossicular chain upon contraction through acoustic or nonacoustic stimulation. On the posterior wall of the middle ear cavity is the pyramidal eminence that houses the stapedius muscle. The tendon of the stapedius muscle emerges from the pyramidal eminence to attach to the head of the stapes. Innervation of the stapedius muscle is by the facial nerve. On the anterior wall of the middle ear is the semicanal of the tensor tympani muscle.[12] The tendon of the tensor tympani muscle inserts to the manubrium and neck of the malleus. The trigeminal nerve innervates the tensor tympani muscle. The chorda tympani, a branch of the facial nerve, also courses through the superior part of the middle ear cavity on its path to taste receptors on the tongue.

The role of the ossicles is to facilitate sound transmission. Sound energy in the air must be delivered efficiently to the cochlea, a fluid-filled chamber. Because of the difference in the densities of air and cochlear fluids, sound energy will be impeded by the greater density of the latter, resulting in some loss of this energy. Such impedance mismatch would be expected to decrease auditory sensitivity. The ossicles rotate in such a way that they perform a lever action, transferring a greater force to the stapes than that exerted on the tympanic membrane. This effectively increases the gain of the human auditory system by about 30 dB.[13]

The eustachian tube plays an important role in middle ear function. By opening and closing during chewing, swallowing, or yawning, the entry of air through the eustachian tube allows air pressure in the middle ear space to match that of ambient atmospheric pressure and, subsequently, effective sound transmission.

Bony Labyrinth

Within the petrous portion of the temporal bone are cavities that interconnect to form the osseous or bony labyrinth. Removal of surrounding bone permits a clear view of the complex system known as the *bony labyrinth*: the bony semicircular canals, the bony cochlea, and the vestibule between them. The orientation of the human osseous labyrinth is such that the semicircular canals lie posteriorly and to the side while the cochlea sits anteriorly and medially relative to the vestibule. Posterior and anterior semicircular canals are aligned almost 90° to one another while the horizontal semicircular canal angles up 30° from the horizontal plane. The semicircular canals have visible bulges or dilatations known as *ampullae* that open onto the vestibule.

The cochlea, an extension of the vestibule,[13] is a coiled structure measuring about 32 to 35 mm in length. It is wrapped around a bony structure called the *modiolus*, the base of which is the internal auditory meatus through which the cochleovestibular and facial

nerves pass to reach auditory nuclei in the brainstem. There are two cochlear ducts, the scala tympani and the scala vestibuli, that are partially separated by the bony spiral lamina.

On the bony vestibule's lateral wall is the oval window which is covered by the stapedial footplate. The oval window connects the vestibule to the scala vestibuli. The round window is located in the inferior portion of the vestibule facing the middle ear cavity. It is the lateral terminus of the scala tympani.

Perilymph, one of two labyrinthine fluids and a filtrate of cerebrospinal fluid, fills the osseous labyrinth. The cochlear aqueduct, a small passage starting near the round window and continuing to the subarachnoid space, is believed to facilitate the transport of perilymph to the labyrinth.[15]

Membranous Labyrinth

Inside the bony labyrinth is a smaller, similarly shaped structure known as the *membranous labyrinth* (Figure 8.2). There are three divisions: the endolymphatic duct and sac, the membranous semicircular canals and the utricle, and the cochlear duct (or scala media) and saccule.[16] The saccule, utricle, and membranous semicircular canals contain the sensory organs for detecting angular and linear head motion. Auditory sensory epithelia (organ of Corti) reside in the scala media. The membranous labyrinth is filled with endolymph, a fluid different in chemical composition from perilymph. The endolymphatic duct and sac regulate the pressure of endolymphatic fluid.[17]

Because the focus of this discussion is the auditory system, only a brief discussion of the membranous semicircular canals will follow. The utricle is a sac-like structure inside the bony vestibule. The semicircular canals have five openings into the utricle. An enlarged bulb or ampulla at each opening contains the vestibular sensory epithelia, the crista ampullaris, supported by connective tissue. The crista contain hair cells whose cilia embed into a gelatinous structure called the *cupula*. Angular head movement causing endolymph to move in one direction across the crista will deflect the cupula and cilia and result in a receptor potential. This electrical event results in a discharge of the afferent vestibular nerve fibers. Deflection of the cupula in the opposite direction will fail to generate a receptor potential.

In the saccule and utricle are areas called *maculae* that consist of "fan-like" sensory structures with a covering called the *otolithic membrane.* This membranous structure is a

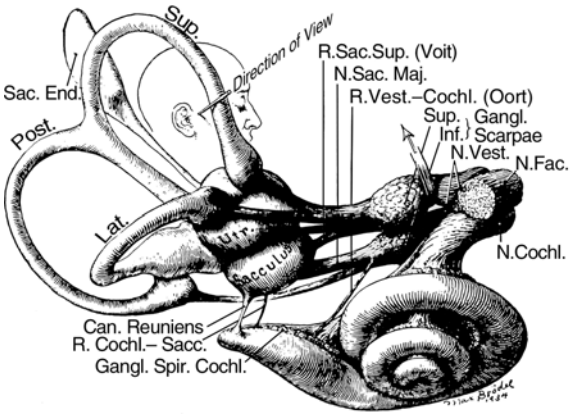

FIGURE 8.2
The membranous labyrinth. (From Dallos, P., *The Auditory Periphery,* Academic Press, New York, 1973. With permission.)

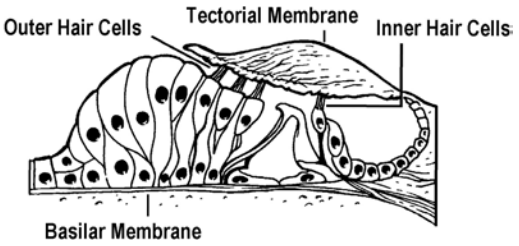

FIGURE 8.3
Structures of the organ of Corti.

gelatinous mass with a thin layer of calcium carbonate particles called *otoconia*. The sensory receptors are hair cells with stereocilia that project into the otolithic membrane. Movement of this membrane in one direction will cause stereocilia to bend in the opposite direction, resulting in a physiologic response. The otolith organs thus respond to linear as well as angular head movements.[16]

The Cochlea

The spiral ligament, a crescent-shaped thickening of periosteum attached to the lateral wall of the cochlea, projects inward and anchors the basilar membrane laterally (Figure 8.3). On its medial side, the basilar membrane is attached to the spiral lamina, a bony shelf that partially divides the cochlear scalae. Thus, the basilar membrane is the roof of the scala tympani and the floor of the scala media. The roof of the scala media is formed by Reissner's membrane. The basilar membrane, about 32 mm long, is composed of transverse fibers lying perpendicular to its long axis. Unlike the scala media, the basilar membrane is wider toward its apex and narrower toward its basal end. This arrangement has had important implications for the development of the many theories of hearing.

The sensory epithelium for hearing, or the organ of Corti, rests on the basilar membrane. A single row of receptor cells, the inner hair cells (IHC), and three rows of outer hair cells (OHC) wind their way from base to apex. Inner hair cells appear "flask-like" in shape and have two rows of stereocilia.[13] The shape of outer hair cells is more cylindrical and each sensory cell has three to four rows of stereocilia arranged in a "W" shape. The tips of the tallest of the stereocilia are embedded in the tectorial membrane. The shorter of the OHC stereocilia are free-standing while the IHC stereocilia are either free-standing or loosely attached to the tectorial membrane.[15] In simple terms, the hearing process is initiated by sound pressure acting on the tympanic membrane. Through a piston-like motion, the ossicles convey sound energy at a significantly higher gain to the oval window. A pressure gradient develops across the basilar membrane and organ of Corti creating a pressure wave that travels apically. Shearing forces act on the tectorial membrane which, in turn, deflects the hair bundles toward their kinocilium, thereby depolarizing the hair cell and leading to a receptor potential. This physiologic excitation increases the number of spike discharges from afferent neurons culminating in a whole nerve action potential. Only IHCs participate in the generation of an action potential. OHCs are the key elements in a cochlear amplifier which increases the sensitivity and frequency selectivity of the hearing organ.[18]

The Auditory Nerve

As discussed previously, receptor cells depolarize when their stereocilia bend in response to shearing forces from the tectorial membrane during the traveling wave. Each IHC may

be innervated by several afferent neurons while many OHCs may be innervated, through multiple branching, by a single neuron. Approximately 30,000 nerve fibers comprise the auditory nerve; about 90 to 95% of these are Type I radial neurons — thick myelinated fibers that synapse with IHCs. Thin, scarcely myelinated Type II, or outer spiral fibers, make up a smaller percentage (5 to 10%) of all afferent neurons and these synapse with the OHCs.

An olivocochlear efferent system exists alongside the afferent neuronal pathway. Efferent fibers arise from either the lateral or medial superior olivary complex.[18] Lateral efferent axons tend to be unmyelinated, originate in the vicinity of the lateral superior olivary complex, and directly synapse with afferent dendrites at the base of the IHCs. From areas near the medial superior olivary complex are larger neurons whose axons are myelinated and synapse directly on OHCs. The role of the efferent system appears to involve the lowering of the sensitivity of the hearing organ in response to high-intensity sounds, reducing the effects of low-level background noise on moderate intensity acoustic stimuli, and may serve to facilitate selective attention.[19]

Central Auditory Pathways

Primary auditory fibers are the central processes of bi-polar neurons. The peripheral processes attach to the cochlear hair cells, while the central fibers enter the brainstem to terminate on diverse cells in the dorsal and ventral cochlear nuclei (Figure 8.4). The latter is divided into anteroventral and posteroventral sections. A tonotopic arrangement is evident in the cochlear nuclei, whereby afferent nerve fibers responsive to high frequency stimuli and, thus, originating from the basal end of the cochlea, terminate on cells of the dorsal side of the dorsal cochlear nuclei. The cochlear apex is sensitive to low-frequency sounds; nerve fibers from this cochlear area connect to cells on the ventral portion of the dorsal cochlear nuclei and to the ventral cochlear nuclei.

Secondary auditory nerve fibers are those that are arranged into three striae: the dorsal acoustic stria, the intermediate acoustic stria, and the ventral acoustic stria. Fibers from the dorsal acoustic stria project from the dorsal cochlear nuclei and cross the midline. Some nerve fibers terminate on the contralateral superior olivary complex with the majority entering the contralateral lateral lemniscus. From there, fibers project to the central nucleus of the inferior colliculus of the midbrain.

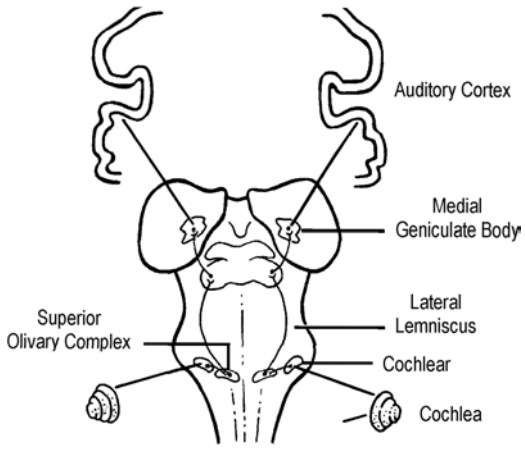

FIGURE 8.4
Central auditory pathways.

From cells in the posteroventral cochlear nucleus arise the intermediate acoustic striae to connect to cells in the periolivary and retro-olivary nuclei. From there, they cross the midline and terminate on the contralateral periolivary and retro-olivary nuclei. Afferent fibers continue contralaterally and join the lateral lemniscus and terminate in the inferior colliculus. Efferent auditory nerve fibers that attach to outer hair cells arise in these olivary nuclei to make up the olivocochlear bundle and, as described above, play a role in altering the sensitivity of auditory sensory receptors.

The ventral acoustic stria begins in the ventral cochlear nucleus and forms the trapezoid body. Many of its fibers course to cross the midline and form the lateral lemniscus. This nerve fiber bundle ascends to terminate on the central nucleus of the inferior colliculus within the midbrain.

The lateral lemniscus is comprised mainly of crossed secondary nerve fibers from the three acoustic striae. A few fibers from its nucleus will cross the midline and terminate at the contralateral inferior colliculus. From the inferior colliculus, ascending fibers continue on to the medial geniculate body of the thalamus. Fibers originating within the medial geniculate body form the geniculocortical fiber tract that connects to the transverse temporal gyrus in the temporal lobe.[20]

Typically, the presence of sound is perceived through air-conduction, whereby the ear detects and processes sound carried through air. Sound transmission can also take place through the vibration of bones of the skull or teeth. Hearing sensitivity can become impaired due to defects occurring at the peripheral level (i.e., from the ear canal to the auditory nerve inclusive) or at the central level (i.e., from the brainstem to the auditory cortex). Four types of hearing losses are recognized clinically and are discussed below. In order to assess an individual's hearing sensitivity, it is necessary to perform preliminary, yet essential, procedures.

Clinical Examination

Patient History

By careful questioning, a clinician should be able to gather enough information about a person's hearing status to help guide audiologic testing. Was hearing sensitivity normal or was hearing loss documented or suspected prior to injury? Was there exposure to excessively loud occupational or recreational noise, toxic industrial chemicals, or use of ototoxic medications? Did the person report tinnitus or "ringing of the ears" prior to injury? Did background noise appear to detrimentally affect the person's ability to comprehend speech? Were family members becoming sufficiently concerned with the person's hearing difficulty that hearing aid use was contemplated? During hospitalization, was there bleeding from either ear or was trauma to either pinna noted? Did radiologic studies discover fracture of temporal bone? Was the person found to exhibit hearing difficulty by hospital staff? Was hearing sensitivity assessed during hospitalization or shortly after discharge?

Standard Audiologic Procedures

Following the taking of a case history, the person is prepared for standard audiologic procedures. Many people with TBI who are seen as outpatients are capable of cooperating during testing and providing reliable responses. Standard pure tone and speech audiometric techniques are the basis for conventional audiologic studies of cooperative patients.

By evaluating air-conduction and bone-conduction sensitivity, the audiologist can determine whether hearing sensitivity is within normal limits or whether hearing impairment is present unilaterally or bilaterally, and its severity can be established.

Speech audiometric data aid in determining the impact of hearing loss on the person's ability to perceive speech at normal intensity levels (sometimes referred to as *conversational speech levels*). Along with pure tone data, speech audiometric data can help ascertain communication problems likely to be experienced by the individual with hearing impairment.

It should be obvious that hearing testing is best performed in a quiet setting. Controlling the acoustical environment ensures that all persons receive hearing testing in optimal listening surroundings and that test data are reliable and accurately reflect hearing status at the time of examination. For these reasons, quantitative data obtained through standard audiologic procedures, rather than qualitative measures (e.g., "whisper test," watch test, single tuning fork test, etc.), are preferred.

A clinical audiometer is an electronic instrument used to generate pure tones and various types of noise stimuli. These, as well as recorded or live-voice speech stimuli, are presented to a listener through circumaural or insert earphones or a bone oscillator placed on the mastoid bone or forehead. When loudspeakers are used instead of earphones, hearing sensitivity is assessed in what is known as *soundfield* testing.

The Audiogram

With a person wearing earphones, pure tones ranging from 250 to 8000 Hz are presented at different sound intensity levels. Bone-conduction thresholds can also be established in the frequency range of 250 to 4000 or 6000 Hz. Thresholds are determined at each specific frequency. Theoretically, a threshold represents the sound intensity level at which a listener is able to successfully detect a stimulus 50% of the time. Clinically, a pure tone threshold represents the faintest sound a person can hear. These test results can be depicted on a form known as an *audiogram* (Figure 8.5). In this graphical representation of hearing sensitivity, pure tone thresholds are plotted in terms of frequency vs. intensity level, relative to normal hearing level.

Whereas pure tones are simple acoustic stimuli, speech is a complex stimulus. Conventional speech audiometric testing can be performed with single words, nonsense words or phrases, short sentences, or continuous discourse. Use of speech stimuli for evaluation of hearing sensitivity is essential because of the significant impact of hearing loss on one's ability to communicate orally.

Together, pure tone and speech stimuli help delineate the patient's hearing sensitivity. An individual with normal hearing sensitivity will typically have air-conduction and bone-conduction thresholds falling between –10 and 26 dBHL. Air-conduction thresholds may differ from bone-conduction thresholds by 5 to 15 dBHL. Because the normal hearing range is fairly wide, pure tone thresholds approximating 25 dBHL (and, therefore, technically within normal limits) may present mild auditory problems. Hearing sensitivity in the normal range facilitates, for most individuals in quiet surroundings, almost effortless reception of speech and nonspeech sounds. Of course, this may not hold true in geriatric cases because of aging effects on sensory and neural function.

Acoustic Immittance

Acoustic immittance encompasses tympanometry as well as measurements of middle ear compliance or impedance and eustachian tube function. In addition, testing for the presence of stapedial muscle contractions in response to loud acoustic stimuli is included. As described above, the middle ear serves to effectively transfer as much of the acoustical

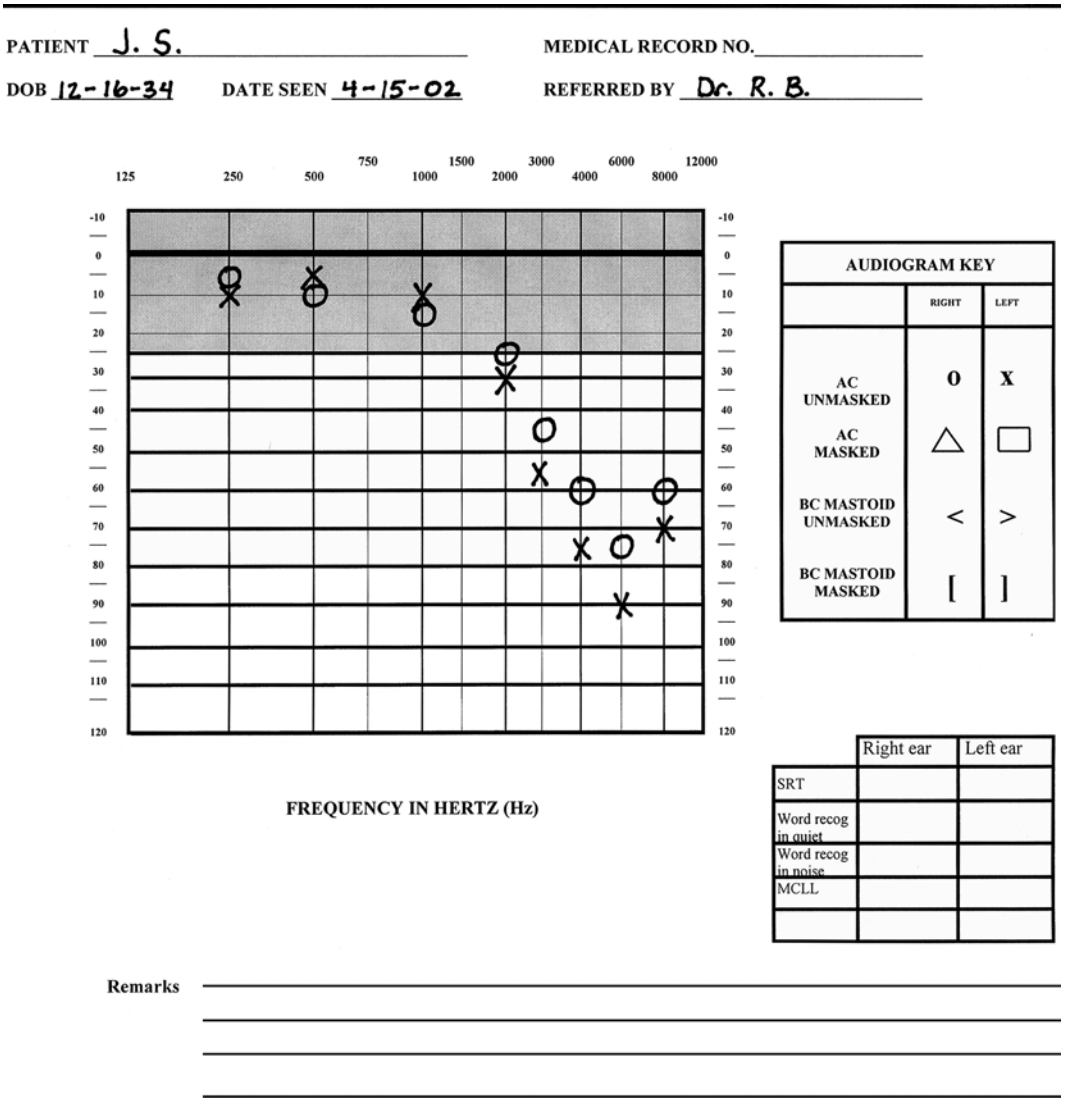

FIGURE 8.5
Audiogram depicting loss of high frequency hearing sensitivity.

stimulus to the inner ear as possible through the action of the ossicular chain. Acoustic impedance refers to the amount of opposition to sound transmission posed by the middle ear. In ears with no otologic disease, acoustic impedance is minimal. Ears with tympanic membrane or ossicular chain defects will demonstrate increased acoustic impedance, resulting in significant reflection of sound off a stiffened tympanic membrane and out through the ear canal. This implies a reduction of sound energy flow to the inner ear.

By presenting a pure tone to the ear while varying air pressure in a closed ear canal, tympanometry quantifies the effect on transmission of that stimulus through the middle ear. A tympanometer measures how middle ear compliance varies as ear canal pressure changes to values above and below ambient atmospheric pressure. The data obtained permit assessment of the integrity of the tympanic membrane, the stiffness of the middle ear, the operational function of the eustachian tube, and the status of the ossicular chain (Figure 8.6). Patients with occluded ear canals will demonstrate abnormally low ear canal

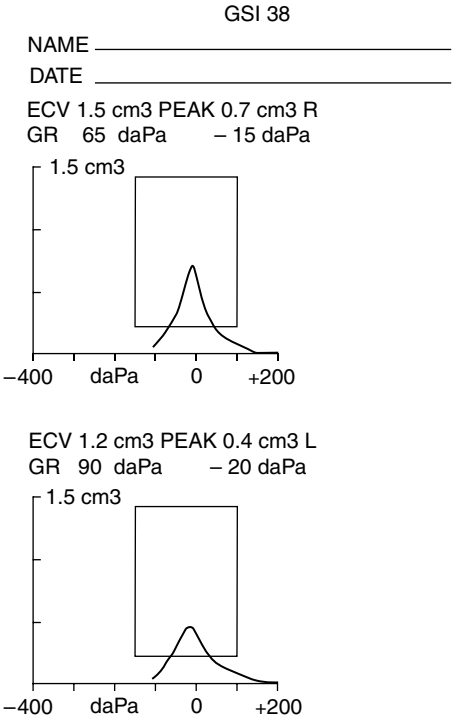

FIGURE 8.6
Tympanogram.

volume. Perforations of the tympanic membrane will yield larger-than-normal ear canal volumes, as the measurement is that of the combined volume values of both ear canal and middle ear space. Ossicular chain fixation will cause abnormally restricted movement of the tympanic membrane and increased resistance to sound transmission as air pressure is varied. Discontinuity of the ossicular chain will do the opposite; because of increased flaccidity, the tympanic membrane is hypermobile, and abnormal high middle compliance values are recorded by the tympanometer.

Acoustic Reflex Testing

The acoustic reflex is a contraction of the stapedius muscle when a sufficiently loud acoustic stimulus is presented to a healthy ear. This acoustic reflex arc has been described by Hall[21] as consisting of afferent auditory nerve fibers that terminate on the ventral cochlear nuclei, neurons arising from the ventral cochlear nucleus terminating near the ipsilateral facial motor nucleus as well as ipsilateral and contralateral medial superior olive (MSO), neurons from the MSO or peri-MSO that end ipsilaterally and contralaterally at the facial motor nucleus, and, finally, the facial motor nerve fibers that innervate the stapedius muscle (Figure 8.5).

In the normal ear, acoustic reflexes can be elicited by ipsilateral or contralateral stimulation. Pure tones, white noise, or bands of noise in the range of 70 to 100 dB above pure tone threshold are effective stimuli. The acoustic reflex is a stiffening of the tympanic membrane that, in turn, increases the resistance to sound energy flow. Instrumentation is used to detect the sudden increase in acoustic impedance upon eliciting an acoustic reflex.

If conductive hearing loss (discussed below) is present, testing usually fails to elicit an acoustic reflex, often because of differing circumstances. For instance, persons with

conductive hearing loss due to middle ear disease or trauma usually do not register the expected change in impedance because middle ear stiffness is already abnormally high. Thus, it is rare that these individuals would present with acoustic reflexes. On the other hand, a person with disarticulation of the ossicles has a middle ear with an abnormally high degree of flaccidity. In such a case, no acoustic reflex may be present because of the loss of continuity within the ossicular chain itself and between the ossicular chain and the tympanic membrane.

Individuals with neurosensory hearing loss (discussed later) may or may not present with acoustic reflexes. If the neurosensory hearing loss (i.e., elevated pure tone thresholds) is mild, acoustic reflexes may be recorded, suggesting that recruitment is present. Recruitment is a clinical symptom in which the ear's ability to process loudness is impaired. A person with recruitment usually complains that certain sounds are annoying or even painful to hear. This is frequently the result of damage to the cochlea. In cases where the neurosensory hearing loss is moderate to severe, acoustic reflexes are generally absent.

Conductive Hearing Loss

Individuals with bone-conduction pure tone thresholds better than air-conduction thresholds exceeding 10 to 15 dBHL are said to have *conductive* hearing loss. Common causes of conductive hearing loss include cerumen impactions, perforated tympanic membranes, middle ear disease, ossicular chain fixation or decoupling, and eustachian tube dysfunction. Less commonly encountered are atresia (i.e., absent ear canal), ear canal stenosis (i.e., narrowing of the ear canal orifice), active bleeding or dried blood occluding the ear canal, fracture across the osseous portion of the ear canal or across the middle ear, hemotympanum or blood occupying the middle ear space, vascular tumor in the middle ear space, and foreign debris in the ear canal or middle ear.

A patient with conductive hearing loss typically exhibits difficulty responding to verbal or nonverbal stimuli unless presented with louder-than-normal intensity levels. Most conductive hearing losses exist as long as the underlying medical condition persists. Medical and/or surgical treatment may help resolve most conductive hearing losses, and hearing sensitivity may return to normal in most cases.

Neurosensory Hearing Loss

Air-conduction and bone-conduction thresholds lying outside of normal and approximating one another indicate neurosensory hearing loss. Most individuals will acquire neurosensory hearing loss as a result of the aging process. Temporary or chronic exposure to dangerously loud sound without hearing protection is one of the leading causes of hearing loss. Autoimmune ear disease, endolymphatic hydrops, perilymphatic fistula, genetic or hereditary factors, viral infiltration into the cochlea, metabolic disease (such as hypothyroidism), and anemia are other bases for neurosensory hearing loss. Most individuals with typical neurosensory hearing losses are not medically treatable, except through amplification. Hearing aids, alternative listening devices, and the advent of middle ear, cochlear, and brainstem implants have made audition possible for many people with neurosensory hearing loss.

Mixed Hearing Loss

When low-frequency bone-conduction thresholds are in the normal range but those in the mid-to-high frequency range approximate diminished air-conduction pure tone thresholds, the hearing loss is referred to as *mixed*. Otosclerosis, a disease involving the growth

of bone around the stapes footplate, commonly causes mixed hearing loss. The stapes footplate becomes increasingly fixated and unable to freely pivot within the oval window, resulting in diminished hearing sensitivity. Individuals suffering from presbycusis (i.e., hearing loss secondary to the aging process) may also exhibit mixed hearing loss should an outer or middle ear lesion exist concomitantly. For instance, a person with earwax blockage of the ear canal, TM perforation, or middle ear disease will exhibit hearing loss due to conductive as well as neurosensory involvement. The conductive component of a mixed hearing loss may be resolved through medical or surgical treatment. The neurosensory portion of the hearing loss, however, may be permanent.

Fractures of the temporal bone can be longitudinal or transverse. Longitudinal fractures occur more frequently, usually spare Cranial Nerve VIII, and commonly cause conductive hearing loss due to damage to middle ear structures and the tympanic membrane. Transverse fractures tend to produce total loss of auditory function because of the severe damage to the labyrinth.[16] Labyrinthine concussions can induce permanent change to hearing ability, especially to high frequency hearing sensitivity.

Central Hearing Loss

People with central hearing loss generally have difficulty with cognitive processing of complex sounds while maintaining normal or neurosensory hearing loss. What is striking, from a clinical perspective, is the person's apparent ability to perceive sounds in a seemingly normal manner, but obvious difficulty or failure to recognize specific sounds. It is not surprising that these individuals are mistakenly deemed to have functional or "non-organic" hearing loss. For instance, a person may completely fail to attend to, recognize, or discriminate speech stimuli in light of apparently normal peripheral hearing sensitivity on audiometric testing. Central auditory processing and associated cortical or subcortical lesions that underlie central hearing loss are beyond the scope of this chapter. For this information, the reader is encouraged to review Pinheiro and Musiek's text.[23]

Electro-Diagnostic Procedures

Otoacoustic Emissions

The existence of "echoes" emanating from the cochlea and out the ear canal was first described by Kemp in 1978.[24] Briefly, acoustic stimuli presented to the ear at threshold were found to generate a return wave or echo detected within the ear canal. These echoes or emissions are the result of distortions in the traveling wave, and their presence reflects the health of OHCs. The ability to test for the presence of these otoacoustic emissions has provided clinicians with another tool for assessing the functional integrity of the human cochlea.

Testing is accomplished using a probe, having both a microphone and a stimulus generator, which is inserted into the ear canal. Clicks or pure tones are stimuli used to elicit responses that are then detected by the microphone inside the probe. These otoacoustic emissions (OAEs) are then analyzed to assess cochlear function in all patient age groups. Evoked OAEs are of two types: distortion and transient. The distinction is based on the type of stimulus used to elicit the cochlear response.

Transient OAEs are evoked using click or tone burst stimuli. Because such stimuli include a broad range of frequency components, their energy stimulates the basal as well as apical regions of the cochlea. Distortion-product OAEs are generated by using two pure

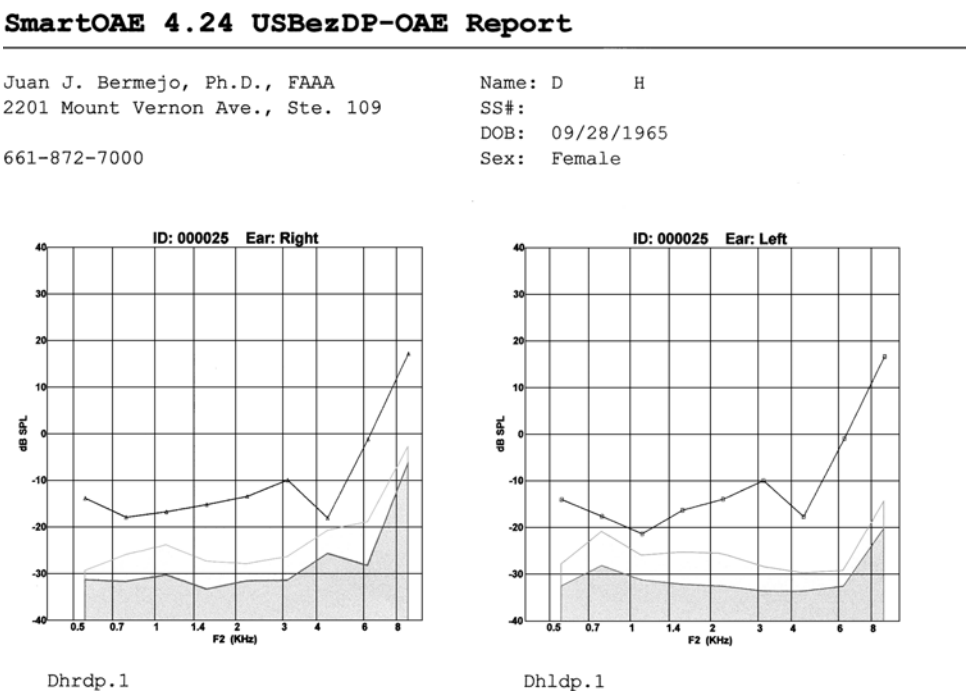

FIGURE 8.7
Distortion-product otoacoustic emissions from a patient with normal hearing sensitivity.

tones (by convention, labeled F1 and F2). These stimuli are most effective when separated in frequency by an F2/F1 ratio of 1.22.[19] For instance, F2 may be a 1600-Hz pure tone while F1 may be 1311 Hz. Their ratio is thus 1600 Hz divided by 1311 Hz or 1.22. Distortion-product OAE findings are graphed, as in Figure 8.7.

Clinically, OAEs are used to assess the integrity of cochlear outer hair cells through an analysis of their amplitude. Most individuals with hearing loss exceeding 45 dBHL would be expected to have absent OAEs.[19] OAE testing thus serves to supplement other behavioral audiologic data to ascertain presence or absence of hearing loss and to distinguish sensory from neural hearing impairment.

Auditory Evoked Responses

There has always been a need to improve identification of hearing loss in difficult-to-test individuals. Individuals with TBI may be unable or unwilling to cooperate for standard behavioral audiometric testing. There may be a need to assess the neural integrity of cortical structures responsible for cognition, memory recall, speech recognition, language function, or attention. For these purposes, a battery of electrophysiologic techniques has been evolving since the 1930s. Known collectively as *Auditory Evoked Responses,* these cortical responses to diverse acoustic stimuli have been used to delineate normal from abnormal cortical function, to identify neuroanatomic generators of these responses, and to evaluate their potential as clinical diagnostic measures. Over the last 40 years, it has become clear that some of these techniques are more useful than other evoked potential methodologies in estimating hearing sensitivity.

The Auditory Evoked Responses include electrocochleography (ECochG), Brainstem Auditory Evoked Response (BAER), Auditory Middle Latency Response (AMLR), Auditory

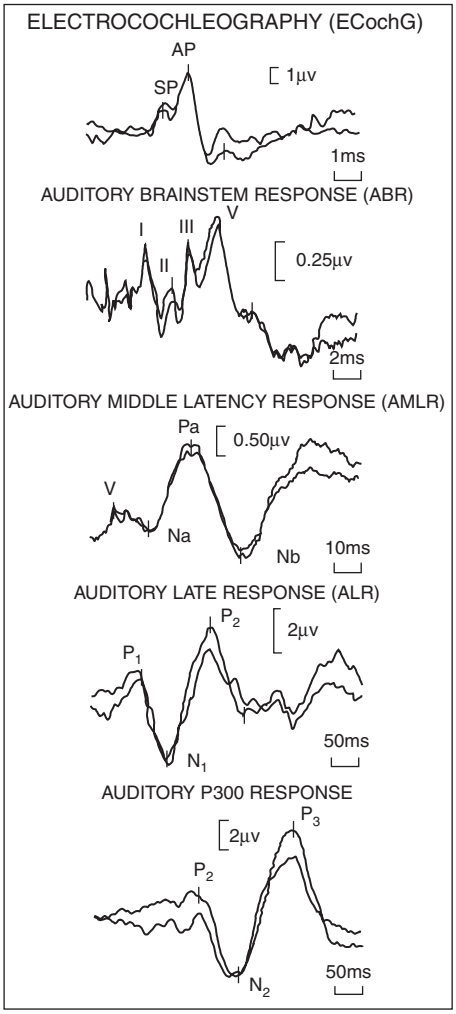

FIGURE 8.8
Waveforms representing the auditory evoked responses that are presently investigated clinically. (From Hall, J. W., *Handbook of Auditory Evoked Responses*, Allyn & Bacon, Boston, MA. © 1992 by Pearson Education. With permission.)

Late Response (ALR), and Auditory P300 Response (Figure 8.8). These electrophysiologic procedures utilize electrodes to measure tiny electrical voltages arising from various auditory neural substrates in response to clicks, tone pips, tone bursts, tones, or speech stimuli.

The utility of the tests is in the assessment of the neurophysiologic status of the cochlea (ECochG), the auditory nerve and auditory centers in the lower and middle brainstem (BAER), and higher level auditory processing centers (AMLR and ALR). These evoked responses are known as *exogenous* because their appearance is not dependent on any cognitive effort by the listener. That is, the evoked potentials from persons with normal hearing will appear whether the stimuli are attended to or not. On the other hand, the Auditory P300 Response is known as an *endogenous* or *event-related evoked* response. Its appearance requires considerable cognitive effort such as attention to specific, randomly occurring auditory stimuli. These cognitive responses are believed to reflect the listener's capacity to attend or to ignore.

The ECochg and BAER techniques are used more frequently to complement or supplement standard behavioral audiologic findings. The sensory or neural events recorded via these two procedures represent very fast (i.e., in milliseconds) processing of incoming auditory stimuli occurring at the periphery of the auditory system. The AMLR and ALR generally reflect auditory processing as it progresses through the brainstem and onto the auditory cortex. The auditory P300 response is a cumulative neural event arising from the involvement of cortical structures and sensory association areas.

ECochg

ECochg testing is performed to evaluate the status of cochlear function. A transtympanic or extra-tympanic electrode is used to record electrical voltages in response to clicks presented to the ear. Responses arise within a 3- to 5-millisecond time window following stimulus onset and consist of the cochlear microphonic (CM), the summating potential (SP), and the compound action potential (CAP) (see Figure 8.8). The CM reflects electrical voltages generated at the sensory hair cell level within the cochlea. The SP is also generated within the cochlea and is, most likely, a product of distortion occurring in the processing of sound by sensory hair cells. The CAP is actually the collective response from hundreds of auditory nerve fibers departing the cochlea on their way to the brainstem.

ECochg components are analyzed with respect to amplitude and time of occurrence or latency. While not a true hearing test, ECochg is useful for determining outer hair cell function and the integrity of the auditory nerve. Because of its dependence on intact high frequency hearing sensitivity, ECochg response parameters may be affected by different cochlear pathologies. For example, ECochg may be reduced in amplitude when sensory hearing loss above 1000 Hz is present. The relationship between the SP and the CAP may be larger than normal in cases with endolymphatic hydrops.[21] Thus, ECochg may be an appropriate component in a test battery for establishing auditory function in a person with TBI, especially if standard audiometric testing is not deemed possible.

BAER

The BAER is perhaps the most commonly used neurophysiologic technique for evaluating the auditory nerve and nuclei in the lower brainstem, as well as auditory structures in the pontine and midbrain regions. Typically, clicks are used as stimuli, although tone bursts may be used to elicit frequency-specific auditory neural responses. Clicks are presented at a rate between 10 to 25 per second. Stimulus intensity is varied to elicit consistent neural responses at the lowest presentation level. Electrodes, placed on the scalp and on the earlobes or on the mastoid bones, are used to detect subcortical responses. These are submitted to signal averaging to generate five to seven waveforms (refer to Figure 8.8). These are patterns of negative and positive voltages occurring within a 10-millisecond time window (i.e., after the ECochg response). Auditory nerve conduction, interwave latencies, wave amplitudes, and the presence or absence of expected waveforms are analyzed for departure from data norms. Wave I and Wave II are attributed to the auditory compound action potential. Wave III is thought to arise from the cochlear nuclei. The superior olivary complex is believed to generate Wave IV, while Wave V probably has its origins in the lateral lemniscus and inferior colliculus.[21]

BAER testing is usually performed on persons unable to cooperate during routine behavioral audiologic evaluation. Because BAER recordings are generally unaffected by sedation or sleep and require only that the patient rest quietly, clinicians have a reliable technique for estimating hearing sensitivity in this clinical population. Some individuals

with suspected brainstem lesions secondary to head trauma will undergo BAER to help identify possible site of lesion, although the use of MRI, CT scan, and other more advanced neuroradiologic studies have, over recent years, become the method of first choice. However, BAER recordings can provide information about the neural integrity of auditory structures in a compromised brainstem. In addition, serial BAER recordings can be used to assess improvement in the neural activity of auditory brainstem generators as a person progresses through TBI rehabilitation.

Middle Latency Response (MLR)

While auditory recordings such as the BAER and ECochg are known as *fast* electrophysiologic responses, the MLR occurs after the BAER, but before the *slow* cortical responses such as the ALR and the P300 response (refer to Figure 8.8). Typically, clicks or tone-bursts are presented at a stimulation rate of 7 to 10 per second. Stimulus intensity is generally held to below 60 to 70 dB above threshold to minimize the large myogenic (i.e., postauricular muscle) response discussed below. Electrodes are placed over the lateral temporal aspects of the scalp to record negative and positive voltage waves in response to auditory stimuli. Typically, 4 to 5 peaks and troughs with latency of 12 to 15 milliseconds extend out to about 50 milliseconds. A first prominent positive peak (Pa) occurs at about 25 to 30 milliseconds, a large negative trough (Na) at about 40 to 45 milliseconds, and a second large positive peak (Pb) at about 50 to 55 milliseconds. The auditory structures responsible for generating the MLR are believed to be the auditory thalamus and primary auditory cortex.[21,22]

Of concern in recording the MLR is the ability to generate large muscle activity through the use of a high-intensity sound. This myogenic response can be recorded within the 15 to 50 milliseconds MLR time window by an electrode placed near the ear. During ECochg and BAER testing, this myogenic response does not usually figure prominently in recordings because it typically appears after 10 milliseconds (i.e., after the BAER time window). However, use of high intensity stimulation can often cause the appearance of a robust tri-phasic myogenic response that is easily misinterpreted as the neurogenic MLR being sought.

Since its discovery in the 1960s, MLR testing has been performed in hopes of more easily identifying persons with hearing loss or brainstem and central nervous system disorders. Specific to TBI rehabilitation, using MLR has proven less useful than the BAER technique. The person's arousal state can influence the amplitude of the MLR, with natural or sedation-induced sleep reducing the amplitude of the waveform. Muscle artifact from body movement or from the presentation of the stimulus itself, if intense enough, will appear as a prominent triphasic response that mimics the MLR. MLR parameters are more easily affected by stimulus duration and latency than are BAER recordings.

Auditory Late Response (ALR)

The origin of the ALR is debated among researchers because different studies have shown variability in response parameters that is contingent on cephalic vs. noncephalic placement of the reference electrode. Most researchers concur that the origin of the ALR is the vicinity of the fissure of Sylvius and the primary auditory cortex in the temporal lobe.[21,22]

The ALR is evoked using tone bursts with long duration or plateaus exceeding 3 to 4 milliseconds at very slow stimulus rates in the order of –0.5 or 1 per second. Evoked potential recordings are generally obtained within the range of 50 to 250 milliseconds. The nomenclature used to identify the components of the ALR consists of P1, N1, P2, and N2 waves.

Clinical application of the ALR is very limited because of better, faster, more reliable electrophysiologic procedures that are used to estimate hearing sensitivity. As a measure

of cortical function, the ALR suffers serious limitations, as it is easily affected by arousal state, sleep, sedation, and medications that impact CNS function.

Auditory P300 Event-Related Potential

The ability to record the auditory P300 response depends very much on the participation of the listener. This endogenous or event-related potential (ERP), the P300, owes its appearance to attention to the presence, or in some cases, the absence, of a specific auditory stimulus. In a typical testing paradigm, a listener will have electrodes attached to the scalp. Clicks, tone bursts, speech stimuli, nonspeech stimuli, or practically any acoustic signal can be used as the "constant" or "frequent" stimulus. The listener may hear the constant stimulus 90% of the time. An auditory evoked response waveform is generated whether or not the listener attends to the constant stimulus (Figure 8.9). The technique calls for another acoustic stimulus, differing on some predetermined parameter, to be introduced, infrequently and at random, to the listener. The listener is instructed to attend (e.g., simply by counting) to the occurrence of the target stimulus. For instance, the letter/e/may serve as the "constant" stimulus and the letter/o/may serve as the "rare" stimulus. Completely at random, the letter/o/may be presented 10% of the time. Separate scalp recordings are then made in response to both the presentation of and attention to this rare stimulus. It is the listener's act of attending (a cognitive act) to the presence of the rare stimulus that generates the P300 waveform.

The P300 response is typically seen in the range of 250 to 700 milliseconds. It is comprised of P1, N1, P2, N2, P3, and N3 peaks and troughs, with P3 generally occurring at about 300 milliseconds. In general, the appearance of P300 depends on both the random occurrence of a rare stimulus and the ability of the listener to attend to the rare stimulus.

Efforts are less to identify neural generators of the P300 response than to identify those producing the auditory evoked responses described above because the P300 response, itself, is viewed as the product of a cognitive effort, such as attention. Nevertheless, there is some speculation that the P300 response recorded intracranially may arise from the hippocampal region and the amygdala.[21]

Clinical application of P300 recordings have been performed on persons with mild to severe TBI. Again, it should be clear that estimating hearing sensitivity has not been the

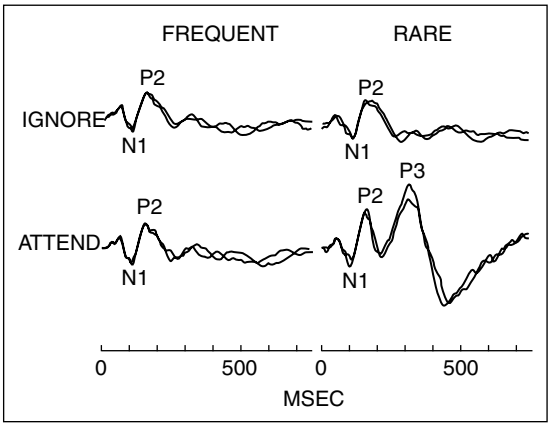

FIGURE 8.9
Auditory Late Response waveforms from a subject under attending or ignoring test conditions. (From Squires, K. C. and Hecox, K. E., Electrophysiological evaluation of higher level auditory processing, *Semin. Hear.*, 4(4), 422, 1983. With permission.)

focus of such use. Instead, interest is primarily on establishing the relationship between P300 latency and amplitude and various cognitive tasks. For instance, several recent studies of interest to TBI rehabilitation examined P300 recordings to investigate whether mild TBI caused deficits in attention,[24–28] increased distractibility during attending tasks,[29] or impaired information processing time.[30–33]

The role of auditory P300 in TBI rehabilitation continues to be of clinical interest because of efforts to uncover the relationship between neurophysiologic events at the cerebral level and a TBI individual's performance on behavioral scales.

Summary

The person with TBI is typically confronted with a lengthy rehabilitation process. Skills once performed unconsciously may now require supreme conscious effort, often with the assistance of various TBI rehabilitation specialists. To ensure that therapeutic goals and objectives are met as efficiently as possible, effective communication between therapist and patient must take place. For this to occur, rehabilitation personnel must be cognizant of a patient's ability to hear well enough to actively participate in his/her rehabilitation. Audiologists serve to provide the comprehensive audiologic assessments, using various and diverse audiologic techniques, needed to allow patient participation to be more effective.

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9

Traumatic Brain Injury: Aging and Related Neuromedical Issues

Alan Weintraub and Mark J. Ashley

CONTENTS

Introduction

Neuromedical issues are faced by a rapidly growing population of over 5 million persons living with traumatic brain injury (TBI) in the United States.[1] As the TBI population ages, survivors, practitioners, caregivers, and financially responsible parties, alike, must consider the neuromedical issues associated with aging and the complex sequelae of TBI. These parties must attempt to anticipate the issues to be faced by this population and further attempt to put in place mechanisms that might address those problems.

The highest incidence of TBI is bimodal in nature. Individuals 15 to 24 years of age constitute the first grouping while the second is comprised of those people aged 75 years and older. Prevalence is estimated at around 5.3 million individuals in the United States.[2] with incidence reported at 90 per 100,000.[3] Thurman et al.[1] estimates that between 80,000 and 90,000 persons per year become disabled as a result of TBI. As such, TBI presents a

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major public health concern, both as a diagnosis in itself and, in particular, as the effects of aging are applied.[4]

Age has been identified as contributory to outcome for persons who sustain TBI, though in a nonlinear way. It seems logical to assume that TBI inflicted upon a chronologically older brain would yield more devastating sequela, and perhaps a more disabling outcome, when compared to a similar injury sustained by a younger brain.[5–8] While this seems to hold true for cases of severe injury,[9,10] there is less support for injuries of lesser severity. This may be due to the neurobiology of injury and the potential for greater neuroplasticity in the younger brain.[11] A prospective study by Rapoport and Feinstein[12] found an inverse relationship associated with age and mild TBI. Older subjects (60+ years) fared better than their younger counterparts (18 to 59 years) with higher Glasgow outcome scores, less physical symptomatology, less psychosocial impairment, and less psychological distress. A reason for these surprisingly better outcomes in an elderly mild TBI population raises relevant theoretical considerations. While the younger brain has clear biological advantages for recovery of function, the older person usually will have well-established "real-life" knowledge, structures, and routines in their day-to-day experience that may give them compensatory advantage to facilitate a better functional outcome. Additionally, environmental demands associated with older adult lifestyles are often diminished in comparison to the demands placed upon younger adults.

Consequently, it is difficult, at best, to attempt to make definitive statements about likely long-term neuromedical issues following TBI based "solely" upon the age of the individual and even the level of severity of a given injury. Clearly, additional factors play into the long-term neuromedical outlook. It seems logical to consider these two factors together with other pertinent information that may bear on the long-term scenario. Insight must be gleaned from review of known, frequently encountered acute medical complications associated with TBI, rehospitalization experiences for individuals with TBI, the pathophysiology of TBI, neurological conditions associated with aging and/or TBI, and morbidity and mortality statistics.

This chapter will review various neuromedical issues associated with TBI, along with the interplay that may exist between TBI and other neurological conditions/diseases associated with advancing age.

Acute Medical Complications and Rehospitalization Rates in TBI

TBI impacts the central nervous system and numerous other organ systems due to the traumatic mechanistic nature of injury, such as motor vehicle accidents, falls, and so on. An early review of medical complications and associated injuries provides valuable insight into different types of intracerebral, extracerebral, and systemic complications in TBI.[13] These authors reported differences in outcome as measured by DRS scores[14] and length of stay for both acute and rehabilitation hospitalization as they related to severity of intracerebral and extracerebral injury and observed complications. Intracranial hemorrhages and other cerebral complications included subdural, epidural, subarachnoid, intraparenchymal, and other hemorrhages. Of individuals studied, 68% had one or more intracerebral hemorrhages. Other cerebral complications included intracranial hypertension, cerebrospinal fluid (CSF) leak, hydrocephalus, and seizures. Extracerebral complications included respiratory failure, pneumonitis, urinary tract infection (UTI), soft tissue infection (STI), coagulopathy, renal failure, and septic shock. Associated injuries included

TABLE 9.1

Intracerebral Complications

Complication	Percent
Intracranial hypertension	20
Seizure	17
CSF leak	8
Hydrocephalus	5

TABLE 9.2

Extracerebral Complications

Complication	Percent
Respiratory failure	39
Pneumonitis	26
Urinary tract infection	21
Soft tissue infection	16
Coagulopathy	5
Septic shock	3

TABLE 9.3

Associated Injuries

Injury	Percent
Fractures	62
Cranial nerve	19
Hemo/pneumothorax	11
Intra-abdominal injury	7
Spinal cord injury	2
Peripheral nerve injury	2
Brachial plexus injury	<1
Amputation	<1

fractures, cranial nerve injuries, hemothorax/pneumothorax, intra-abdominal injury, spinal cord injury, peripheral nerve injury, brachial plexus injury, and amputation. The frequency of these complications is shown in Table 9.1 to Table 9.3.

Englander et al.[15] also reported that respiratory complications were seen in 39% of 637 individuals during acute hospitalization. Twenty-one percent of individuals required gastrostomies and 23% required jejunostomies. More detailed information was available from this study pertaining to upper extremity fractures (humerus, radius, or ulna), which occurred in 11% of the study population, and pelvis or lower extremity fractures, which occurred in 21% of persons studied.

Of the four reported intracerebral acute medical complications, only hydrocephalus and seizures appear to impact the long-term neuromedical status of people with TBI. Of the seven reported extracerebral complications, it could be argued that respiratory and coagulopathic complications might reasonably bear some long-term neuromedical importance for persons with TBI.[16] It is less clear that early infectious complications, once resolved, impact long-term neuromedical status. Finally, of the eight associated injuries reported, cranial nerve injuries, SCI, peripheral nerve, and brachial plexus injuries might bear some significance from a strict neuromedical perspective, but only cranial nerve injury and SCI[17] seem to bear on likely neuromedical conditions impacting the central nervous system.

TABLE 9.4

Etiology of Rehospitalizations by Year Postinjury

Reason	Year 1[a] (n = 79 [22.5%])	Year 2[a] (n = 59 [21.0%])	Year 3[a] (n = 40 [20.0%])	Year 5[b] (n = 75 [17.0%])
Rehabilitation	3 (3.8%)	0 (0%)	0 (0%)	1 (1.3%)
Seizures	8 (10.1%)	8 (13.6%)	6 (15.0%)	14 (18.7%)
Neurologic disorder	4 (5.1%)	8 (13.6%)	2 (5.0%)	2 (2.7%)
Psychiatric	5 (6.3%)	9 (15.3%)	6 (15.0%)	12 (16.0%)
Infectious	9 (11.4%)	10 (16.9%)	3 (7.5%)	6 (8.0%)
Orthopedic/reconstructive	35 (44.3%)	14 (23.7%)	10 (25.0%)	10 (13.3%)
General health maintenance	11 (13.9%)	10 (16.9%)	9 (22.5%)	27 (36.0%)
Unknown	4 (5.1%)	0 (0%)	4 (10.0%)	3 (4.0%)

[a] *Source*: Cifu et al., Etiology and incidence of rehospitalization after TBI: A multicenter analysis, *Arch. Phys. Med. Rehabil.*, 80(1), 85–90, 1990.

[b] *Source*: Marwitz et al., A multicenter analysis of rehospitalizations 5 years after brain injury, *J. Head Trauma Rehabil.*, 16(4), 307–317, 2001.

A second source of insight into the nature of long-term neuromedical issues associated with aging in TBI is found in literature that reviews rehospitalization rates and reasons in the TBI population. People with disabilities, in general, are more likely to be rehospitalized than the nondisabled population.[18,19] Several studies have examined medical complications resulting in rehospitalization a number of years postinjury in TBI. Cifu et al.[20] found that rehospitalization rates were relatively stable over the first 3 years postinjury when all reasons for rehospitalization were grouped together. An increase in rehospitalizations due to behavioral/psychiatric problems, seizures, and general health maintenance from years 1 to 3 was observed. Rehospitalization for infectious processes peaked in year 2 and decreased somewhat in year 3 (Table 9.4).

A report of rehospitalizations was conducted 1 and 5 years after TBI for 1547 consecutive cases[21] enrolled in the NIDRR Model Systems for Traumatic Brain Injury. Of these, 799 were eligible for 5-year follow-up. The authors reported findings that were similar to those of Cifu et al.[20] in that rehospitalization for seizures and psychiatric problems increased from year 1 to year 5 (Table 9.4). It is interesting to note that between the two studies by Cifu et al. and Marwitz et al.,[21] rehospitalization rates for general health maintenance increased over the time periods studied. Clearly, disabled persons are less able to participate in their own health maintenance at the level seen in the general population and general health may be an issue of concern in the discussion of aging. In persons who have sustained TBI, cognitive, social, financial, and physical disabilities may serve as barriers to self-initiated health maintenance activities and practices.

Psychiatric issues also pose a substantial concern for the aging TBI population. Rehospitalization rates for psychiatric issues remained relatively stable between the two studies from year 2 (15.3%) to year 3 (15%)[20] and year 5 (16%).[21] Burg et al.[22] reported finding an incidence of self-reported TBI of one or more injuries in psychiatrically hospitalized individuals of 66%. This increase in psychiatric rehospitalization correlated with substantially more aggression toward family members and caregivers between years 1 and 5 postinjury.[23] Specifically, Brooks et al.[23] reported the incidence of threats of violence at a rate of 15% at year 1. By year 5, these incidents were reported by 54% of caregivers. Physical assault of a family member was reported by 10% of caregivers in year 1 and 20% in year 5.

Rehospitalization rates for seizures increased steadily over years 1, 2, and 3 in the Cifu et al.[20] study, peaking at 15% in year 3. The Marwitz et al.[21] study found seizure rehospitalization rates at 18.7% at year 5.

Rehospitalization rates for orthopedic/reconstructive procedures remained surprisingly high in the first 3 years postinjury ranging from 44.3% in year 1 to a relatively stable 23.7 to 25% in years 2 and 3, respectively. By year 5, the rate dropped to 13.3%, still fairly high for 5 years postinjury. Rehospitalization rates of 8% at 5 years postinjury for infectious disease are also high and may be a reflection of antibiotic resistant organisms which have increased in recent years.

In summary, the rehospitalization data up to 5 years postinjury suggests that seizures, neurological disorders, psychiatric/behavioral disorders, and maintenance of general health are issues of concern. Acute hospitalization complications and relatively short-term rehospitalization rates out to 5 years provide limited insight into likely neuromedical concerns for a population that can be reasonably expected to live from 10 to 55 years postinjury depending upon age at injury, injury type, injury severity, and functional status.[24]

Pathophysiology of Traumatic Brain Injury

To speculate in more detail over the anticipated neuromedical sequela of TBI with aging, clinicians must appreciate the pathophysiologic complexity and heterogeneity of TBI. Cytoarchitectural changes associated with chronic TBI logically serve as a basis for potential neuromedical aging-related developments and conditions. As such, consideration of the nature and type of injury to neural structures may be important in understanding the nature of long-term neuromedical issues that may develop. TBI can result in focal or diffuse metabolic, hypoxic, ischemic, or traumatic axonal damage.[25] Focal damage can be reasonably expected to impact certain motor, sensory, or cognitive functions, depending upon the neural structures or systems involved.

Diffuse axonal injury (DAI) is recognized as a primary component of neurophysiological dysfunction in 40 to 50% of all brain injury which arises from forces applied to the head.[26] DAI tends to predictably affect specific regions of the human brain, such as the parasaggital white matter of the cerebral cortex, the corpus callosum, and the pontine-mesencephalic junction adjacent to the superior cerebellar peduncles.[27] At the cellular level, direct forces of sufficient magnitude breach the neuronal/axonal cytoplasmic cellular membrane, initiating a cytotoxic, biochemical cascade of events which impacts neuronal health and function in the immediate vicinity of the primary damage.[28] The damage inflicted by this cytotoxic biochemical cascade, however, is not restricted to the locality of the primary site of damage and can reach far distant cellular structures within the central nervous system.[29]

Neurofilamentary changes arising from DAI consist of mechanical failure of the axonal cytoskeleton and/or the biochemical cascade that brings about Wallerian degeneration.[30] Neurofilamentary changes associated with Wallerian degeneration, however, are not immediate. Wallerian-type axonal degeneration progresses from axonal swelling to swelling of the axonal bulbs, leading to the development of small clusters of microglia.[31] At a cellular level, this includes residual endogenous brain peptides and small proteins,[32] immunoreactive astrocytes in injured areas,[33,34] beta-amyloid protein deposition,[35] and neurofibrillary tangles.[36] These changes occur from days to months to years after injury. Active myelin degeneration occurs as the final stage in the neurodegenerative process in the first 2 years after DAI.[37]

Some evidence also exists for the presence of chronic perivascular iron deposition (siderosis) associated with previous perivascular hemorrhage in cortical, subcortical,

brainstem, and cerebellar structures.[38] Primary areas of involvement include the parasaggital white matter, the corpus callosum, the internal capsule, and the deep gray matter.

Cognitive Decline

The relationship between a history of TBI, age or aging, and cognitive decline must be examined from two perspectives. The first considers whether cognitive decline associated with normal aging is, in some manner, impacted or accelerated by interaction with some neurological mechanism associated with the abnormal brain following TBI. The second considers whether the cognitive impairment often seen following TBI persists throughout life or worsens over time in comparison to the cognitive performance of persons without TBI. The clinician considering cognitive decline must be able to differentiate normal age-related cognitive decline from early signs of dementia, especially in attempting to prognosticate and make recommendations to individuals and their families. Several studies have attempted to examine the reality, persistence, and perception of TBI-related progressive cognitive impairments with aging.

Subjects with mild to moderate TBI were evaluated several years postinjury for cognitive performance and compared to two groups of age-matched normals. Middle-aged persons and older persons with, and without, TBI were also matched and compared. The TBI subjects reported the belief that they suffered no long-term sequela associated with the TBI, though test results demonstrated cognitive performance to be impaired. The authors reported TBI sustained early in life, which results in permanent sequela in specific domains of cognitive functioning, did not interact with changes in cognitive function arising from normal aging. In fact, middle-aged persons with TBI actually performed at the level of older, non-TBI subjects.[39]

Goldstein et al.[40] reported that deficits in cognitive performance persisted over time for persons with TBI when compared to a normal population. Additionally, these authors found that the magnitude of the difference in cognitive performance between persons with and without TBI remained stable over time. These findings suggest that the effect of TBI on cognitive performance is additive to declines in cognitive performance associated with normal aging.

Thus, it appears that individuals with TBI may accommodate to some level of decrement in cognitive performance over time. Without reference to potentially escalating neurobehavioral sequelae with aging, these studies show that differences exist between individuals with TBI and those without. These differences persist, but seem to remain stable in magnitude.

Dementia and Alzheimer's Disease

Along the continuum of cognitive decline associated with normal aging comes a point at which the level of cognitive decline interferes with normal function and becomes dementia. The prevalence of the "dementia syndrome," in and of itself, increases with advancing age.[41] There is also some degree of intellectual and cognitive dysfunction affecting about 15% of the population over the age of 65.[42] This makes it difficult to investigate whether TBI directly causes dementia and/or Alzheimer's disease (AD). The research issue is further clouded by difficulty in proper characterization of normal cognitive decline and early onset dementia.

The contribution of TBI to the development of AD and other dementias has been a topic of considerable focus in the literature. The literature has revealed an intriguing relationship between a history of TBI and AD, in particular. The linkage of TBI to AD will be examined but it is important to consider the scientific limitations in research design and methodology. Much of the literature provides retrospective reviews of coincidental diagnoses such as stroke or TBI and the development of AD or other dementia.[43] Correlational studies are useful in pointing to potential causal relationships; however, attribution of causality due to the finding of correlation is inappropriate. Care must be taken to avoid such common error in the application of statistical analysis.[44]

The presence of neurofibrillary tangles has been identified in the brains of boxers who suffered from the syndrome of Pugilistica Dementia. AD-like pathology appeared to arise from a protracted history of repeated blows to the head.[45] Beta-amyloid protein deposition was not found, however, in these subjects. Conversely, in a study by Roberts et al.,[35] immunocytochemical methodology further clarified the neuropathology of pugislitica dementia. The use of immunocytochemical methodology allowed identification of both substantial beta-amyloid protein deposition and development of neurofibrillary tangles in pugilistica dementia similar to that found in AD. Increased expression of beta-amyloid precursor protein is found as an acute-phase response to traumatic neuronal injury. Additionally, such increased expression is a marker of immunoreactivity. The authors suggested that the extensive overexpression of this response may lead to the deposition of beta-amyloid protein, thereby initiating an AD-type process within days postinjury.[35]

Several retrospective and case-controlled studies demonstrated a higher incidence of AD in individuals with a history of TBI.[46–49] Salib and Hillier[50] examined the relationship between TBI and AD and other dementias, looking at relative risk/odds ratios. While there was an association found between a history of TBI and the development of AD (only in males) and other dementias, greater risk ratios were observed for other dementias rather than AD. In this study, head trauma was not identified to be a significant risk for AD. The interval observed between TBI and the development of AD was several decades.

Later research added still further information in determining the relationship between a history of TBI and the development of AD. Mayeux et al.[51] determined that it was the presence of apolioprotein-epsilon-4 (APOE-4) that materially increased the risk of AD. TBI, in the absence of the APOE-4 allele, did not increase the risk of AD and only the presence of the APOE-4 allele in persons with a TBI did so.[51] While the presence of the APOE-4 allele increased the risk of AD, cerebral deposition of beta-amyloid with age, a genetic mutation, or brain injury were felt to further contribute to the pathogenesis of AD.[52,53] The effects of brain injury and APOE genotype on AD risk was studied by Guo et al.[54] evaluating 2233 subjects who met criteria for probable or definitive AD. The study continued to demonstrate a relationship between TBI injury severity and genetic subtype.

A population-based study conducted by Nemetz et al.[55] investigated the incidence of persons with TBI who later developed AD. It was concluded that the incidence of AD was no different than that of the normal population. The onset of AD for persons with a history of TBI, however, was observed to occur an average of 10 years earlier than for those without a history of TBI. These findings are substantiated by the work of Mehta et al.[56] In a prospective, population-based study of 6645 participants who were free of dementia at baseline, the authors compared them to a cohort of individuals diagnosed with dementia. Their findings included no increased risk of AD or dementia associated with a history of trauma with a loss of consciousness. Multiple head traumas, time since head trauma, and duration of unconsciousness also did not significantly influence the risk of dementia. Finally, the presence of the APOE-4 allele was not found to interact with the time to onset of dementia.

Still other factors may bear on the earlier manifestation of AD and the association of TBI with other dementias. Brain trauma damages the blood–brain barrier permitting

extravasation of serum proteins into the surrounding parenchyma.[57,58] The introduction of serum proteins into the surrounding parenchyma may portend an activation of an immunological response later in life in instances where the blood–brain barrier is again compromised. Since permeability of the blood–brain barrier is not well understood in normal aging, the issue of potential leakage as a trigger for a secondary immunological response needs further exploration.[59]

Study of regional cerebral blood flow (rCBF) in AD reveals diminution of rCBF in the posterior temporal and inferior frontal/parietal areas in subjects who developed AD.[60] Therefore, the nature of the TBI itself may yield predictive insight into whether AD will more likely manifest. For example, focal and multifocal injuries to the brain tend to predominate in the frontal poles and anterior temporal structures of the brain.

Utilizing positron emission tomography (PET), regional brain metabolism for individuals with cognitive symptoms of dementia was found to be a sensitive indicator of both AD and neurodegenerative disease by Silverman and colleagues.[61] A negative PET scan indicated that cognitive impairments were unlikely to progress over at least a 3-year period.

A salient neuroimaging feature of AD and the frontotemporal dementias is progressive brain atrophy, also a characteristic of chronic TBI. Chan and colleagues[62] obtained serial MRI images in order to quantify rates of cerebral atrophy in individuals with AD, frontotemporal dementia, and controls. They found the annual rate of atrophy was significantly greater in demented individuals (2.7%) than in controls (0.5%). While the results of this study were able to distinguish normals from individuals with dementia, it could not differentiate between the types of dementia, such as AD or frontotemporal dementia. These atrophy measurement techniques are presently confined to the research environment. In the future, brain atrophy measurement techniques may provide a means of assessing the differential characteristics of post-TBI cerebral atrophy due to aging contrasted with an index of a more specific separate dementia entity, such as AD or frontotemporal dementia. The implications of this regional volumetry technology may help in the development of treatments with the goal of delaying a progressive neurodegenerative process.

The loss of neural structures associated with TBI earlier in life does reduce overall neuronal availability and thereby diminishes the redundancy of neural structures. As such, a diminished reserve may contribute to an earlier manifestation of dementias. To the extent that AD and other dementias may have a genetic basis, persons with TBI may experience the development of these dementias in concurrence with the TBI sequela, just as they might other diseases, such as cancer or heart disease.

As one attempts to draw conclusions regarding TBI and its relationship to the development of AD or other dementias, multidimensional factors need to be considered. The clinician must evaluate the potential interrelationships between age, various neuropathologies associated with different injury types, idiopathic neuronal atrophy, the potential contribution of repetitive trauma, genetic predisposition, and immunosusceptibility. These relationships may all play a role in the timing of the onset of dementia, the rapidity of progression of dementia, and/or the development of other neurodegenerative disorders.

Other Neurological Disorders

The majority of studies investigating the relationship of TBI and neurological disease have focused on brain injury as either a precipitating risk factor for the *de novo* development or exacerbation of the progression of AD, Parkinson's disease, Amyotrophic Lateral Sclerosis, and Multiple Sclerosis.[63–68] Given case reports relating post-TBI syndromes that resemble Parkinson's syndrome,[69,70] the theoretical consideration of trauma as an etiology of Parkinsonism is necessary.[71] Goetz and Stebbins[72] found that TBI seemed to modify the course of Parkinson's Disease (PD) in a small series of ten individuals. Following TBI,

they found a transient increase in disability status lasting a few weeks, but after 1 year, there was no difference in disability compared to age-matched controls.

Williams et al.[68] examined the medical records of 821 people with TBI, between 1935 and 1974, who were more than 40 years old. These people were followed for the development of dementia and other degenerative neurological diseases. Utilizing a standardized morbidity ratio (SMR), there was no evidence that brain trauma was a significant risk factor for the development of Parkinsonism, Parkinson's disease, or Amyotrophic Lateral Sclerosis.

Over the past several years, the issue of injuries precipitating multiple sclerosis (MS) or promoting new relapses of MS has also been passionately debated in the literature. Well-designed studies have concluded that TBI and other types of injuries do not precipitate MS nor lead to relapses of MS. Sibley et al.[64] reported a large number of prospectively studied individuals with MS and identified a subgroup of 67 individuals who incurred a total of 140 episodes of "closed head injury." It should be noted that only nine of these episodes were associated with a period of definite or probable loss of consciousness, with none lasting more than a few minutes. Siva et al.[66] examined individuals with significant TBI to determine whether any of these individuals subsequently developed MS. The study did not consider individuals with MS who incurred TBI.

However, to these authors' knowledge, there are no other studies describing the interaction of "significant TBI" with underlying MS. Many clinicians have wrestled with the issue of a coincidental MS relapse vs. the consequences from the TBI. It has been postulated that the pathobiologic interaction of TBI with damage to axons in previously demyelinated pathways may explain these unexpected clinical scenarios.[28,29]

The majority of studies addressing trauma and multiple sclerosis concern the issue of trauma as an environmental etiologic trigger of MS or relapses of MS. In 1987, Poser suggested that TBI may exacerbate the underlying disease process of MS.[73] Bamford et al., Sibley, Siva et al., Sibley, and Kurland et al.,[63–67] on the basis of longitudinal studies of cohorts, found no indication that either the onset or exacerbation of MS was the result of physical trauma. A major limitation of these studies was that their design did not evaluate the consequences of "significant TBI" in people with MS.

In general, the effect of preexisting neurological disorders and their attendant neuropathology interacting with the pathobiology caused by TBI appear significant, but how this modifies outcome is unknown. Conversely, how the pathobiology of TBI modifies the subsequent course of the underlying neurological disease is also unknown. In this regard, demyelinating diseases such as MS may interact differently than neuronal diseases such as Parkinson's Disease in the setting of TBI and with the consequences of aging. This, again, may be an additive effect related to neuronal loss with increasing brain age, thus magnifying the pathobiologic effects of the TBI and the neuropathology of other neuronal diseases such as Parkinson's disease and demyelinating diseases such as multiple sclerosis.

Seizures

Seizures are considered to be the clinical manifestation of an abnormal and excessive discharge of a set of neurons within the brain, including cortical cells. While seizure phenomena can be associated with an acute insult to the central nervous system or a generalized systemic metabolic disturbance, this does not necessarily constitute a condition of "epilepsy."[94] Epilepsy is defined as a condition characterized by recurrent, unprovoked seizures.[96]

Epilepsy occurs within the general population with varying incidence depending upon age. This topic must consider, independently, seizures associated with "normal aging," aging-related diseases, TBI, and their potential interactions.

Normal Aging

Seizure incidence appears to be highest in children, though incidence increases substantially in people over the age of 70.[74,75] Hauser et al.,[74] in a prospective epidemiologic population-based study, followed the incidence of epilepsy and unprovoked seizures in Rochester, Minnesota, over a 50-year period. Incidence in people over age 70 was found to be two to three times greater than in children. Incidence at age 40 was 30/100,000 and, by age 80, increased to 140/100,000. There was no gender difference observed. Generalized seizures occurred most frequently in children, whereas the elderly had a higher incidence of partial onset seizures. In people over age 75, partial epilepsy was five times more frequent than at earlier ages. Approximately two-thirds of seizures in people under age 40 were tonic–clonic seizures. The rate of tonic–clonic seizures decreased to 54% for the age group 40 to 65 years and to 40% in people 65 years and older.[74] Overall, the cumulative incidence of epilepsy ranged from 1.2% from 0 to 24 years, 3% from 25 to 74 years, and 4.4% from 75 to 85 years. Age-specific incidence is highest in the first year of life. Incidence decreases during childhood and remains stable up to age 54, when incidence begins to increase again.[74]

Hauser et al.[74] determined the three most common etiologies for seizure disorders in people over age 65 were cerebrovascular disease, degenerative diseases of the CNS, and CNS tumors. Approximately two-thirds of all cases had a cerebrovascular etiology. Included in this category are cerebrovascular accident (embolic stroke and intracerebral hemorrhage), hypertension, vasculitis, and arteriovenous malformation.[76–81] Seizures are fairly common within the first 2 weeks of cerebral infarction and are considered to be an acute effect of the infarction.[82,83] Cerebral cortex involvement, the presence of multiple lesions, hemorrhage, and embolic infarcts have been identified as risk factors for recurrent seizures following stroke.[84]

Degenerative diseases are associated with an incidence of seizures that ranges from 10 to 22%.[85–88] McAreavey et al.[85] found that people with dementia who had seizures were younger and more cognitively impaired than a control group of people with dementia only. There did not appear to be any dementia etiologic differences between the two groups.

Hauser et al.[74] found CNS infections, tumors, and neurological defects arising from birth or trauma to be of equal frequency as antecedents to seizure disorders in people between 15 and 34 years. Neoplasms and trauma were equally frequent antecedents in people 35 to 64 years and cerebrovascular disease emerged as the most frequent. Cerebrovascular insults preceded the diagnosis of epilepsy in 15% of this age group. In the greater than 65 years group, 28% of all newly identified seizure cases were preceded by cerebrovascular disease and 20% of seizures had associated degenerative disease.

Management of seizures is impacted by physiological changes in aging.[89] Pharmacokinetics, routes of administration, drug interactions, pharmacodynamic interactions, and even drug cost must all be considered as they influence treatment selection.[75] Aging is associated with decreases in serum concentration of plasma proteins and albumin necessary for pharmacological binding, absorption, and bioavailability.[90,91] Inefficiencies in hepatic and renal function with advancing age also impact metabolism and excretion.[90,91] Swallowing and cognitive decline may contribute to difficulty with an oral route of administration. Nasogastric, intramuscular, and rectal options for drug delivery must be made available.[92] Finally, in people over 60 years of age, the average number of drugs taken at one time is 7, with up to 13 taken over a year.[93] The risk of pharmacokinetic and pharmacodynamic polypharmacy interactions is quite high.

Traumatic Brain Injury

Seizures play a relatively prominent role in a discussion of either aging or TBI. Seizures represent the second most frequent intracerebral complication, occurring at a rate of 17%. Only intracranial hypertension, as an intracerebral complication, is higher and, then, by only 3%.[13] Seizures increase in frequency from year 1 to year 5 as a reason for rehospitalization and become the second most common reason for rehospitalization, following general health maintenance.[20,21]

Studies of seizure incidence and prevalence in the general population logically have individuals with TBI as a subgroup. Consequently, direct comparison of data sets between the two groups should be cautiously interpreted. The causes of epilepsy which are germane to the discussion of "aging-related" posttraumatic seizures can be idiopathic, tumor, trauma, and vascular, which may include hypoxic/ischemic cerebral insult.[95] A thorough review of the subject can be found in the chapter in this text by Hernandez et al. Also, Dalmady-Israel and Zasler[96] published a critical review of the literature related to current concepts of definition, incidence, and risk factors pertaining to posttraumatic seizures. This review, together with an overview of the topic by Yablon,[97] offers a good literature review of posttraumatic seizures over the past 50 years, including incidence, natural history, and predictive characteristics. These articles discuss rehabilitation management topics, such as anticonvulsant prophylaxis, symptom management, and other problems encountered in the rehabilitation setting.

Posttraumatic epilepsy (PTE), to some degree, is the result of neuronal biochemical changes related to the injury process and may play a role in seizures or recurrent ictal episodes.[98] In addition, differences in types of force, mechanical factors, and anatomic injury may help determine one's predilection for developing posttraumatic seizures.[98] A positive correlation between brain injury severity and the development of one or more seizures has been identified. When brain trauma results in cortical injury and neurological deficits without interruption of the dura matter, PTE incidence ranges between 7 and 39%. Where dural disruption and neurologic abnormalities coexist, the incidence increases dramatically to between 20 and 57%. Interestingly, however, injury severity and the persistence of ictal episodes do not appear to have a correlation.[99]

In practical terms, rehabilitation professionals have considered missile penetrating injuries, depressed skull fractures, intracerebral/intracranial hematomas, and early epilepsy, defined as seizures within the first week after brain trauma, as the highest at-risk group for developing PTE.[100–103] Feeney and Walker[104] developed a mathematical model to estimate the probability of posttraumatic seizures. This classic study found individuals with central parietal injury, dural penetration, hemiplegia, missile wounds, and intracerebral hematomas to be at greatest risk for development of PTE.

Clinician's experience and Feeney and Walker's[104] work suggesting dural penetration to be a key risk factor has been substantiated in the literature. While the risk of seizures is, in fact, very high following penetrating missile injury and has been estimated at 35 to 53%,[105] the risk in diffuse–closed head injury, without contusion or laceration of the cortex, is much lower, approximately 5%.[106]

PTE can occur in the early period following TBI. The early period is defined as occurring within the first 7 days of injury.[107] PTE can also have its first manifestation many months or years postinjury, thereby defining late seizures. The risk of PTE after cerebral parenchyma–penetrating injury remains for up to 15 years. Approximately 95% of individuals who remain free of seizures in the first 3 years after injury remain seizure-free long-term.[108–110] Approximately 56% of individuals with TBI, without missile injuries, who develop late seizures do so within the first year of injury.[111]

Age at the time of injury appears to figure into the risk of developing PTE.[100] In a study by Kennedy and Freeman,[112] risk of early posttraumatic seizures was found to be higher in children, though fewer developed late seizures, defined as after the first week post-trauma. When late seizures occurred, approximately 40% were noted to have focal features, 70% became unconscious, and 20% had disturbed consciousness, with or without focality, defined as partial-complex seizures.

In a study of 490 consecutive people with TBI, Asikainen et al.[113] studied factors active in the development of early and late seizures and their subsequent influence on long-term outcome. They determined that young children were more prone to early seizures than adolescents and adults, who were more prone to late seizures. The main risk factors for late posttraumatic seizures were the known presence of early seizures and depressed skull fracture. Brain injury severity, as measured by a low Glasgow Coma Scale (GCS) score, prolonged unconsciousness, and posttraumatic amnesia, without localized brain pathology, was not found to be a risk factor for the development of late PTE. It was recommended that people with TBI who developed seizure disorders have appropriate anticonvulsant therapy and thorough follow-up. Individuals receiving this level of care were able to attain higher rehabilitation goals and functional outcomes, such as employment.[113]

It is always of great interest to be able to discern whether a seizure will be an isolated event or whether recurrence is likely or inevitable. This is of concern for operation of automobiles and mechanized equipment, independence and safety in the community or living environment, and return to school or work. Haltiner, Temkin, and Dikman[114] studied the incidence and risk factors for seizure recurrence after the onset of late PTE. This longitudinal, cohort design showed that, when late seizures developed following severe TBI, the probability of recurrence was high. The importance of aggressive anticonvulsant medication management following a first, unprovoked late seizure was emphasized.

While the importance of treating defined seizures and epilepsy is clear, the issue of suppressive treatment vs. prevention is somewhat controversial. Suppressive treatment is defined as medication intervention to decrease the occurrence of seizures during the time in which the individual is at greatest risk. Prevention refers to an approach of ongoing treatment following the epileptogenic at risk phase. Several older retrospective studies suggested antiepileptic prophylaxis may prevent the genesis of epileptic foci.[115–117]

However, most clinicians now practice in a manner consistent with a study conducted by Temkin et al.[107] This randomized, double-blind study of phenytoin coverage for the prevention of posttraumatic seizures was designed on the assumption that seizure prophylaxis following brain injuries (i.e., medicating to attempt to prevent the first seizure) would prevent the development of eventual posttraumatic epilepsy. Convincing evidence was demonstrated as to the effectiveness of phenytoin-seizure prophylaxis when treating during the first week following severe TBI. When compared to placebo, treatment with phenytoin was associated with a 73% decrease in the risk of seizures in the first week. However, no significant protective effect was detected between day 8 and the end of the second year of study. Therefore, the early, but not late, effect of phenytoin appears to have an early suppressive effect (i.e., during the vulnerable epileptogenic phase), but not necessarily a true long-term prophylactic or preventative effect. This hallmark study concluded that phenytoin reduces the incidence of seizures in the first week after injury, but not thereafter.

While managing a person with TBI over his/her entire life, the clinician must be cognizant of the unique presentations of the types of seizures that present with aging and the elderly, appropriate methods of diagnosis, and the complexity of different treatment paradigms.[92,118,119] Care should be taken to avoid over-attribution of seizures to a history of TBI alone in the aged.

Cerebral Atrophy, Ventricular Size, and Hydrocephalus

Posttraumatic ventriculomegaly is a frequent neuroimaging finding following moderate to severe TBI.[120,121] Ventriculomegaly following TBI remains a controversial condition as to what it signifies. Chronic neuroimaging findings of cerebral or subcortical atrophy do not necessarily have clinical implications.

Chronically-aging TBI reveals a relationship between cortical atrophy and ventricular volume in neuroimaging studies. Volumetric measures of brain morphology show that the generalized effects of most traumatic diffuse axonal injuries are more evident via ventricular dilatation, while the effects of focal and multifocal injury appear to be more evident in cortical atrophy measures.[122]

Computerized tomographic (CT) volumetric studies of the cortical/subcortical mass to ventricular size ratio[123] have shown that marked encephalomalacia occurs over many years postinjury.[122,124] As the processes of neurodegeneration and gliosis associated with injury advance over time, cortical/subcortical volume decreases, while there is an associated compensatory increase in ventricular size. Over time, the CT pattern in TBI is one of mild to moderate ventricular enlargement and normal sulcal prominence, except in cases of focal injury. This process is far greater than that seen in normal aging, though a similar, less pronounced change in cortical volume and ventricular size is seen in normal aging. Magnetic resonance imaging (MRI) of aged persons with a history of DAI demonstrates progressive atrophy within the corpus callosum over many years.[125–127]

Normally, cerebrospinal fluid (CSF) is produced by the choroid plexus in the ventricular system. CSF is extruded into the ventricles and flows from the ventricle of origin to the sequential ventricle(s) via the Aqueduct of Sylvius, ultimately exiting the ventricular system to be reabsorbed by the arachnoid villi in the superior sagittal sinus. Noncommunicating or obstructive hydrocephalus develops when an obstruction blocks the flow of CSF and a buildup of CSF occurs behind the obstruction, causing the ventricle(s) behind the obstruction to enlarge. Obstructive hydrocephalus can occur as a result of hematoma, subarachnoid hemorrhage, or meningitis.[128] Communicating hydrocephalus occurs when CSF production continues at a normal rate, but reabsorption in the subarachnoid space is slowed, causing a buildup of CSF within the ventricular system. Ventricular enlargement stretches fibers in the surrounding regions, thereby impairing function. Clinically-significant hydrocephalus, whether obstructive or communicating, may be of a high or normal pressure variant.[129]

Differentiation of ventriculomegaly, in which the underlying process is due to subcortical atrophy, and "hydrocephalus," which implies an active obstruction of cerebrospinal fluid or diminished reabsorption, is quite difficult at times. The progression of ventricular enlargement, which results from cerebral atrophy associated with diffuse axonal injury and normal aging, can further complicate this clinical differentiation. The importance of differentiation of the typical symptoms of normal pressure hydrocephalus[130] from symptoms related to brain trauma, itself, is reviewed by Beyerl and Black.[131] The imaging criteria of Kishore et al. are still widely accepted for progressive ventriculomegaly with the distended appearance of the anterior horns of the lateral ventricles, enlargement of the temporal horns of the third ventricle, with normal or absent sulci, and, if present, enlargement of the basilar cisterns and fourth ventricle.[120] Periventricular decreased density on CT imaging was also felt to be a diagnostic indicator of communicating hydrocephalus, as well as enhanced trans-ependymal and periventricular flow patterns on MRI scan.

The classic triad of normal pressure hydrocephalus is impaired gait, incontinence, and dementia.[130,132,133] In early stages of this phenomena, gait may be unsteady or apraxic and

cognitive decline can be noted, as opposed to an absolute loss of consciousness in more severe cases.[134]

Even though ventricular shunting is frequently regarded as a routine procedure, clinicians must be cognizant of the possibilities of mechanical, biological, or technical complications.[135] Complications of ventricular shunting for hydrocephalus can include shunt failure, hemorrhage, delayed wound closure, infection, and seizures.[136] Dan and Wade[135] reviewed the incidence of seizures after ventricular shunting in 180 of 207 consecutive cases for hydrocephalus arising from various causes. A total of 9.4% developed seizures. Incidence appeared to be age-related, with a 15.2% occurrence in children younger than 1 year, 10% occurrence in people aged 1 to 49 years, and 6.9% incidence in people over age 49. Risk of postshunt seizures decreased with time after surgery, from 5% in the first year to 1.1% after the third year. The incidence of seizures rose with multiple shunt revisions. Cortical puncture site for ventricular catheterization significantly affected rates of seizures. In 168 individuals with a posterior parietal insertion, incidence of seizures was 6.6%. In 11 individuals with frontal catheter placement, 54.5% experienced seizures.

Shunt implantation outcomes were also reviewed in 48 individuals following severe TBI where implantation was performed a mean of 27 months postinjury.[136] Improvement in clinical status occurred in 52.1% of cases, whereas 47.9% showed no improvement. Immediate seizures occurred within 1 hour of surgery in five cases. Seizures occurred within the first week of surgery in one case and, after the first week, in 29 cases. Prior to shunt implantation, 14 individuals had seizures, while 17 developed seizures after shunt implantation. Postoperative complications that required shunt revision were shown by 15 individuals. Three individuals had postoperative complications that did not require shunt revision, one of whom developed marked cerebral edema.

In summary, clinical differentiation between cerebral atrophy due to aging and subcortical atrophy due to trauma must be made. The clinical and imaging differentiation is furthered by determination of the degree to which the observed recovery pattern is or is not consistent with an expected recovery pattern related to the underlying pathophysiologic correlates of injury. Where incongruence between the observed and expected recovery patterns exists, the interaction of communicating hydrocephalus, with or without pressure, should be considered. Careful selection for shunt placement should be based on a realistic appraisal of the risk/benefit ratio for surgical complications vs. better outcomes. Favorable outcomes from CSF shunting in appropriately selected individuals are reported, and technical considerations include timing, the type of shunt valve used, seizure prophylaxis, and methods of long-term follow-up.[137] A recent technological advance is found in the development of programmable shunt valves. An improved understanding of intracranial pressure dynamics and their clinical correlates, before and after CSF shunting, may lead to a more scientific rationale for the application of these valves and their safe use.

Neuroendocrine Dysfunction

TBI has been associated with neuroendocrine dysfunction in both the acute and chronic states.[138–142] Endocrine abnormalities following brain trauma vary with the comparative degree of injury to the hypothalamus, the anterior or posterior pituitary, the upper or lower portion of the pituitary stalk, and the connections of these structures to other subcortical and brainstem structures.[143] These traumatic neurohypophyseal system injuries acutely may lead to abnormalities in salt and water metabolism, including syndrome of

antidiuretic hormone (SIADH), temporary or permanent diabetes insipidus (DI), thyroid function, control of body temperature, abnormalities in ACTH-cortisol levels, and glucose metabolism, to name a few. Yuan and Wade[143] felt it was unusual to find "classic" features of hypothalamic or pituitary dysfunction in the TBI population. Koiv et al.[138] found serum catecholamine and ACTH levels were reduced in people with severe brain injury who had CT scan evidence of severe alterations in mesencephalic/diencephalic regions. In these cases, cortisol levels were elevated.

Neuroendocrine dysfunction following chronic TBI has only recently been systematically evaluated as a potential contributor to outcome. Lieberman et al.[140] studied 70 adults with TBI on average who were 4 years postinjury. Serum TSH, free T_4, insulin-like growth factor I, prolactin (PRL), testosterone (males), and cosyntropin stimulation were evaluated. Abnormal results were followed by dynamic tests of gonadotropin, thyrotropin stimulation hormone (TSH), and growth hormone (GH) secretion. The authors reported that 31.4% of subjects had no abnormalities. A single abnormal axis was found in 51.4% of the subjects (26 adrenal, 8 thyroid, and 2 GH) and twelve subjects had dual axis abnormalities (5 adrenal and thyroid, 4 adrenal and GH, 1 GH and thyroid, 1 gonadal and thyroid, 1 adrenal and PRL). There was no correlation with initial GCS. GH deficiency was found in 15% of subjects and low morning cortisol levels in 46% of these cases. Hypogonadism and diabetes insipidus were not observed.

Kelly et al.[139] reported some degree of hypopituitarism in nearly 40% of persons who had suffered moderate to severe head injury. Long-term anterior pituitary dysfunction was most common, while thyrotroph and corticotroph deficiencies were less common. The authors suggest that pituitary–hypothalamic axis testing is warranted for people with moderate to severe brain injury or subarachnoid hemorrhage, particularly those who experienced hypotensive or hypoxic events, evidence of diffuse brain swelling, and/or basilar skull fractures that involve the sella turcica. While direct trauma to the pituitary gland may account for dysfunction, the authors feel that vascular causes may be more prominent.

Neuroendocrine function may be important for rehabilitative success, neuromedical function, and overall health. It is illustrative to consider examples of how specific endocrine abnormalities may correlate and further contribute to an individual's functional life challenges. Neuronal growth is regulated by cytoskeletal proteins and depends on thyroid hormone equilibrium.[144] The highest concentration of thyroid hormone receptors has been found in the adult rat hippocampus, amygdala, and cerebral cortex.[145] Both thyroid and estrogen have been demonstrated to impact dendritic tree density in the cerebral cortex.[146–150] Thyroid deficiency can result in cerebellar ataxia, leading to instability and a predisposition to falling and reinjury. Thyroid deficiency can also further contribute to cognitive and emotional difficulties in the domains of memory and new learning. Glucocorticoid receptors, like thyroid receptors, are found in concentration in the hippocampus.[151] The subsequent paralimbic neurobehavioral consequences of glucocorticoid insufficiency include apathy, depression, irritability, and psychosis.

The direct result of endocrine dysfunction as it relates to TBI and aging may lead to an array of chronic physical, neurobehavioral, and functional disabilities. This comorbidity should be further explored in individuals who display chronic symptoms of fatigue, loss of muscle strength, decreased energy, cognitive dysfunction, inability to regulate body temperature, emotional lability, decreased aerobic capacity, and decreased bone mineral density. Combined with the direct effects of TBI, an endocrinopathy may further result in a diminished sense of well-being, social isolation, and overall reduced quality of life.[152,153]

Endocrine function should be monitored in brain-injured individuals who may be particularly susceptible beyond the postacute phase of management. TBI individuals at particular risk with aging to this comorbidity are those with known basilar skull fracture,

history of severe DAI with dysautonomia, protracted posttraumatic amnesia, or those with a history of SIADH or diabetes insipidus.

Sleep

Sleep is beneficial for the rejuvenation of human functioning, and animal studies have shown it necessary for survival. Deprivation and disturbance of this rejuvenating process can have many adverse effects. With aging, these effects include excessive daytime sleepiness, fatigue, frustration, depression, poor quality of life, impaired performance, decreased productivity, and increased health care costs.[154] Sleep disturbance is a relatively common complication following TBI. Beetar et al.[155] reported that subjects with brain injury had significantly more insomnia (56%) and pain complaints (59%) than nonbrain-injured subjects. Poor sleep maintenance was the most common sleep problem. Clinshot et al.[156] reported 50% of brain-injured individuals had difficulty sleeping during inpatient rehabilitation. Another study reported 30% of individuals with brain injury were found to suffer from insomnia.[157] Interestingly, they reported that the more severe brain injury was associated with less likelihood of sleep disturbance.

Many of the sequelae of sleep disturbance may be particularly disruptive to the neurobehavioral functioning of individuals with TBI. This includes agitation, poor performance, decreased attention, memory, confusion, somatic complaints, and decreased seizure threshold. One study revealed self-reported sleep disturbance in 73% of rehabilitation inpatients and 52% of outpatients with brain injury, and two other studies reported a correlation between sleep pattern abnormalities and cognitive deficits following brain injury.[158–160]

The particular sleep disorders individuals with TBI are at risk for include posttraumatic hypersomnia, narcolepsy, central sleep apnea, obstructive sleep apnea, nocturnal seizures, periodic limb movement disorder (PLMD), and insomnia.[161] In a study of 20 individuals between 1 and 9 months post brain injury who complained of excessive daytime sleepiness, eight subjects had sleep apnea/hypopnea syndrome.[162] Sleep apnea was found in 47% of individuals with brain injury in acute inpatient rehabilitation.[163] In 71 brain-injured individuals in a residential/day rehabilitation program, excessive daytime sleepiness was reported in 65% of subjects. Eleven percent (11%) had sleep apnea/hypopnea, 25% had periodic limb movement disorders, and one subject had narcolepsy.[164] Finally, Castriotta and Lai[165] found seven of ten individuals with brain injury had complaints of excessive daytime sleepiness, sleep disordered breathing, and narcolepsy. They reported that all subjects were treated with either continuous positive airway pressure (for sleep disordered breathing) or Provigil® (for narcolepsy and posttraumatic hypersomnia) which resulted in subjectively improved quality of life and substantial improvement in daytime function.[165]

The incidence of sleep disorders for persons with TBI is much higher than that in the general population. Sleep apnea/hypopnea is estimated to occur in 2 to 4% of the general populace. PLMD occurrence is about 5% and hypersomnolence occurs in between 0.3 and 13% of the general population.[164] Sleep disorders clearly contribute to a number of other neuromedical conditions including reduced seizure threshold, psychiatric and behavioral disorders, cognitive dysfunction, and overall feeling of reduced psychological well-being.[166–169] From a social perspective, sleep disorders have been associated with increased incidence of motor vehicle collisions[170,171] and unintentional injuries.[172]

Sleep disturbances can be assessed using subjective measures such as self-rating scales.[173,174] However, sleep disturbance can also be measured using more objective

techniques that range from monitoring changes in select physiologic processes (heart rate, temperature, cortisol levels, blood/oxygen levels, etc.) to full polysomnography and sleep lab studies.[175,176]

A combination of subjective and objective measures, combined with serial clinical evaluation throughout the aging process, will assist clinicians in appropriate management strategies.[177,178] Depending on etiology, management strategies include extension of time in bed, naps, surgery, various medical devices (e.g., oral appliances, continuous positive airway pressure), and pharmacotherapy.[178,179]

Mortality and Life Expectancy

One of the most frequently asked questions concerns what impact TBI has on life expectancy. This issue presents a number of pragmatic concerns for families of people with TBI and bears on the development of suitable support systems that will be able to effectively address lifelong issues.[180] Logistical and financial planning for the individual and public health planning on a larger scale require the most accurate appraisal possible of what will need to be provided for an individual living with TBI and for how long.

There is a significant amount of literature describing the risk factors, shortened life expectancies, and causes of death in persons with chronic, disabling CNS conditions that may be illustrative in the discussion of such issues in TBI.[181–184] In certain sub-groups of persons with severe mental and physical disabilities, several studies have shown abbreviated life expectancies. In a study examining life expectancy of profoundly handicapped persons with mental retardation, Eyman et al.[185] collected data on mortality and other factors for 99,543 persons with developmental disabilities. This comprehensive review between 1984 and 1987 examined subgroups with functional disability related to mobility, personal activity of daily living abilities (i.e., self-feeding), and incontinence. People with severe mental retardation were found to have decreased life expectancy, either as children or adults, if they had severe limitations in mobility, were dependent on nutritional tube feeds, and were incontinent. This subgroup represented the most medically-fragile group and had an average life expectancy of less than 5 years. However, as mobility, nutritional, and bowel and bladder independence improved, so did life expectancy, adding a range of up to an additional 23 years. This study did not, however, account for differences in environmental factors, such as the level and intensity of care and how enriched the environment in which the person was being cared for was, thus allowing them to thrive. Roboz[186] found that people with mental retardation had the highest mortality when there was extensive brain damage and a completely bedridden condition was present. This study in a non-TBI disabled population with mental retardation demonstrated the influence of functional predictors of long-term morbidity and mortality and the contribution of comorbid neurological factors.

Much of the literature on mortality after TBI in adults has focused on predictors of early mortality, i.e., less than 1 year after injury. Mortality studies involving hospitalized individuals have found that approximately 90% of those individuals admitted to a hospital with TBI are discharged alive.[187,188] Risk factors such as age, admission GCS score, associated injuries, hypotension, hypoxia, and intracranial hemorrhage are associated with survival. A study by Marshall et al.[189] reported 6-month mortality at 36% among those with an admission GCS score of less than 8, by itself, or associated with the presence of subdural hematoma and elevated intracranial pressure. In another study, 1-year mortality

was found to be associated with factors such as age, GCS score, injury severity, and presence of intracranial hemorrhage. While neither of these studies focused on individuals who received inpatient rehabilitation, Fiedler et al.[190] examined first rehabilitation admissions for TBI in 1998 using data from the Uniform Data System for Medical Rehabilitation. They found mortality within this population was 1 to 2% 3 months postdischarge. This study was focused on functional independence as a correlate of mortality. It did not attempt to determine survival status in those persons lost to follow-up, nor was any analysis done to identify predictors of mortality.

Most relevant to issues of aging are studies reporting on mortality and life expectancy beyond 1 year after TBI. In a study of Vietnam veterans with penetrating cerebral injuries, the cause of death after TBI appeared to have similar patterns to those seen in the general population as soon as 2 years postinjury.[191] However, earlier studies implicated seizures as a cause of death unique to the TBI population.[192,193] More recently, seizures appeared as the third leading cause of death in reviewing a California database analyzing post-TBI mortality.[16] However, in this study, both circulatory and respiratory causes of death were more common than seizures and both of these causes appeared consistently over time and across populations.

A preliminary study utilizing the NIDRR-funded TBI Model Systems National Data Base has identified a range of possible predictors of future mortality.[194] These include age, previous TBI, having an injury that was caused by a fall, blood alcohol level (BAL), posttraumatic amnesia, and discharge disposition. However, only age at the time of injury and BAL were significant predictors of mortality in this study's multivariate analysis. Alcohol was not shown to be a significant risk factor in a similar study conducted in Australia.[195]

Overall, a few studies do suggest that life expectancy for individuals with TBI is shorter than for those in the general population.[24,192,193] However, the evidence explaining why life expectancy is shorter is very mixed.[16,24,191,194–197] In persons who have sustained severe TBI and are considered "low functioning" or dependent, life expectancies seem to be much shorter. Ashwal et al.,[198] in a study reporting on the most severely injured of TBI survivors, found that those who remained in a persistent vegetative state had a mortality rate of 82% at 3 years postinjury and 95% at 5 years postinjury.

People with TBI who remain in a persistent vegetative state represent a subgroup of TBI with the least functional status and mobility. There is some suggestion that a distinction might be made even between life expectancy for persons with the "minimally conscious state" vs. "persistent vegetative state." In this vain, Jennett and Plum[199] differentiated the persistent vegetative state (PVS) from other types of chronic unconsciousness and suggested that life expectancy for PVS differed when compared to other types of unconsciousness. The Multi-Society Task Force on PVS,[200] in a literature review of the medical aspects of the persistent vegetative state, examined data available on survival. The review concluded that a reduction of life expectancy to approximately 2 to 5 years for both children and adults resulted when neurological injury was severe enough to produce PVS. Examination of the records of 251 individuals diagnosed with PVS resulted in the conclusion that survival beyond 15 years was rare.

Morbidity and mortality show differences between those people in coma immediately after a nontraumatic vs. a traumatic injury with the nontraumatic group having a poorer prognosis.[200] Rates of death and PVS combined are higher at 1 year postinjury for the nontraumatic group than for the traumatic group. By 1 year, 85% of nontraumatically injured people who immediately entered coma remained in PVS or died contrasted with 48% for the traumatically injured group. A shortened life expectancy in PVS was noted to be due to several factors. Reported causes of death include infection (usually of the pulmonary or urinary tract), generalized systemic failure, sudden death, respiratory

failure, and other disease-related causes, such as recurrent strokes or tumors. It was stated that age was an important factor both in young infants and children and that the elderly have a shorter life expectancy than do young or middle-aged adults. It was not well-delineated whether the cause of the vegetative state or the subsequent medical complications were the etiologies of death.

In contrast, two studies of "highly functioning," ambulatory adults suggested that life expectancy was reduced by 3 to 5 years.[192,193] Roberts[201] followed approximately 500 individuals with severe disabilities up to 25 years. An estimated reduction in life expectancy of 4 to 5 years was found among individuals who became mobile enough to walk unaided. Strauss et al.[24] reviewed life expectancies across all severity levels of TBI. They also found diminution of life expectancy to be dependent upon level of mobility. That is, life expectancy for people with no mobility ranged from 10 to approximately 15 years depending upon age at the time of injury. The shortest life expectancies were associated with higher age at injury. This trend remained stable for people with poor mobility and fair to good mobility. Those with poor mobility ranged from 17.9 to 34.2 years life expectancy and those with fair to good mobility ranged from 26.5 to 54.8 years life expectancy, again depending upon age at injury. The youngest people at injury had the greatest decrease in life expectancy.

There appears to be some reduction in life expectancy related to TBI associated with other comorbidities. Weiss et al.,[197] in a study examining post World War I head-injured veterans, found that the occurrence of posttraumatic seizures was a prognostic factor for a higher death rate after the age of 50 years. While other indicators of injury severity did not lead to differences in death rates, there were significantly more deaths due to cerebrovascular causes in the head-injured group compared to controls. In post World War II studies, Corkin et al.[196] found that penetrating head injury, coupled with posttraumatic epilepsy, shortened life expectancy in persons who survived the initial postinjury period when compared to head injury alone. Educational level was found to be independent of the influence of seizures on life expectancy, meaning people with more education survived longer than those with less. Walker and Blumer[202] also found the death rate of World War II veterans with posttraumatic epilepsy to be higher than that of normal men. In addition, wounds involving the right cerebral hemisphere seemed to shorten life span more than similar injuries of the left hemisphere.

Strauss et al.[24] reviewed the records of 946 persons who sustained TBI, ages 5 to 21, and were receiving disability services in California between 1987 and 1995. The study explored risk factors associated with mortality after TBI: male gender, no mobility, poor mobility, tube fed, fed completely by others, attempts to finger feed, and ADL assistance. Cognitive skills did not contribute to prediction of mortality. Age at injury was not found to systematically relate to mortality risk either. Time since injury was found to impact relative risk of mortality. After the initial acute period, time since injury in the first 1 to 2 years showed less than half the risk of mortality when compared to children with cerebral palsy. However, in the longer run, mortality rates between the two groups seemed to converge. The greatest predictor of mortality appeared to be mobility. Known causes of death were listed as late effect of accidental history (n = 19), subsequent vehicle and other accidents (n = 3), infections (n = 3), pulmonary (n = 2), epilepsy (n = 2), cerebrovascular (n = 1), suffocation (n = 1), burning (n = 1), suicide (n = 1), unspecified (n = 2), and missing (n = 3).[24]

The findings of causes of death reported by Strauss et al.[24] are similar to those reported by Roberts.[201] While Roberts reported that causes of death for people with TBI were not very different from the general population for many causes, some stood out as being different. These included meningitis, epilepsy, accidents, suicides, and respiratory disease. The causes of death reported by Roberts and Strauss et al. closely follow the causes for rehospitalization reported by Cifu et al.[20] and Marwitz et al.[21]

The mortality risk factor of "functional status" has also been explored in the literature related to TBI mortality. In particular, feeding and mobility are reported to be major determinants of life expectancy in both children and adults.[24] One study found that mobility was a stronger predictor of mortality than consciousness in "poorly" responsive individuals.[203] Shavelle et al.[16] reported standardized mortality ratios (SMR) for those with TBI that range from a low of 180% in ambulatory individuals to 196% in those who are partially ambulatory and as high as 660% in nonambulatory individuals. These studies are beginning to lend credence to the concept of function as a predictor of mortality. In future prospective, longitudinal studies, knowledge of objective functional measures at rehabilitation admission, discharge, and in selected time frames postinjury may, themselves, be predictive of survival, life expectancy, neuromedical complications, and other relevant comorbidities.[184]

Finally, medical–legal issues encompassing life expectancy and the need for long-term planning seem relevant.[204] The logistics and costs of these long-term planning considerations are immense.[180] The anticipated progression of communicative, physical, and neurobehavioral changes over a lifetime is not yet an exact science. Planning for later life events and end of life can be furthered to a degree by not only the knowledge of neuromedical complications and long-term issues but also recognition of associated functional changes arising from either the neurological injury or associated nonneurological injuries.[180] It is not possible, at this time, to fully enumerate the exhaustive implications of aging on such functional skills and limitations since investigation into these arenas has only just begun for the TBI population. The work done thus far in SCI should serve as an excellent model for this endeavor.[17,181–183] This will only help to further the understanding of the efficacy of specific medical rehabilitative interventions and allow better understanding of society's duty in resource allocation.[205]

Procedures for estimating life expectancy in a "specific" person with TBI is a complex and challenging endeavor. Statistical methods are often valuable in making life expectancy estimates for persons with spinal cord injury and other neurologic disabilities when grouped by particular characteristics. However, in a heterogeneous TBI population characterized by different injury types and severity with discrepant medical, neurologic, and functional disabilities, a statistical methodology may be inaccurate. Furthermore, the impact of pre- and comorbid variables and different rehabilitative and long-term supportive care paradigms may also have a differential impact on long-term morbidity and mortality. In an article by Kraus[206] reviewing accuracy of life expectancy estimates in life care plans, it was felt important to consider nonbiographical and noninjury factors, as well as the injury itself. This article emphasizes a host of important variables which may impact life expectancy, such as income, access to healthcare, health behaviors, and psychosocial adaptations.

Successful Aging

Successful aging is a wonderful goal for an individual with the disabling physical, cognitive, neurobehavioral, and emotional disabilities associated with TBI. Successful aging is defined as an optimal state of overall functioning and well-being. Successful aging can be difficult to achieve, even in the general population. In a cross-sectional aging study that obtained information from 599 participants in Leiden, Netherlands, successful aging from a public health perspective, was defined as a state of being.[207] All participants were classified as "successful" or "not successful" based on optimal scores for physical, social,

psychocognitive functioning, and feelings of well-being using validated quantitative instruments. Although 45% of the participants had optimal scores for well-being, only 13% had optimal scores for overall functioning. In total, 10% of the participants satisfied all the criteria and could be classified as "successfully aged." The qualitative interviews showed that most elderly people viewed success as a process of adaptation rather than a state of being. The participants recognized the various domains of successful aging, but valued well-being and social functioning more than physical and psychocognitive functioning. Therefore, aging people with TBI are not unlike the elderly population and should view successful aging as a process of adaptation.

A study is now being conducted by the Rocky Mountain Regional Brain Injury System at Craig Hospital in Englewood, Colorado. This study includes collaboration with 17 TBI Model Systems of care as funded by the National Institute on Disability and Rehabilitation Research.[208] Over 2500 TBI systems national data base cases, starting in the year 1989, will be evaluated and compared to a cohort of all individuals with TBI rehabilitated at Craig Hospital over the past 40 years. The study will investigate mortality and life expectancy in TBI survivors following inpatient rehabilitation, evaluate the causes of death compared to the general population, and attempt to determine the risk of death in certain neurologic and clinical subgroups. This study will also evaluate the effects of different types of improved care and their relationship to long-term survival.

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10

Therapy, Neuroplasticity, and Rehabilitation

Robert P. Lehr, Jr.

CONTENTS

Introduction

Therapists engaged in the rehabilitation of the traumatically brain-injured person are well aware that their therapeutic skills are effective and can produce significant results. The techniques that produce these results are those of a repetitive nature that build on previous therapeutic procedures and are multimodal in nature.

These therapies are what have been described as being activity-dependent.[1] Being activity dependent means the therapy is focused to the point that the recipient of the therapy is actively engaged in the therapeutic process. These therapies are designed by the therapist to elicit a key response from the client and this leads to one part of a successful rehabilitative program. These learned skills have their foundation in the nervous system, and we now know that there are physical changes that take place at the synaptic level to produce the rehabilitative results. It is the synapse that is the ultimate target of the therapeutic process. The purpose of this chapter is to provide therapists with a better understanding of these neuronal changes and how the human brain is altered by their therapies.

Neuroplasticity is the ability of the brain to change its structure and organization as the organism encounters its environment.[2] The human brain is composed of a collection of neurons that have been shown to be pliable and subject to changes in structure, individually, as well as collectively, if the interaction between them is initiated with purposeful intent. Just because the brain is active does not mean it is learning. Learning comes from a purposeful activity in which the learner is fully participating. As you will recall, just

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sitting in the classroom did not guarantee the acquisition of the material of the lecture. It was not until you actively studied the material, committed it to memory, or put it to use that you learned the material. In a like manner, the traumatic brain-injury (TBI) client must be committed and actively engaged in the therapeutic process.

Let us now look at some of the learning processes therapists initiate and see them on the cellular level. It is hoped that this insight will stimulate in the reader a better appreciation of the processes involved and perhaps lead to some innovative therapies.

The early prediction by Hebb[3] that there would be observable changes in the neurons or their synapses was further elaborated by neuroscientists to suggest that the behavioral changes an organism makes in response to the influences of the environment would be reflected in changes in synapses in the central nervous system.[4] Neurobiologists (Bailey and Chen,[5] Kandel,[6] and others) followed with elegant experiments that demonstrated the importance of this synaptic organization and the interactions that occur between the neurons. Using very simple animals, such as marine snails and moving on to rodents and mammals, these investigators were able to clarify the role of the synapse in learning.

Learning is a complex process that has several levels. We will look at learning in terms of habituation, sensitization, classical conditioning, and operant conditioning. These are by no means the only concepts involved in learning, but they will allow us to illustrate some changes that take place at the cellular organization of the brain and to place them in the context of therapy.

Habituation

Kandel,[6] using the California marine snail *Aplysia,* has demonstrated the simple form of learning known as *habituation*. This form of learning is characterized by the reduced response to a presentation of a novel stimulus. The experimental setup is demonstrated in Figure 10.1. When a stimulus is applied to the siphon, the snail responds by reflex withdrawal of its gill, mantle, and tail. With repeated stimulation to the siphon, there is a depression of the reflex response. The decreased response is characterized by a decrease in the synaptic transmission from the presynaptic sensory neurons to the interneurons

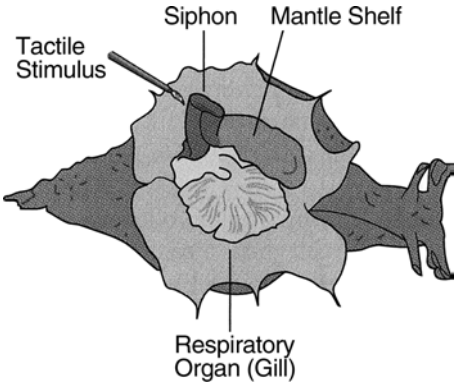

FIGURE 10.1
Marine snail *Aplysia*: experimental setup. (From Kandel, E.R., Cellular mechanisms of learning and the biological basis of individuality, in *Principles of Neural Science*, 4th ed., Kandel, E.R., Schwartz, J.H., and Jessell, T.M., Eds., Elsevier, New York, 2000, chap. 63, p. 1248. With permission.)

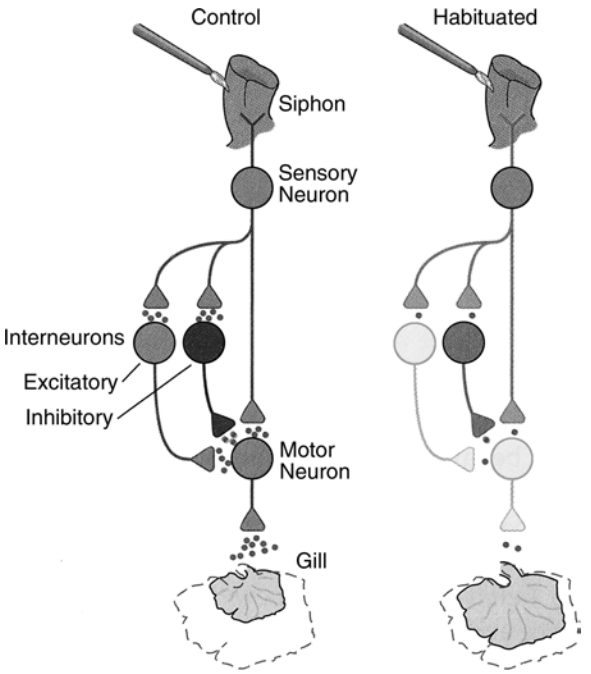

FIGURE 10.2
Marine snail *Aplysia*: gill-withdrawal reflex circuit. (From Kandel, E.R., Cellular mechanisms of learning and the biological basis of individuality, in *Principles of Neural Science*, 4th ed., Kandel, E.R., Schwartz, J.H., and Jessell, T.M., Eds., Elsevier, New York, 2000, chap. 63, p. 1248. With permission.)

and motor neurons in the reflex circuit (Figure 10.2). There is a decrease, over time, of the amount of transmitter released. These changes are internal to the presynaptic neuron and can last for a few minutes or a few hours. This is known as *short-term habituation.*

When stimulation occurs over several training sessions, there has been demonstrated an actual reduction in the number of synapses present to the postsynaptic neuron, and this process is known as *long-term habituation.* While this has not been demonstrated in humans, it can be speculated that this is what occurs when we condition a client that has symptoms of dizziness by constant exposure to a revolving swing. The constant presentation of a stimulus that produces the dizziness will, in time, habituate. First, there is a reduction of neurotransmitter, and then, eventually, a reduction of synaptic connections so that a stable equilibrium may be obtained, without nausea.

Sensitization

In *sensitization*, the process involves an additional neuron and is more complex. The additional neuron is one that "facilitates" the signal by reinforcement (see Figure 10.3). It is an enhancement of the reflex response after the presentation of a strong stimulus. After a strong stimulus, the organism is more attentive to all stimulations to itself and the nature of the synapse physically changes. There is an increase in the size of the synaptic zone[7] (Figure 10.4) and in the number of vesicles containing neurotransmitter in the active zone.[8] These changes in the circuit demonstrate that there is a "memory" of what has happened to them. These changes last several minutes and are known as *short-term sensitization*.

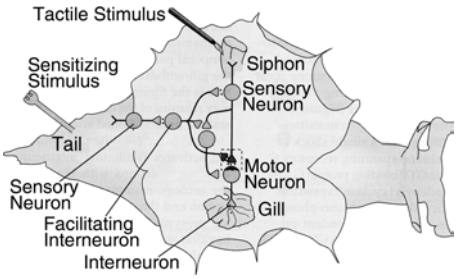

FIGURE 10.3
Marine snail *Aplysia*: gill sensitization. (From by Kandel, E.R., Cellular mechanisms of learning and the biological basis of individuality, in *Principles of Neural Science*, 4th ed., Kandel, E.R., Schwartz, J.H., and Jessell, T.M., Eds., Elsevier, New York, 2000, chap. 63, p. 1251. With permission.)

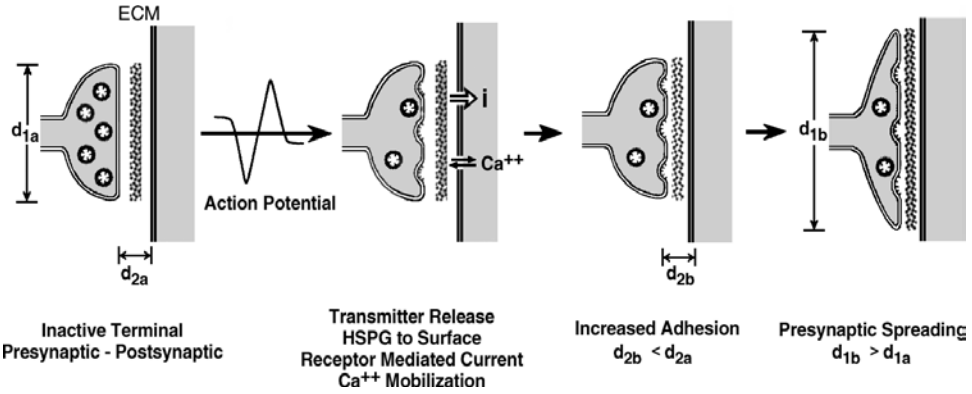

FIGURE 10.4
Schematic model for adhesion-mediated changes associated with synaptic modification. The hatched area between cells represents the extracellular matric (ECM). (From Schubert, D., The possible role of adhesion in synaptic modification, *Trends Neurosci.*, 14(12), 128, 1991. With permission.)

Long-term sensitization also occurs following several training sessions. This process produces proteins that enhance the short-term mechanisms and also promotes the growth of axons with new synapses. These newly produced proteins have been shown to be persistently active for up to 24 hours without requiring a continuous signal of any sort. This is an exciting opportunity for the therapy regimen. These new synapses cause the postsynaptic neuron to increase its dendritic branches to accommodate the new synapses from the axons of the presynaptic neurons.[8]

This synaptic plasticity is "activity dependent" and, with the increased axonal sproutings, increased neurotransmitters, and correspondent dendritic field expansion, there are changes in the surrounding tissue. There are increases in the glial cell components and an increase in the vascular supply to the region. These changes are rapid and have been identified to take place within 10 to 15 minutes.[9] The therapist must move quickly to reinforce the target behavior when the client demonstrates the acquisition of that sought behavior.

Additionally, exercise has been demonstrated to increase the number of synapses in the cerebellum of experimental animals that undergo complex motor skill learning, but not mere motor activity.[10] These demonstrations of the plasticity of the brain at the cellular level show that a new foundation for the behavior has been formed, and the repetition of the behavior will reinforce the newly formed synaptic connection. As we repeat the activity in a therapy setting, we increase the effectiveness of the corresponding synapses and this, in turn, contributes to the reacquisition of the skills.

Types of Learning

Learning and memory are closely associated and sometimes difficult to separate except for academic purposes. For the therapist, however, they are intertwined in a more specific way. The rehabilitation process involves the returning to wholeness of the entire person and, as such, makes demands on many systems, from the locomotor to the cognitive. The cellular mechanisms involved in the learning and memory processes we are discussing are the same. The two types of learning we discussed above, habituation and sensitization, are forms of *nonassociative* learning where the organism learns the properties of a single stimulus.

In another form of learning, *associative*, the organism learns about the relationship between two stimuli or between a stimulus and a behavior.[11] For the therapist, it might be more productive to view the learning/memory process as being based on the classification of *explicit* and *implicit* memory. It is not our purpose to engage in an extensive discussion of memory but to set the stage for the learning process within the therapeutic setting.

Explicit memory deals with facts and events. This form of memory is recalled by a deliberate conscious effort. Facts and remembering events are the purview of the entire rehabilitative team. It is also the area where the cognitive functions of the skills of daily living are rehabilitated. The skills to plan the day, to shop for groceries, and to make change for a dollar are some of the items of concern, and these require the reestablishment of the explicit memory.

Explicit memory has been shown to involve *long-term potentiation* (LTP) in a part of the brain known as the *hippocampus*. In fact, the presence of LTP in the hippocampus was the first confirmation of Hebb's rule that learning would be based in the physical changes in the synapse. LTP represents the receptiveness and increased facilitation of the excitatory synaptic potentials in the postsynaptic neurons that can last for hours, weeks, or months.[8] The relationship, in time, of two presenting stimuli increases the efficacy of the two synaptically related cells and is a reminder to the cells of that relationship.

This synaptic enhancement can take different forms in different parts of the hippocampus. Recent research has shown that the hippocampus is a key component in early memory and in the final distribution of information to the multimodal association areas of the cerebral cortex. The left hippocampus seems to be involved with verbal memory, whereas the right hippocampus seems to be more involved with the representation of the environment and the ability to find our way in it.[8] Suffice it to say that the association of the hippocampal and multimodal association cortical neurons is established in the synapses of their respective neurons. The reinforcement with repeated practice is what produces a successful therapeutic regimen.

Implicit memory, on the other hand, refers to how to perform an act. These memories of a specific task do not require conscious effort to recall or to reestablish. They require concentration and a focus on the task at hand but not the conscious effort of recall. Implicit memory is seen in the training of skilled movements and perceptual skills. These are the skills of walking, driving a car, or performing other motor tasks.[8]

Implicit memories involve habituation and sensitization but they also include two other processes, *classical conditioning* and *operant conditioning*. These processes involve the concept of association. In classical conditioning, there are two stimuli presented, which, after a series of associations with each other, begin to produce a new response. These associations are established in the synapses of the cooperating neurons. This new response then enables the organism to predict the environment.

In operant conditioning, the associative relationship is between the organism and a subsequent behavior produced. The organism learns that, for a specific action, there is a

related reward. Thus, if behavior is controlled, then the individual receives an appropriate reward for that action. This is the foundation for the wide use of behavioral modification programs (see Chapter 14).

Classical conditioning relies on an association in which a stimulus that had been previously incapable of producing a response is paired with a strong stimulus that does produce the response, and the association between the two will eventually produce the response from the weaker stimulus. Classical conditioning results in a greater and longer-lasting enhancement. This process is one in which there is a presynaptic facilitation of the synaptic transmission. It is the pairing, in time, of a meaningful relationship that produces the result. The internal mechanisms of the process are solidly established and involve several enzymes and genes.[8] The combinations of enzymes and genes are the same that we saw in the process of long-term sensitization. The production of the cellular proteins by this process forms the foundation for the results seen in the therapeutic program.

Hierarchical Learning

Rehabilitation, as a process, requires the work of several respective professions. Among these, the professions of physical and occupational therapy hold, as a major tenet, the developmental concepts in neurodevelopmental therapy.[12,13] Neurodevelopmental theory says that there is a basic developmental sequence in the individual from the time of conception to adulthood. The function that is expressed is built on previously learned foundations. We must crawl before we walk. Therefore, it is important that the process of restoration of function should follow the same sequences that occurred in development.

Kandel's group[6] has shown that the stages of learning mentioned above are sequential. The infant *Aplysia* is first capable of only habituation, then, with maturity, dishabituation occurs, and finally, sensitization. These sequential stages of learning confirm that learning is a process that builds on previously developed mechanisms and is not complete at birth. This understanding seen in the simple snail lends support to the foundation of some long-standing therapies of rehabilitation[3,4] that suggest a hierarchy exists in the development of the individual, and successful therapy must be carried out in the same order.

It is clear that learning is a hierarchical process and has a neuronal basis. It is not so clear in the cognitive area where we have only begun to investigate the cognitive functions with modern imaging techniques and cellular neurophysiological experiments. The literature on cognition is rich indeed and has provided a foundation of strategies that has been successfully incorporated into the rehabilitation environment (see Chapter 12).

Cognitive scientists will tell us that we are first able to describe objects using very simple descriptions of color, size, and shape. From this base, we can move to the descriptions of their usefulness and, eventually, to the features of the object, allowing use of the object for other extended purposes.[14]

Current concepts in the neural sciences are beginning to reveal a neural concreteness to constructing the visual image from the features of the object. The neural pathway for vision is known to have two parallel pathways that convey different types of information.[15] One pathway, the P pathway, is concerned with form, size, and shape or *what* the object is. The P pathway projects to the temporal multimodal association cortex. The other pathway, the M pathway, is concerned with movement and depth perception or *where* the object is located. This M pathway projects to the parietal multimodal association cortex.

As these two pathways project to separate areas of the cerebral cortex, this helps explain the selective loss of some features of an object. As an example, object agnosia, the ability

to name an object, is associated with Brodmann areas 18, 20, and 21 on the left temporal cortex, whereas color anomia, the ability to name a color, is associated with the speech zones or connections for Brodmann areas 18 and 37. The mechanism of the complete visual construct is pulled together by a yet unknown *binding mechanism.*

The binding mechanism takes the properties of form (rectangle), color (yellow), and dimensions in depth (box), and says, "We have a long yellow box!" Thus, the binding mechanism pulls together a single representation of an object from several multimodal association cortices. Treisman et al.[16] and Julesz[17] have suggested that such associations require focused *attention*. They further divide the process into two steps. One is the *preattentive* stage in which the object is scanned for the size, shape, color, and movement by the parallel processing P and M pathways. A serial processing that is responsible for identifying how to categorize the visually constructed object follows. This categorization is dependent on the hippocampus and the eventual storage of the information about the object in the various association cortices.[10]

Attention is a function of working memory. Baddeley[18] proposed a model in which verbal working memory has two components: a subvocal rehearsal system of a phonological log accessed by reading words or numbers, and a short-term memory store activated by speech. This "articulatory loop" allows us to retain phone numbers or addresses for short periods of time. He also demonstrated a nonverbal working memory that he called a *visuospatial scratchpad.* Both of these components are greatly dependent on the multimodal association areas of the frontal lobe and its executive function.

Until recently, we have assigned the basal ganglia to a simple role in motor behaviors. Recent work has demonstrated that they also play a key role in cognition, mood, and behavior.[19] Three circuits have been described that originate in the prefrontal association and limbic regions of the cortex and interact with specific areas of the basal ganglia. These areas of the frontal cortex are frequently the ones implicated in the deficits and behaviors seen in the traumatically brain-injured individual in the rehabilitation setting.

The first circuit is the *dorsolateral prefrontal* circuit (Figure 10.5) and this is the one frequently characterized by the term *director of executive functions.* It is the one most closely corresponding to the "articulatory loop" described by Baddeley[18] that is important for working memory. The circuit begins in the prefrontal cortex, projects to the basal ganglia, then to the thalamus, and back to the prefrontal cortex. This circuit undertakes cognitive tasks such as organizing behavioral responses and using verbal responses in problem solving.

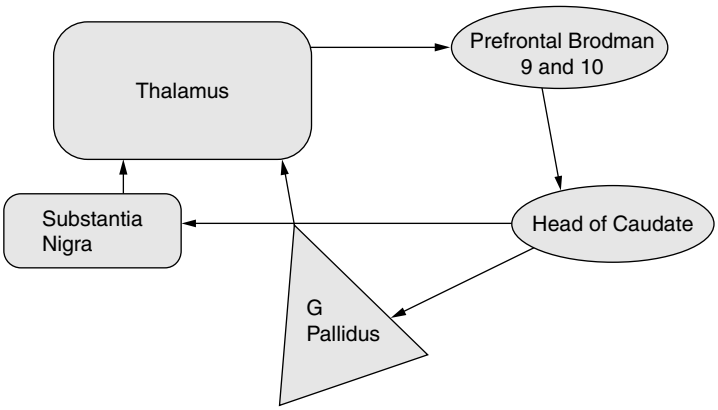

FIGURE 10.5
Dorsolateral prefrontal circuit.

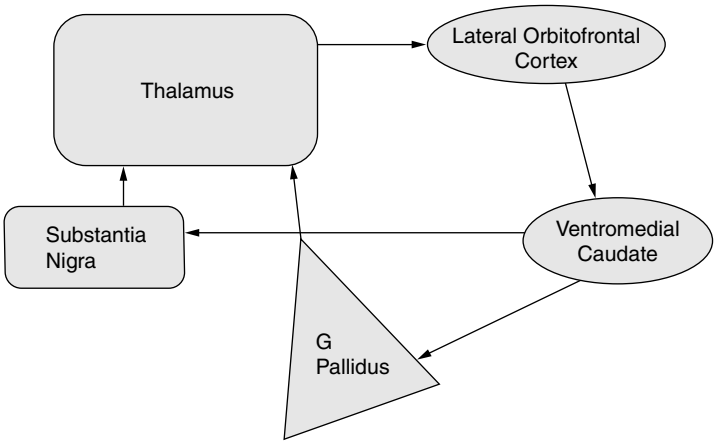

FIGURE 10.6
Lateral orbitofrontal circuit.

The second circuit is the *lateral orbitofrontal* circuit (Figure 10.6). This circuit begins in the lateral orbitofrontal cortex, projects to the basal ganglia and to the thalamus, and returns to the orbitofrontal cortex. This circuit seems to be involved in mediating empathetic and socially-appropriate responses. Injury to this area results in the individual being irritable and failing to respond to social cues.

The third circuit is the *anterior cingulate* (Figure 10.7). This circuit is distinguished by its role in motivated behavior, and it may play a role in conveying reinforcing stimuli to diffuse areas of cortical and subcortical regions.[20] This circuit begins in the anterior cingulate gyrus on the medial surface of the cerebral cortex and projects to the ventral striatum, which, in turn, receives inputs from the hippocampus, amygdala, and entorhinal cortices. From the ventral striatum, the projection goes to other parts of the basal ganglia, then to the thalamus, and back to the anterior cingulate gyrus. This particular circuit includes dopamine-containing neurons in the midbrain that have inputs to the basal ganglia. It has been suggested that these neurons may deliver reward-predictive signals. This circuit may be deeply involved in procedural learning and, as such, this circuit may be important in the behavior modification programs in which reinforcement and reward are utilized.

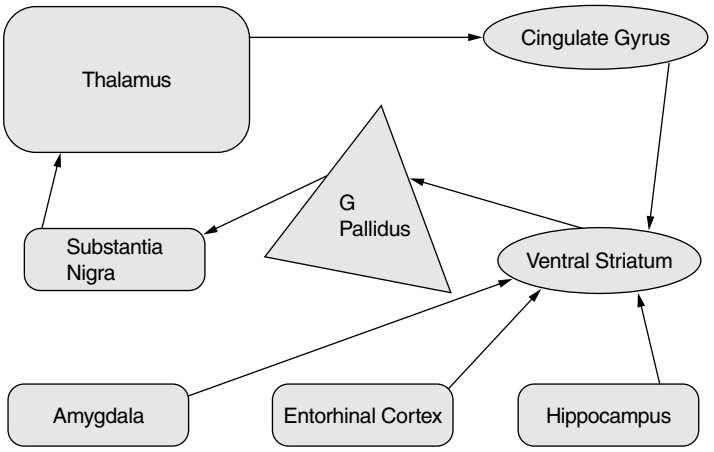

FIGURE 10.7
Anterior cingulate circuit.

Multimodal Rehabilitation

Multimodal rehabilitation refers to a therapeutic approach that attempts to address the individual as a whole person. This places a responsibility on the rehabilitative team to address all of the rehabilitative possibilities. The process must address the physical aspects of movement and awareness of the environment as well as the cognitive, behavioral, social, and psychological aspects of the individual.

We have just discussed the role of the multimodal association cortices and their role in learning and memory. It was shown that the long-term storage of memories was a function of the hippocampus distributing the component parts of the memory to the parietal, frontal, and temporal lobes. In a similar manner, we noted the distribution of the visual pathways to the multimodal, parietal, and temporal cortices. And the three circuits of the basal ganglia were related to the limbic and frontal association cortices. Saper, Iversen, and Frackowiak provided an excellent overview of the association areas of the cerebral cortex and how these structures form the foundations for the cognitive capabilities of the brain.[21]

In each of these descriptions of the related pathway, we mentioned the route through the thalamus. The thalamus is a central structure of ancient origin. Before the development of the cerebral cortex, there was a thalamus that performed the functions of integrating the sensory and motor functions of the organism. It acts as a gatekeeper for information that is conveyed to the cerebral cortex.[22] In this role, it is central to the integration of all the sensory modalities, except olfaction. In addition, it plays a role in the extrapyramidal motor output from the basal ganglia, as well as the three mentioned basal ganglia-cortical circuits concerned with cognition, mood, and behavior.

The thalamus is composed of several nuclei that have different roles (Figure 10.8). Some of the nuclei function for specific sensory modalities such as vision and auditory functions. Others have a motor integrative function such as pathways to the extrapyramidal tract.

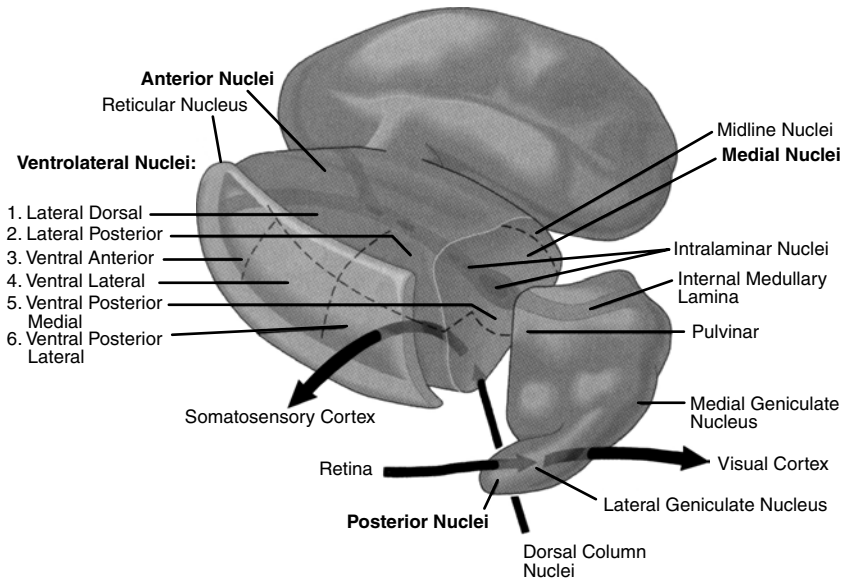

FIGURE 10.8
The major subdivisions of the thalamus. (From Amaral, D.G., The functional organization of perception and movement, in *Principles of Neural Science*, 4th ed., Kandel, E.R., Schwartz, J.H., and Jessell, T.M., Eds., Elsevier, New York, 2000, chap. 18, p. 343. With permission.)

Then, others are of a diffuse nature to serve the organism's arousal system. In any case, it is important for the therapist to remember that the thalamus holds the potential to be involved in many of the observed deficits of the head-injured person.

Neurogenesis in Adult Humans

The old concept that we are born with all the neurons we will ever have and that some neurons die off over our lifetime was recently found to be false. This long-held belief was overturned in an elegant experiment. P. S. Eriksson of Goteborg University, Sweden, and F. H. Gage of the Salk Institute, San Diego, California, demonstrated that new neurons, as defined by biological markers, are generated from dividing progenitor cells in the dentate gyrus of adult humans.[23] Further, they indicated that the human hippocampus retains its ability to generate neurons throughout life. Exciting prospects and intensive investigations are under way. Their work was built upon that of Elizabeth Gould who had demonstrated this phenomenon in macaque monkeys. She has subsequently shown that some of these new neurons have an apparent transient existence of only nine weeks.[24]

This transient existence perhaps holds some promise for utilization for future therapies. Arsenijevic et al.[2] have demonstrated that there are multipotent precursor cells able to generate neurons, astrocytes, and oligodendrocytes in the human brain. And, further, that these precursor cells are widely distributed, having been found in many brain regions studied, including the temporal and the frontal cortex, the amygdala, the hippocampus, and the periventricular zone. This work demonstrates a possible new platform to study adult human neurogenesis and potentially generate neural cells for transplantation.

The possibility of transplantation and the rehabilitation of the individual in an enriched environment hold promise for development and recovery of lost functions. The synaptogenesis stimulated by the activity-dependent therapeutic setting should give the cellular basis of learning we have been discussing a strong chance to bring about the rehabilitative results we want.

However, these prospects remain speculative, but tantalizing, and will require much further experimental effort to develop to their potential for rehabilitation.

Constraint-Induced Therapy

More recent has been the discovery of constraint-induced (CI) therapy for stroke victims.[25] This therapy restricts the movements of the undamaged appendage in order to make maximum use of the appendage that has been impaired. This therapy is not limited to appendage movement but has been seen to be useful in therapy for language disorders, such as aphasia.[26] Such restriction of movement to the impaired structure causes changes in the brain, altering the synapses, and enhancing the neuronal connections. These changes can take several forms such as the assumption of the function by the same region in the other hemisphere, or a change in the type of sensory processing from one modality to a new one, or an enlargement of a functional brain region due to its expanded use.[27]

In a like manner, it has been demonstrated that exercise, and not just motor activity, can produce physical changes in the brain structure.[28] Gómez-Pinilla has demonstrated in

experimental animals that an increase in challenging exercise activity potentiates the effects of physical activity on trophic factor induction in the cerebellum, and that the trophic factor involvement in behavior may provide a molecular basis for the enhanced cognitive function associated with active lifestyles and may guide development of strategies to improve rehabilitation. In addition to the experimental animals, changes that take place in the human motor cortex have been demonstrated with neuroimaging.[29]

This change wrought by the action of the therapist on the impaired person brings about the positive result of rehabilitation. It is the active interaction of the therapist, client, and the environment that causes physical changes in the structure of the brain that have formed the basis of all the therapies ever used. It is only in the last decade or so that we have been able to demonstrate that these changes are taking place at the level of the neurons. These changes in the brain tissue have been demonstrated conclusively by the new neuroimaging technology.[30]

Summary

These are exciting times for researchers and rehabilitation specialists alike. The prospect of new possibilities is incentive to press the frontiers of knowledge. However, it should be remembered that therapies have worked for years without a clear understanding of the underlying foundations of the changes wrought on the brain itself. The constant repetition of the target activity has brought about restoration of function. It is with the deeper knowledge of the changes in the brain that do occur that insights into new therapies may develop.

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Posttraumatic Epilepsy and Neurorehabilitation

Theresa D. Hernández, Paul M. Levisohn, and Dean K. Naritoku

CONTENTS

Introduction

Two percent of patients with traumatic brain injury (TBI) experience early seizures, defined

as occurring while the patient is still suffering from the direct effects of the head injury,

usually within the first 24 hours of injury, though up to 2 weeks later in those with severe

head trauma. 1 There is a 3.6-fold increase in late seizures (after the acute effects of head

trauma have resolved). The majority of these late-occurring seizures occur in the first year

following TBI, though some increased risk continues for 4 years after the trauma. By

definition, the occurrence of multiple seizures (two or more) is defined as epilepsy. While

epilepsy (i.e., late-occurring seizures) has long been recognized as a common sequel to

brain injury, progress in understanding the pathophysiology and treatment of posttrau

matic epilepsy has been limited. Consequently, clinicians have little information regarding

appropriate therapy of posttraumatic epilepsy, and as a result, therapy of posttraumatic

epilepsy has remained empirical and arbitrary. The decision to initiate or withhold anti

epileptic drug therapy has far-reaching implications for rehabilitation of the traumatic

brain-injured patient. Inappropriate use of anticonvulsants may cause unnecessary cog

nitive impairment in those persons not requiring medication. At the same time, experi

mental data suggest that certain types of seizures may retard functional improvement

during recovery from brain injury, while other types have no deleterious consequences.

Thus, it is crucial to differentiate patients who will require and benefit from antiepileptic

drug therapy from those who will not.

Evaluation of Episodic Behavioral Changes

Episodes of abnormal behavior occur commonly after severe head injuries and present a

diagnostic challenge for the treating physician. There are many potential etiologies for

these episodes; therefore, it is crucial to determine the correct diagnosis in order to select

the most appropriate and efficacious therapies to avoid iatrogenic complications. Several

disease entities result in fluctuations of mental status in the posttraumatic brain-injured

state. These include posttraumatic encephalopathy, seizures, postictal state, and numerous

encephalopathies of toxic and metabolic etiologies. Episodic dyscontrol and disinhibition

from frontal injury may occur. The encephalopathy caused by the posttraumatic state is

discussed in detail by Gelber elsewhere in this volume. Mentation and attention tend to

fluctuate in the TBI patient and may be mistaken for seizures, especially when there is a

superimposed encephalopathy of another etiology. Simple staring spells are rarely due to

seizures in the setting of TBI. Nonepileptic spells (psychogenic seizures) and misinterpre

tation of behaviors by caregivers may be difficult to differentiate from epileptic seizures.

Metabolic encephalopathies are characterized by fluctuating mentation and may also be

mistaken for seizures. Inappropriate use of antiepileptic drugs in these situations will not

only be ineffective but may result in worsening of confusion or agitation.

There are many common etiologies for acute encephalopathies. Medication-induced

encephalopathies rank among the most common and easily remedied causes of confu

sional states. As a result of the brain injury, TBI patients possess a lower tolerance to the

central nervous system side effects of psychotropic drugs and other medications. Medi

cations with anticholinergic properties are tolerated especially poorly and should be

avoided because of their tendency to cause confusion, hallucinations, and memory loss,

especially in older patients. 2,3 Antihistamines and many over-the-counter preparations fall

into this category and are often overlooked as causes of transient or prolonged confusion.

Several centrally acting sedatives, especially benzodiazepines and barbiturates, have

extremely long half-lives. From a pharmacokinetic standpoint, long half-lives result in a

greater interval before steady state is achieved; thus, adverse effects on the central nervous

system may not be apparent until several days after the start of medications, and cause

and-effect may not be apparent. As a general rule, sedative agents (including benzodiaz

epines, opioids, and barbiturates) exacerbate encephalopathies; therefore, they frequently

aggravate confusion or agitation in TBI patients and should be avoided. Other drugs

commonly used in the TBI patient may have profound effects on the central nervous

system. The medication list should always be reviewed for histamine antagonists (e.g.,

cimetidine) and narcotics for the possibility that they are inducing the confusional state.

Several systemic derangements are commonly associated with the posttraumatic state.

Head injury may cause the syndrome of inappropriate antidiuretic hormone (SIADH) and

result in hyponatremia, which, in turn, may cause confusion. Systemic infections are

common in the TBI patient because of reduced mobility and presence of indwelling

catheters. Any infection may manifest as an abrupt decline in mental status or agitation.

An acute decline or fluctuation in mental status may herald a pulmonary, urinary tract,

or wound infection. In patients with open head injuries and skull fractures, the possibility

of a central nervous system infection should always be considered when there is an abrupt

decline in mental status. When in doubt, a lumbar puncture must be performed after

careful assessment for potential causes of increased intracranial pressure. Hypoxia may

also cause agitation and confusion and is commonly caused by pulmonary emboli from

deep venous thrombosis or fat emboli. Stroke is usually not a cause of global cognitive

dysfunction except in cases of multifocal, brainstem, or

diencephalic strokes.

Syncope (fainting) may be confused with seizures, especially if there is associated tonic

posturing. As the patient loses consciousness, there is dimming of vision and the patient

appears pale and clammy. The patient generally falls limply to the ground or slumps over,

if sitting. Occasionally, a brief tonic or tonic-clonic seizure occurs, adding to the confusion

regarding the diagnosis. In contrast to epileptic seizures, the patient with a syncopal

episode generally regains consciousness and orientation rather quickly. Medications such

as tricyclic antidepressants, beta-blockers, and neuroleptics may result in systemic

hypotension and lead to syncope.

Panic disorder may mimic epilepsy and is frequently seen in patients after trauma. Panic

episodes may be mistaken for complex partial seizures because of altered consciousness

that may occur. Panic episodes and other spells of psychogenic etiology are often misdi

agnosed as medically intractable seizures, and these diagnoses should be considered in

patients who are not responsive to antiepileptic medications. A careful history will help

sort out this differential diagnosis. Typically, in the case of a panic attack, the patient

complains of feeling dissociated, smothered, and in need of fresh air. The patient may

have perioral numbness, tingling of digits, and a feeling of impending doom. Generally,

full awareness of surroundings is retained and the patient

is able to maintain conversation.

Episodes of syncope may occur in patients with panic disorder. They are usually brief and

vasovagal in nature. As opposed to patients with complex partial seizures, those with

syncope due to panic attacks generally retain full awareness and can maintain a conver

sation until loss of consciousness. Antiepileptic drugs are ineffective for panic disorder,

whereas alprazolam and imipramine are very effective. 4

Clinical Evaluation of Seizures

Seizures should be considered when episodes of discrete and stereotypic behaviors occur

with altered or lost consciousness. While an electroencephalogram (EEG) is often support

ive, the diagnosis of epilepsy must be made on clinical grounds. The patient may provide

only a vague or incomplete history, and the diagnosis often depends on a careful history

taken from observers. Seizures are distinct, stereotyped episodes, with a definite start and

end. With the exception of status epilepticus, seizures usually last only a few minutes.

Afterwards, mentation will often clear within a few minutes with return to baseline,

although postictal somnolence may persist. Prolonged confusion of hours to days is rarely

caused by seizures and should alert the clinician to the possibility of other causes outlined

above. Directed aggression is not seen during seizures or the postictal state, though

confusion and undirected aggressive behaviors may be seen.

Under the International Classification of Seizures, 5 seizures are classified by whether

they appear to start from a localized cortical region (partial or localization-related seizures)

or from the entire brain at once (primary generalized seizures). Partial seizures are further

divided by whether they impair consciousness (complex partial seizures) or not (simple

partial seizures). Partial seizures are caused by localized cortical abnormalities and tend

to be acquired in nature, whereas primary generalized seizures appear to be caused by

genetic factors. The partial onset seizure category encompasses seizure types that previ

ously went under several terminologies, including Jacksonian, psychomotor, and temporal

lobe seizures. Tonic-clonic (grand mal) seizures that result from spread of the ictus from a

focal onset are described as partial seizures with secondary generalization.

The distinction in seizure onset has important implications for the pathophysiology and

therapy of the seizure. Antiepileptic drugs tend to be selective for the seizure type and

are analogous to cardiac antiarrhythmic drugs, which are fairly selective for arrhythmia

type. Because posttraumatic seizures occur as a result of localized injury to the cerebral

cortex, the resulting seizures are usually of partial onset, with or without secondary

generalization. The behavioral manifestations of posttraumatic seizures relate to area of

onset, usually in the penumbra of injury. Thus, injuries to the convexity of the brain often

result in sensory or primary motor manifestations at seizure onset, such as a migrating

paresthesias or twitching and jerking of an extremity. Seizures of the temporal lobe may

result in psychic phenomena such as a sensation of fear or deja vu, followed by automa

tisms, whereas frontal seizure foci often result in aversive motor or more complex behav

iors, described as hypermotor.

During typical complex partial seizures, the patient will often stare and become nonre

sponsive or poorly responsive to commands. Automatisms frequently occur and take the

form of lip smacking and swallowing or chewing (oral-alimentary automatisms) and

fidgeting with objects. Although the patient may spontaneously speak or seem to respond

to commands, the language is inappropriate to the situation. The patient may affirm or

disagree when questioned but, typically, gives little more than simple responses and does

not follow complex commands. Generally, combativeness occurs only when the person is

restrained. Thus, when directed aggression occurs, such as seeking out and striking a staff

member, the episode most likely is a conscious act and not the result of a seizure. After a

complex partial seizure, there is often a several-minute period of confusion and disorien

tation which represents the postictal state. The patient will often feel tired or exhausted

and will frequently go to sleep. When present, a history of postictal confusion and lethargy

often helps to identify episodes as seizures, as they generally do not occur or are brief with

spells of other etiologies. Amnesia for the event is often noted in patients with complex

partial seizures. Seizures emanating from the frontal lobes may be confused with nonepi

leptic events due to the bizarre nature of the seizures (hypermotor) reported, occasionally

without impaired consciousness and without a period of postictal mental change.

In TBI patients, tonic-clonic (convulsive) seizures result from secondary generalization

(i.e., spread of the seizure from the seizure focus at the site of trauma to other parts of the

brain, especially the brainstem) which appears to moderate the initial tonic phase of the

convulsion. 6 Thus, the tonic-clonic seizure episode often begins as a brief simple or

complex partial seizure. The warning or aura that patients often describe is actually the

beginning of a seizure that is perceived while the person is conscious and is actually a

simple partial seizure.

Tonic-clonic seizures consist of two phases: the tonic phase and the clonic phase. These

phases are easily identified with a careful history. During the tonic phase, there is a sudden

stiffening of all extremities. The epileptic cry may occur during this phase as a result of

sudden diaphragmatic contraction. After a brief period, the extremities become tremulous.

As the tremor slows in frequency, it evolves into a rhythmic jerking motion — the clonic

phase. As the seizure ends, the jerking slows and ceases. After a tonic-clonic seizure, the

person is invariably groggy and disoriented for several minutes. Absence of the tonic

phase or postictal confusion and somnolence in a person with convulsive behavior should

raise the question of nonepileptic episodes, including psychogenic seizures. However, the

postictal state may be fleeting or indiscernible after brief complex partial seizures and

absent following simple partial seizures. Thus, a minimal or absent postictal state does

not exclude seizures when convulsive activity does not occur. A recent monograph by

Lüders and Noachtar 7 is a useful reference for defining the clinical semiology of seizures.

Acute medical management is similar for both partial and tonic-clonic seizures. If

semiconscious, the patient should be gently directed away from harm. During a convul

sion, the patient should be rolled to one side to avoid aspiration if vomiting occurs.

Contrary to common belief, the tongue cannot be swallowed or bitten off and objects

should never be forced into the patient’s mouth. Insertion of hard objects, such as spoons

or “bite sticks,” may break teeth and cause serious complications of fragment aspiration

and pneumonia. A soft oral airway may be used if it is easily inserted. If available, oxygen

via face mask may be provided, as well as suction if needed.

Epilepsy, by definition, consists of recurrent seizures. As with seizures, epilepsies have

been classified; in the instance of epilepsy, the classification is into epilepsy syndromes,

defined by seizure type, electroencephalographic features, etiology, and natural history.

Primary generalized epilepsies, including absence (petit mal), myoclonic, and general

ized convulsive epilepsy, commonly begin in childhood or adolescence and are usually

idiopathic or genetic in etiology. These epilepsies are diagnosed by their distinctive

patterns on the EEG, which consist of bilateral synchronous epileptiform patterns. Their

onset in patients following traumatic brain injury is highly unusual and should be con

sidered coincidental. It is important to identify these epilepsy syndromes since primary

generalized seizures, especially absence and myoclonic seizures, do not respond to, or

may be worsened by, medications used for partial onset seizures, such as phenytoin and

carbamazepine. 8 It is important to note that epilepsy itself may result in trauma and TBI;

thus, preexisting epilepsy should be considered in patients with TBI and primary gener

alized epilepsy. 9

Etiologic Considerations

Risk factors for posttraumatic epilepsy have been examined in several population studies.

However, it is difficult to resolve the relative risk of specific characteristics of injury, such

as presence of intracranial bleeding and depth of injury, because these markers tend not

to be independent variables. For example, although concussion (with loss of conscious

ness) has been considered a risk factor for posttraumatic epilepsy, patients with mild

concussive injury alone have only a 0.6% risk of seizures within 5 years, which is not

significantly increased over the incidence of new seizures in the general population. 1

Data from World War II, the Korean War, and the Vietnam War have provided the risk

factors for posttraumatic epilepsy. Overall, the risk for epilepsy following nonmissile head

injury was 24% in World War II 10 and 12% during the Korean War. 11 Interestingly, the risk

of epilepsy following penetrating missile injury was about 35% for both World War II and

the Korean War but was much higher (53%) in the Vietnam War. 12 The differences between

studies on Vietnam War veterans and previous war veterans may relate to both improved

care of head injury and differences in the nature of injuries. In particular, high-velocity

rifles were used in combat and, when combined with improved surgical care, may have

resulted in a greater percentage of survivors with epileptogenic lesions.

Risk factors have also been studied in nonmilitary injuries. As outlined above, mild

head injuries do not present an increased risk of posttraumatic epilepsy. The incidence of

posttraumatic epilepsy after moderate head injuries is 1.6%, and 11.6% after severe inju

ries. 1 In review of military and nonmilitary injuries, similar risk factors are evident. Early

seizures (onset less than 1 week after TBI) also appear to be a risk factor for subsequent

seizures in several series, 13 but the increased risk appears to be dependent on the severity

of head injury. 1 In civilian head injuries, early seizures are not predictive of seizure

recurrence when the head injury is mild, yet do appear to increase risk in moderate to

severe injuries. 1 In children, seizures occurring immediately after minor head trauma are

more common, though not necessarily predictive of subsequent epilepsy. 1 The time of

seizure onset also appears to be predictive of seizure recurrence. In wartime injuries, early

seizures are associated with seizure recurrence and the risk of seizure recurrence increases

if the onset is greater than 1 week. 14 More recently, Angeleri and colleagues 15 reported that

the risk of posttraumatic epilepsy was 8.58% higher for those individuals with early

seizures, and 3.43% greater for individuals with frontal or temporal lesions on CT. The

degree of hypoperfusion in the temporal lobes as detected by single-photon computed

tomography (SPECT) has also been correlated with posttraumatic epilepsy. 16 Also associ

ated with increased risk of posttraumatic epilepsy (+3.49%) was the presence of an EEG

focus at 1 month.

The risk of posttraumatic epilepsy in the presence of an intracerebral hematoma was

estimated at 21% in nonmilitary injuries. 1 However, Guidice and Berchou 17 found intra

cerebral hematomas not to be predictive of posttraumatic epilepsy. This may be due to the

fact that CT scans were used routinely in all head-injured patients at their center. Earlier

studies, which did not utilize CT scanning, would not have detected intracerebral hem

orrhage in milder cases that did not require surgery or cerebral angiography. Alternatively,

other studies have argued that the most predictive factor for posttraumatic seizures is

focal CT abnormalities. 13,18 Brain contusion with subdural hematoma was predictive of

posttraumatic epilepsy in a population-based study. 19 In one small series, the development

of posttraumatic epilepsy was correlated with the presence of bone fragments on CT scan

studies; 20 however, the scope of this study could not establish whether the risk of bone

fragments was independent of injury severity. The type of skull fracture also tends to

predict the likelihood of posttraumatic epilepsy. Greater risk occurs in patients with

depressed skull fractures, 1,13 while linear convexity or basilar fractures carry an interme

diate risk. The value of acute magnetic resonance imaging studies in predicting posttrau

matic epilepsy is unclear.

Risk factors for posttraumatic epilepsy include duration of coma, 1,17,19 genetic suscepti

bility to epilepsy, 21,22 and age over 65 years. 19

When the epidemiologic studies are viewed as a group, it appears that the severity of

brain injury best predicts whether posttraumatic epilepsy will occur. While there is debate

on the relative risk of any single factor, it is likely that most identified risk factors are

indicators of a high degree of brain injury, rather than being specific etiologies. Further

more, posttraumatic epileptogenesis is probably dependent on several pathophysiologic

mechanisms (see text below) which may partially explain the large number of identified

risk factors.

Diagnostic Investigations of Posttraumatic Seizures

When faced with the new onset of seizures, laboratory studies should screen for conditions

that may have lowered seizure threshold. Serum chemistries should be drawn to exclude

electrolyte imbalances and, minimally, should include electrolytes, glucose, calcium, and

drug screen. A complete blood count may detect a subclinical infection. Measurement of

arterial blood gas in appropriate circumstances will exclude hypoxia. Imaging studies,

consisting of either computerized tomography (CT) or magnetic resonance imaging (MRI),

may help identify new lesions contributing to the occurrence of seizures. Prior to initiation

of antiepileptic drug therapy, complete blood count and liver function studies should be

measured to define any hematologic or hepatic dysfunction and as a baseline in case of

idiosyncratic reactions to medication.

The EEG is a useful tool for evaluating patients with episodic behavioral changes.

Interictal abnormalities, such as epileptiform spikes or sharp waves, are often present in

patients with epilepsy. A difficulty arises in that interictal abnormalities are transient,

much like the seizures they attempt to detect. Thus, a normal EEG does not exclude the

possibility of epilepsy. Conversely, an abnormal EEG alone does not diagnose epilepsy.

As outlined in later sections, there are important consequences of antiepileptic drug

therapy; thus, it is crucial that the TBI patient not be treated solely on the basis of EEG

findings. The EEG does provide supportive evidence of a seizure disorder when it is

clinically suspected, and its greatest utility lies in its ability to help identify whether the

seizure onset is partial or generalized. Despite its limitations, the EEG is one of the most

important tests in evaluating epilepsy as it provides electrophysiologic information that

cannot be obtained from any other laboratory investigation.

For example, a retrospective study of EEG findings in patients with head injury revealed

no predictive value of focal or generalized EEG abnormalities. 12,23 However, this study

included all abnormalities and did not specifically assess the risk of epileptiform patterns.

The EEG is valuable as a prognostic factor in persons who have already experienced a

seizure. The interictal hallmark of epilepsy is the epileptiform spike or sharp wave. When

well-formed and definite, focal spikes are predictive of seizure recurrence in both

brain-injured patients 24 and in patients with seizures of unidentified causes. 25 Focal EEG

findings 1 month following TBI was associated with an increased risk of subsequent

epilepsy in a prospective study of risk factors following an early seizure. 15

Prolonged EEG monitoring after traumatic brain injury has been promoted as a means

by which to detect subclinical seizures and even predict posttraumatic epilepsy. 26 Postin

jury EEG assessment revealed that subclinical seizures occur frequently despite anticon

vulsant drug administration. 26 As many as 22% of traumatically brain-injured individuals

have postinjury seizures within the first 2 weeks, 26 many of which are subclinical. Postin

jury EEG monitoring may help define the impact of seizure activity on patient outcomes,

especially as regards the risk for subsequent epilepsy.

The EEG study should follow the technical guidelines of the American EEG Society. 27

To briefly summarize, all studies should utilize at least 16 channels of EEG recording to

allow for adequate spatial resolution and localization of EEG abnormalities. Gold disk

electrodes should be used and attached to the scalp with either collodion or electrode

paste to assure low electrical impedance. Needle electrodes should not be used because

of their high impedance and the potential risk of blood-borne pathogens. Standard EEG

montages should be used, per recommendations of the American EEG Society. Digital

EEG recordings are now routinely obtained which allow for reformatting the montages,

if necessary. Drowsiness and sleep-enhanced expression of epileptiform abnormalities and

recording during these stages of consciousness must be performed. The patient should be

partially sleep deprived during the night prior to the EEG study as this will increase the

probability of recording epileptiform abnormalities and avoid the need for sedation.

There has been much debate over the advantages of special EEG electrodes used to

improve the detection of interictal abnormalities. Nasopharyngeal electrodes are now

rarely used. Standard scalp electrodes with high-distance electrode montages are as effec

tive as nasopharyngeal electrodes at detecting epileptiform abnormalities and are consid

erably more comfortable. 28,29 Other scalp electrodes, such as T1 and T2 electrodes, are often

used to increase sensitivity to temporal spikes. 30

Prolonged EEG recording may be extremely useful in cases where the cause of altered

mental status episodes cannot be ascertained by conventional means and the spells occur

with enough frequency to be detected within the designated recording period. Twenty

four-hour ambulatory EEG monitoring is usually available at larger medical centers. These

devices continuously record EEG and EKG activity for 1 to 2 days and may be performed

on an outpatient basis. Newer digital equipment allows for higher quality recordings than

was possible with analog recordings which were often limited to eight channels. Never

theless, there are several limitations to ambulatory recording. Artifact makes interpretation

of ambulatory EEGs difficult and technologists must review large amounts of data. As

EEG technicians or other health care staff are not present to observe the recording, it may

be difficult to later sort artifact from true abnormalities during playback. Moreover, if a

diary is not carefully maintained during the recording period or the patient is unable to

trigger the alarm on the recording unit reliably, it may not be possible to correlate the

episodes in question with the EEG or EKG, or the episode may even be missed entirely.

Intensive neurodiagnostic monitoring involves continuous 16- to 64-channel recording

of electroencephalographic, electrocardiographic, and other electrophysiologic data with

simultaneous video recording of behavior. It is available at most epilepsy centers and

many tertiary care facilities. These studies allow precise correlation of behavioral changes

with electrophysiologic data to determine the exact etiologies of the behavioral episodes.

Intensive neurodiagnostic monitoring is costly and requires hospital admission. However,

it may provide the only means to obtain definitive and conclusive information. As such,

it should be reserved for situations where the diagnosis cannot be determined by usual

means or when nonepileptic spells are suspected. Intensive

neurodiagnostic monitoring

is essential for localization of epileptic foci when epilepsy surgery is contemplated.

Potential Epileptogenesis Associated with Psychotropic Medications

Behavioral and affective disorders are common after traumatic brain injury, and it is often

necessary to treat the brain-injured patient with psychotropic medications. Of concern is

whether these agents lower seizure threshold. In high doses, tricyclic antidepressants

induce seizures, but it is less clear to what extent they are proconvulsant at clinically

effective doses. Many reports of tricyclic-induced seizures are retrospective and do not

take into account the normal incidence of new onset seizures. When drug monitoring

has been instituted to avoid high levels, the risk has been estimated at only 0.4%. 31

Although a 0.2% risk of seizures has been estimated for fluoxetine therapy on the basis

of preclinical trials, fluoxetine is anticonvulsant in experiments using epileptic rodents

with convulsive seizures. 32 In a retrospective study of persons with depression and

established epilepsy, antidepressant therapy actually improved seizure frequency in the

majority (56%) of patients. 33 This raises the question of whether this positive effect on

seizure control occurs indirectly (i.e., through improvement of depression) or, instead,

by directly raising seizure threshold. Interestingly, a double-blind placebo study has

demonstrated imipramine to be effective adjunctive antiepileptic therapy in intractable

atonic, myoclonic-astatic epilepsy, and absence epilepsy in subjects without affective

problems. 34,35 Thus, at nontoxic levels, tricyclic antidepressants may possess anticonvul

sant properties for certain seizure types, despite being proconvulsant at toxic levels. This

bimodal response is frequently seen in other drugs with anticonvulsant properties, such

as phenytoin and lidocaine.

The ability of tricyclic antidepressants to increase seizure frequency may be selective

for seizure type. For example, a selective increase of tonic-clonic seizures may occur with

use of imipramine or maprotiline in patients with mixed seizure types. 35 Neuroleptics are

frequently utilized in the posttraumatic state for agitated behavior and there are several

reports of their proconvulsant effect. Unfortunately, little data exist on the actual risks of

antidepressants and neuroleptics in the setting of traumatic brain injury. However, from

existing information on these agents, it appears that the actual clinical risk of seizure

exacerbation by psychotropic medications is small and is usually far outweighed by the

need to effectively manage a severe affective or disruptive state in the TBI patient. Thus,

these medications should be used when necessary for psychiatric and behavioral prob

lems. As a caveat, though the neuroleptics may not pose a risk for seizures after TBI, there

are data showing that the administration of these drugs is detrimental to neurobehavioral

recovery in this population. 36

Therapy for Posttraumatic Epilepsy

It is common practice to initiate antiepileptic drugs (AED) following acute TBI as prophy

laxis against seizures. Such treatment decreases the risk of early seizures but does not

appear to prevent late-occurring seizures, that is, posttraumatic epilepsy. However, studies

on prophylaxis regarding the use of newer AED is lacking. 37,38 Nevertheless, it is appro

priate to treat those with late occurring seizures, e.g., posttraumatic epilepsy. Initiation of

antiepileptic drug therapy should begin only after careful evaluation of the patient and

seizures have been clearly identified. Almost all clinicians will begin therapy once two

seizures have occurred, but there is debate on whether therapy should be initiated after

the first seizure. Many clinicians will not treat a single seizure without recurrence; others

will treat, depending on the situation. As outlined in later sections and based on recent

meta-analysis of anticonvulsant prophylaxis trials, 39 as well as a Practice Parameter pub

lished by the American Academy of Neurology, there are clearly no firm data to justify

long-term prophylactic AED therapy in TBI patients who have not experienced a seizure. 38

Selection of AED therapy must be based on several factors, including efficacy for seizure

type and side effects. A specific AED may be quite

selective for seizure type, thus neces

sitating seizure classification. Posttraumatic epilepsy is caused by focal or multifocal injury

and consists of partial onset seizures and secondarily generalized tonic-clonic seizures.

Accordingly, appropriate AED for posttraumatic epilepsy are those used for partial onset

seizures. The most commonly used antiepileptic drugs are listed in Table 2.1.

The effectiveness of AED in the treatment of epilepsy of all etiologies has been exten

sively examined. A multicenter, double-blind, randomized study compared the efficacy

of phenytoin, carbamazepine, primidone, and phenobarbital against partial onset seizures.

All of the drugs were equally efficacious in terms of seizure control. 40 However, barbitu

rates were tolerated poorly, resulting in a high dropout rate in these treatment groups.

Similar results were obtained in a British study involving patients with newly diagnosed

partial onset epilepsy which compared the efficacy of carbamazepine, phenytoin, and

valproic acid. 41 Valproic acid exhibited the same efficacy as phenytoin and carbamazepine

against partial onset seizures and convulsion, suggesting its usefulness for these seizure

types. A Veterans' Administration study compared the efficacy of carbamazepine to val

proic acid for partial onset seizures and indicated a modest, but significantly lower, efficacy

of valproic acid against complex partial seizures. 42 Nevertheless, valproic acid appeared

Table 2.1

Guide to AED Dosing and Adverse Effects Medication/

Target Dose mg/d

[Pediatric Dose mg/kg/d] Target Serum Levels Idiosyncratic Dose Related Age Specific/Other

Carbamazepine

800–1000

[10–30] mg/kg/day 4–12 μg/ml Dermatologic, hematologic, hepatic (fatal 1/ 50–200,000) Vertigo, visual disturbance (diplopia), leukopenia Hyponatremia in adults, leukopenia, liver induction, myoclonus in pts. with general S/W

Ethosuximide

[15–40] mg/kg/day 40–100 g/ml Leukopenia, SLE, nephrotic sx, rash Sedation, GI upset Behavioral

Felbamate

2400–3600

[45–60] mg/kg/day 30–100 g/ml Aplastic anemia, hepatic failure, rash (rare) Anorexia, insomnia, headache, irritability Aplastic anemia, drug interactions

Gabapentin

1800–3600

[30–100] mg/kg/day 4–20 g/ml Rash (rare) Somnolence, irritability, wt. gain Renal excretion, no drug interactions

Lamotrigine

300–500

[1–15] mg/kg/day (with

vs. w/o inducer) (dose

depends on presence of

hepatic enzyme

inhibitors) 3–20 g/ml Rash, hypersensitivity reaction Ataxia, diplopia, GI, headache Rash (1–5% in children), StevensJohnson

Levitiracetam

1200–2400

[20–60] mg/kg/day 5–50 g/ml None reported to date Somnolence, ataxia Agitation, aggression

Oxcarbazepine

1200–2400

[15–45] mg/kg/day MHD – 10–55 g/ml Rash (25% crossreactivity with CBZ) CNS diplopia Hyponatremia (3% of adults)

Phenytoin

200–600

[4–8] mg/kg/day 10–20 g/ml Rash (5–10%), hematologic, hepatic, lymphadeonpathy, others Cosmetic, CNS, ataxia, nystagmus Elevated LFTs, induction, reduced vitamin D, possible cerebellar degeneration

Phenobarbital

60–120

[2–6] mg/kg/day 15–40 g/ml Rash, StevensJohnson, SLE Somnolence, irritability Possible irreversible cognitive effects, liver induction

Primidone

750–1500

[5-20] mg/kg/day 4–12 g/ml Rash Sedation, irritability, GI upset Similar to PB

Tiagabine

32–56

[.25–1.25] mg/kg/day 5–70 g/ml Psychiatric CNS, tremor,

weakness, GE reflux, gait difficulty

Topiramate

100–400

[5–25] mg/kg/day 3–25 g/ml Rash (rare), elevated LFTs Somnolence, memory disturbance, anorexia, renal stones, parasthesiae, dysgeusia Language disturbance when used in polypharmacy, avoid ketogenic diet

to be equally effective to carbamazepine against secondarily generalized tonic-clonic sei

zures. Because valproic acid is generally well tolerated, it should be considered for patients

who are unresponsive or intolerant to carbamazepine. Kwan and Brodie 43 likewise have

found that all carbamazepine, valproate, and lamotrigine had equal efficacy in newly

diagnosed patients with epilepsy, though tolerability differed. More patients on carbam

azepine changed medication due to adverse events than those on the other two drugs. 43

All antiepileptic drugs may cause significant problems with adverse effects, especially

neurotoxicity, and pose problems for the TBI patient. Indeed, several antiepileptic drugs

commonly cause ataxia at high levels and may also exacerbate gait abnormalities at lower

levels, in some patients. This may present a problem to the patient who is returning to

ambulation. There is a significant incidence of hyponatremia in carbamazepine-treated

patients over the age of 25, 44 as well as those on oxcarbazepine. 45 Postural tremor is a

common side effect of valproic acid that may pose a problem to the TBI patient and can

be particularly troublesome in patients who are prone to postural tremor. The tremor is

reversible, dose dependent, and responds to a dose reduction or other medications that

block essential tremor (propranolol, primidone). Because the barbiturates, including phe

nobarbital and primidone, are poorly tolerated and result in a high incidence of cognitive

impairment, they should not be used as first line drugs, but rather used in patients

refractory to other antiepileptic medications.

Eight new AED (felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine,

tiagabine, topiramate, and zonisamide) have been approved by the FDA since 1993,

predominantly for use as adjunctive therapy in partial onset seizures. In general, they

appear to have high therapeutic indices, that is, a wide window between efficacy and

toxicity, and have demonstrated to be effective and safe in controlled studies. 46–49 Improved

pharmacokinetics provide an additional advantage of some of these newer AED, including

renal clearance, the lack of significant protein binding, and the absence of CyP450 induc

tion. 49 However, serious idiosyncratic adverse effects can occur. The use of felbamate has

Valproic acid

1000–3000

[20–60] mg/kg/day 50–150 g/ml Hepatic failure, pancreatitis Tremor, weight gain, alopecia, sedation and cognitive changes, thrombocytopenia, prolonged bleeding time Hepatic failure (1/ 500 under age 2 on polypharmacy), elevated LFTs, GI upset with syrup, incidence of PCOS

unknown, liver enzyme inhibition

Vigabatrin

[40–100] mg/kg/day — Visual field constriction, sedation, CNS Psychiatric symptoms (rare), visual field constriction Especially effective of Infantile Spasms and Tuberous Sclerosis

Zonisamide

200–600

[4–10] mg/kg/day 10–30 g/ml Rash, hematologic, hepatic Renal stones, anorexia, somnolence Oligohydrosis in children, avoid in sulfa drug sensitivity

Disclaimer: Doses, therapeutic levels, and adverse effects are based on reported clinical experience and not on

adequate scientific information from clinical trials. Not all drugs are approved for use in children.

Table 2.1 (Continued)

Guide to AED Dosing and Adverse Effects Medication/

Target Dose mg/d

[Pediatric Dose mg/kg/d] Target Serum Levels Idiosyncratic Dose Related Age Specific/Other

been restricted by the FDA for use in severe intractable epilepsy because of a significant

risk of aplastic anemia estimated by the FDA to be 1:2000. Lamotrigine is associated with

a risk of serious rash in approximately 1:1000 patients, usually at onset of therapy.

Vigabatrin has not been approved for use in the United States, in part, because of potential

retinal toxicity. Additionally, treatment-emergent side effects can be troublesome. For

example, topiramate is associated with word-finding difficulties in some patients, partic

ularly at higher doses or when the drug is used in polypharmacy. Gabapentin may cause

weight gain and somnolence. Levetiracetam may cause behavioral side effects. While

monitoring of serum drug levels, complete blood counts, and liver function are not

required with most of the new AED (with the notable exception of felbamate); the difficulty

in assessing clinical status of patients with significant traumatic encephalopathy may make

such monitoring advisable. Practitioners should take advantage of published reviews of

these drugs in textbooks and journals to familiarize themselves with their use.

In a systematic review of efficacy and tolerability of the newer AED, Marson and

Chadwick 50 found no statistical differences between gabapentin, lamotrigine, tiagabine,

topiramate, vigabatrin, and zonisamide. Nevertheless, the addition of these new drugs

will provide alternatives for patients who do not tolerate or respond to current antiepi

leptic drugs. Undoubtedly, they will be tested in posttraumatic epilepsy and may provide

a better armamentarium for this problem.

In general, all AED should be introduced slowly to avoid problems with neurotoxicity,

including somnolence and altered mental status. If introduced too quickly, carbamazepine

may cause severe dizziness; lamotrigine may precipitate a serious rash. However, when

multiple seizures or status epilepticus occurs, loading with phenytoin is often effective in

controlling seizures. For intravenous use, fosphenytoin is better tolerated than phenytoin.

Valproic acid is also available for intravenous use and can be used in relatively high doses

acutely, if necessary. The intravenous preparations of both of these drugs may be useful

for patients who are unable to take oral medications, for instance, after surgical procedures.

With all AED, clinical efficacy and tolerability determine appropriate dosing. Most of the

newer AED do not have well established therapeutic plasma level measurements, but the

presence of significant traumatic encephalopathy may make determination of AED plasma

levels appropriate. Drug plasma levels may be utilized to provide a rough guideline for

therapy but should not be used as the sole indicator of therapy or toxicity. 51 It should be

noted that a plasma steady state is not achieved for up to seven half-lives of a medication

so that levels are rarely useful acutely after dosing changes.

Phenytoin is unique among the commonly used AED in that it saturates its metabolic

enzymes at therapeutic levels which results in zero-order kinetic elimination. As a result,

the effective half-life is variable and becomes longer with higher levels of phenytoin. As

a result of nonlinear kinetics, there is a proportionate increase of serum level at low doses

of phenytoin, but at therapeutic levels, small increments result in marked elevations of

levels. 52 This phenomenon is responsible for what is mistakenly identified as wild fluctu

ations in phenytoin levels. In addition, phenytoin and valproic acid compete for protein

binding, making routine measurements of phenytoin levels inappropriate when used in

combination with valproate. Rather, unbound phenytoin levels should be obtained

through reference laboratories as they are not routinely available in most hospital labora

tories. Also of note are the kinetics of Dilantin Kapseals which allow once a day dosing,

not true for phenytoin suspension or chewable 50 mg tablets.

The use of phenytoin, carbamazepine, and oxcarbazepine suspensions may be useful in

patients who cannot swallow tablets or capsules. However, care must be taken to ade

quately shake the bottle before administering a dose to allow for even distribution of drug

in the solution. Lamotrigine, levetiracetam, and zonisamide can be dissolved and given

as a solution. Both valproic acid and topiramate are available as sprinkle capsules, but

they cannot be given through gastric tubes due to the tendency of the sprinkles to adhere

to the tubing.

Several AED are being evaluated for their potential neuroprotective effects, including

antiepileptogenicity, in both experimental and clinical studies. Temkin performed a meta

analysis of 47 studies of the effectiveness of anticonvulsant drug administration for seizure

prevention and antiepileptogenicity. 39 Of these, 13 were conducted after traumatic brain

injury. There was no good evidence to support that anticonvulsant drug administration

after traumatic brain injury is antiepileptogenic in the long term, though acutely (within

the first week), there was seizure reduction associated with phenytoin 53 and carbam

azepine. 54 Temkin emphasizes the need for “rigorous clinical trials” to determine the drug’s

antiepileptogenic effects as well as any neurobehavioral costs. She goes further to state

that “Clinical use of any drug to prevent epileptogenesis should be avoided until clinical

trials have proven the drug to be effective for that purpose.” 53, pg 522

It is likely that there are individual differences in response to and tolerance of any given

antiepileptic drug. Therefore, additional medications should be tried in patients who have

failed to respond to or who are unable to tolerate initial treatment. In all cases, the

therapeutic plan should strive for a single antiepileptic drug regimen. Monotherapy has

been shown to be more efficacious than polytherapy and minimizes toxicity, drug inter

actions, and cost. 55

Mechanisms and Models of Posttraumatic Epilepsy

When considering the appropriate treatment of posttraumatic epilepsy, it is worthwhile

to understand the mechanisms whereby trauma leads to the epileptogenic state. Studies

of posttraumatic epileptogenesis implicate several potential pathologic etiologies that may

result in a seizure focus. These etiologies can be broadly

separated into those related to

the acute or primary insult (i.e., penetration of parenchyma, shearing forces, and disrup

tion of blood-brain barrier) and those caused by late or secondary sequelae (i.e., vascular

disruption, cicatricial pulling, and synaptic reorganization). Given the wide variations of

brain injury and complications, it is unlikely that any single mechanism is responsible for

posttraumatic epileptogenesis. Thus, posttraumatic epileptogenesis probably utilizes com

binations of several mechanisms, many of which are supported by scientific studies and

concur with clinical aspects of this type of epilepsy.

In 1930, Foerster and Penfield 56 induced seizure activity by electrical stimulation of areas

surrounding a gunshot lesion of cerebral cortex. These findings suggested the presence of

an epileptic zone or penumbra surrounding the site of injury. Furthermore, retraction of

dura that had become adherent to the damaged cortex also triggered seizures. They con

cluded that posttraumatic seizures are most likely to occur after dural penetration, which

induces formation of scar tissue between brain and dura, and subsequent pulling of the

ipsilateral and, sometimes, contralateral hemispheres toward the lesion, as a result of

contraction brought about by normal maturation of the scar (cicatricial contraction). This

hypothesis is supported by clinical findings that head injuries associated with dural pen

etration are associated with the highest incidence of

posttraumatic epilepsy (27 to 43%). 22

Additional putative mechanisms include glial cell proliferation and damage to blood

vessels, axon collaterals, and blood-brain barrier, each of which is known to precipitate

brain injury. 57 Jasper 57 hypothesized that the toxicity of extravasated blood increases neu

ronal activity abnormally in some brain regions and disrupts blood flow in others. These

pathophysiologic changes could result in the alternating periods of seizure activity and

functional neuronal depression that characterize acute status epilepticus induced by brain

contusion. 57 Alternatively, damage to inhibitory axon collaterals by shearing forces may

result in reduction of inhibitory tone and excessive depolarization that ultimately produce

seizure discharges. 57 Overt penetration of dura and disruption of brain parenchyma may

not be absolute requisites for posttraumatic epilepsy.

Lowenstein and colleagues 58 reported that extradural fluid percussion induces profound

decreases in hippocampal hilar neurons and hyperexcitability of dentate granule cells in

rodents. Postinjury hyperexcitability in the granule cell and molecular layer of the dentate

gyrus has been shown to be persistent (observable at 15 weeks) and pervasive (e.g.,

bilateral). 59 Measures taken at earlier time points throughout the hippocampus revealed

dramatic physiological and receptor-mediated disruptions in excitatory/inhibitory bal

ance, with the changes being time dependent and only

observable ipsilateral to the site

of traumatic brain injury. 60,61 Thus, even nonpenetrating brain injury can cause pathologic

changes in distal structures, possibly tipping the balance in favor of posttraumatic seizures.

These findings could help explain the emergence of posttraumatic epilepsy in persons

with milder, low velocity head injuries who do not appear to have frank penetration of

dura or intracerebral bleeding.

Because penetrating brain injuries carry the greatest risk for posttraumatic epilepsy,

alterations in blood flow may play a role. Not only does brain injury disrupt vasculariza

tion at the site of damage, it also affects areas “downstream” from the insult. Disruption

in blood flow could bring about both ischemic and hypoxic conditions which produce

significant increases in synaptic glutamate release and decreased inactivation of glutamate.

Overactivation of glutamate receptors, including NMDA receptor activation, results in

excessive Ca ++ influx, 62 which promotes phosphorylation of the GABA A receptor to its

nonfunctional, desensitized state. 63 Trauma has also been associated with GABA-mediated

Ca ++ influx, 64,65 which would not only lead to depolarization, but also, potentially, to cell

death. Loss of inhibitory neurons, coupled with other trauma-induced disruptions in

normal brain function, could result in a state that both primes the brain for acute seizures

and provides the foundation for long-term epileptogenic

changes.

A related hypothesis implicates blood breakdown products, particularly hemosiderin,

in the cellular events that lead to epileptogenesis. An important role for iron deposition

has been supported by experimental studies in animals. Subpial iontophoresis of ferrous

or ferric chloride into sensorimotor cortex of cat or rat induces a chronic epileptic focus

with many striking similarities to lesions in human posttraumatic epilepsy. 66,67 Electro

corticographic seizure activity is observed within 48 hours after injection and behavioral

convulsions occur between 48 hours and 57 days. These abnormalities recur spontane

ously and persist for more than 12 weeks after injection. 67 Examination of the

iron-induced focus reveals many histopathologic changes found in posttraumatic epi

leptic foci from humans: 66,67 meningocerebral cicatrix, consisting of fibroblasts and iron

laden macrophages, surrounds the iron injection cavity with neuronal loss and gliosis

occurring next to the injection site. Hypertrophied astrocytes encompass the entire iron

focus. It has been hypothesized that a cascade of events is initiated by the iron focus,

resulting in the genesis of a posttraumatic epileptic focus. Breakdown of blood from

brain injury-induced extravasation creates iron deposits that may induce free-radical

oxidant formation and subsequent lipid peroxidation. 68 In support of this hypothesis is

the finding that antioxidant administration reduces the incidence of iron-induced sei

zure activity. 68

The possibility of hemosiderin deposition leading to posttraumatic epilepsy has also

been studied in humans. 15 Following traumatic brain injury, MRI scans were utilized to

detect the presence of hemosiderin, gliosis, or both. Evidence of hemosiderin deposits was

found in 81% of patients. Although there was no correlation between the presence of

hemosiderin, alone, and posttraumatic epilepsy, the presence of cortical hemosiderin sur

rounded by a “gliotic wall” was significantly correlated with the development of post

traumatic epilepsy.

The mechanisms discussed so far largely address seizure activity that occurs acutely

following brain injury. However, the onset of posttraumatic seizures is bimodal — the

highest incidence occurs during the first week (early onset seizures) with a secondary

peak occurring at about 6 months. 69 This latency suggests there is a maturation process

resulting in the genesis of an epileptic focus. Because the latent period can last months to

years after the insult in humans, most of what we know about the mechanisms underlying

posttraumatic epileptogenesis comes from animal models.

Modeling posttraumatic epilepsy in animals poses quite a challenge. First, not only is

it difficult to evoke spontaneous seizures secondary to traumatic brain injury, chronically

monitoring animals to determine when, and if, subconvulsive vs. convulsive seizures

occur is an enormous task. Second, because the goals of animal models vary, it may not

be possible to test all aspects of interest in every model. For example, a model of post

traumatic epilepsy that attempts to mimic the postinsult latent period, may not allow for

neurobehavioral assessment of acute postinsult seizures or anticonvulsant drug adminis

tration. As well, such a model may not use trauma as the precipitating event. Alternatively,

a model designed to assess postinjury neurobehavioral change may not allow for the

assessment of the spontaneous epileptogenic process. With these limitations in mind,

discussion of some of the animal models is worthwhile.

Status epilepticus, induced by excitotoxins (e.g., kainic acid or pilocarpine) 70,71 or elec

trical stimulation 72–74 has been proposed to share commonalities with posttraumatic epi

leptogenesis. 75 The initial precipitating insult of prolonged seizures is followed by a latent

period, after which spontaneous seizures occur. Like experimentally-induced traumatic

brain injury, status epilepticus results in dramatic and significant morphological, physio

logical, and neurochemical alterations. Indeed, the insult-associated plasticity and neu

ronal reorganization seen after experimentally-induced insult via seizures or frank trauma

appears to share similarities. 75,76 Likewise, another useful model involves the cortical

“undercut method” in which the initial brain insult is followed by a dormant period after

which cortical epilepsy is evident. 77

Lastly, the kindling model refers to a phenomenon whereby a brain region can be

rendered permanently epileptic when subjected to brief, repeated electrical stimulations

that, alone, would not induce behavioral seizures. 78 Clinical evidence that “seizures beget

seizures” is supported by a prospective study of unselected patients with new onset of

seizures which demonstrated that the probability of seizure control was inversely related

to the number of seizures experienced prior to initiation of antiepileptic drug therapy. 79,80

Furthermore, the time interval between seizures appears to decrease with subsequent

episodes in untreated patients. 81

The kindling paradigm in which the brain “learns” to seize has been used to study

epileptogenesis and neuronal plasticity. Typically, electrical stimulation is administered

by an implanted depth electrode and, initially, results only in a brief localized epileptiform

discharge on EEG, without a behavioral response. With continued daily stimulation, there

are progressive increases in duration of both EEG epileptiform discharges and motor

seizure activity.

The resulting convulsive behavior evolves through stages that are highly reproducible

from animal to animal and may be graded by levels of

behavioral severity. 82 Stage 0 is no

behavioral response; Stage 1 consists of chewing motion; and Stage 2 consists of head

nodding. At Stage 3, the animal displays clonus (jerking) of forelimbs, and at Stage 4,

there is forelimb clonus with rearing onto hind limbs. The fifth, and most severe, stage

consists of forelimb clonus with rearing and falling.

Electrical kindling of seizure activity induces neuronal changes within the brain that

result in more severe generalized seizures from a stimulus that initially produced only

focal seizure activity. Numerous transient and long-term changes occur during, and as a

result of, electrical kindling, with the most dramatic being seen within the excitatory and

inhibitory amino acid transmitter systems. 83–88 For example, kindling significantly reduces

neuronal sensitivity to GABA; the changes are long lasting and may be seen at 4 and 12

weeks after the last fully kindled (Stage 5) seizure. 89–92 Loss of sensitivity to GABA evolves

during the course of kindling, and correlates with seizure severity. 89 These changes are

believed to result from a compensatory desensitization of the receptor in response to

increased GABA release during the electrical kindling process. 93,94 Thus, the very mecha

nisms utilized by the brain to suppress kindling appear to be counterproductive and

ultimately facilitate the kindling process.

Because sequelae of brain injury also elicit aberrations in the excitatory and inhibitory

tone, 60 using the kindling model to produce postinjury epileptogenesis is a useful tool,

particularly in combination with focal cortical damage. In this model, 95,96 injury severity

is controlled using a reproducible focal cortical lesion 97,98 that induces behavioral deficits

in animals similar to those seen in humans with brain injury. 99 This focal cortical lesion

in animals does not routinely produce spontaneous convulsions, yet it does lower the

seizure threshold in the amygdala. In our laboratory, we observed a 37% decrease in Stage

5 seizure threshold following cortical lesion in comparison to fully kindled animals with

out lesions. Electrical kindling of the amygdala after focal cortical lesion is a useful and

unique model as it allows for the study of the neurobehavioral impact of epileptogenesis

(with and without anticonvulsant drug administration), while still controlling seizure

severity, timing, and number.

Posttraumatic Seizures, Epilepsy, and Anticonvulsant Prophylaxis:

Implications for Neurobehavioral Recovery

Brain damage resulting from traumatic brain injury can significantly impair physical,

cognitive, and social function. Recovery from such deficits can be variable, and permanent

neurological disability occurs in as many as 90,000 survivors of brain injury in the United

States each year. 100 These disabilities are further compounded by posttraumatic epilepsy,

which results not only in spontaneous and unpredictable seizure recurrence but also in

toxicities associated with antiepileptic drug therapies. Individuals with posttraumatic

epilepsy pose a special case in that they are neither patients with only a brain injury nor

patients having only epilepsy. Thus, the treatment requirements for posttraumatic epilepsy

extend beyond those available for either the epilepsy or brain injury alone. This makes it

difficult to generalize from the anticonvulsant drug toxicity and efficacy profiles obtained

from epileptic subjects without brain injury, and few anticonvulsant drugs have been

systematically investigated in traumatic brain injury patients alone. 36,38,101–103 Treatment

strategies that acknowledge these complexities will improve patient quality of life.

The controversy surrounding whether or not anticonvulsants should be administered

prophylactically requires assessing the potential neurobehavioral impact of seizures vs.

the risk of AED administration. 101,104,105 Anticonvulsants are often administered after brain

injury even though they have not been found to be effective in preventing later develop

ment of posttraumatic epilepsy. 38,39 Several early studies suggested a beneficial effect of

prophylactic anticonvulsant therapy, 106,107 but later controlled studies failed to support

these findings. For example, when studied in a double-blind, placebo-controlled, random

ized manner, phenytoin administered following TBI had no impact on the later develop

ment of epilepsy, though it did reduce the incidence of early seizures (i.e., those occurring

within the first week after injury). 37,53

The lack of effectiveness of anticonvulsant drugs in preventing posttraumatic epilepsy

is also paralleled in experimental kindling studies. Although many antiepileptic drugs

may block fully kindled convulsions in animals, they do not prevent the kindling process

and do not prevent the increases in seizure severity. Specifically, phenytoin and carbam

azepine may block seizures but do not consistently prevent epileptogenesis from occur

ring. 85,108 In contrast, phenobarbital and benzodiazepines do appear to be

antiepileptogenic in that they are effective in slowing the progression of amygdala

kindled seizures. 109–111 Valproic acid has also been found to retard the rate of amygdala

kindling but only when used at high doses with significant toxicities. 112,113 Antagonists

that directly compete for the NMDA receptor inhibit the progression of electrically

kindled seizures but have relatively less effect on seizures once kindling has been

achieved. 114 This suggests a potential antiepileptogenic role of NMDA receptor antago

nists that is independent of its ability to block acute seizures. A full scale trial is underway

in which magnesium, which blocks the N-methyl-D-aspartate (NMDA) channel, is being

administered after traumatic brain injury. 39 Other transmitters have been targeted to

determine their antiepileptogenicity in the kindling model as well. Administration of the

alpha adrenergic receptor agonist clonidine can significantly retard the rate of evolution

of kindled seizure stage but, by itself, does not block the fully established kindled

seizure. 115,116 Thus, a key role of noradrenergic neurotransmission in the regulation of

epileptogenesis has been proposed. 117,118

The search for effective antiepileptogenic drugs may necessitate a change in current

experimental drug development paradigms so that potential prophylactic drugs may be

screened. Use of models of epilepsy, rather than acute seizures, holds great promise for

future development of antiepileptogenic drugs. These models include the electrical kin

dling paradigm, studies in genetically seizure-prone animals, and models in which the

focal insult (e.g., status epilepticus, cortical “undercut”) is followed by a dormant period

and epilepsy. 75,77 Ultimately, however, the effectiveness of a drug as an antiepileptogenic

agent will require prospective, placebo-controlled trials in TBI and other high-risk patients.

Currently available antiepileptic drugs do not appear to affect the pathophysiologic

processes resulting in spontaneous seizure recurrence and may be merely masking the

outward manifestations of seizure activity. The question is, does this come at a cost to the

traumatically brain-injured patient? The neurobehavioral effects of anticonvulsant drug

therapy is known. Indeed, it has been argued that, since brain injury carries only an

approximate 5% risk for posttraumatic epilepsy, the remaining 95% needlessly receive

anticonvulsant medication. 119 This group of patients is exposed to the toxicities of anti

convulsant administration without any potential benefit. Even in normal volunteers, anti

epileptic drugs cause significant cognitive impairment, albeit minor in many cases. 120

Barbiturates commonly cause cognitive impairment, even at low doses. 121 For many drugs,

however, toxic levels can account for some of their untoward effects. For example, it was

initially suggested that carbamazepine induced less cognitive impairment than pheny

toin. 122 When the data were reexamined so that patients with toxic phenytoin levels were

removed from the study, no significant differences in cognitive impairment could be found

between treatments. 123 A subsequent study, which maintained levels in therapeutic ranges,

verified these findings. 121 Although valproic acid is thought to cause minimal problems

with cognition, withdrawal of this medication improved psychometric scores. 124 In a study

that included completely randomized assignment of drug vs. placebo, phenytoin admin

istration after traumatic brain injury was associated with impaired function on several

neuropsychological measures of cognition, which are among the most common and dis

abling problems faced by individuals with brain injury. 101

Phenytoin and carbamazepine

have each been shown to adversely affect psychomotor function following brain injury,

though this is reversible upon drug discontinuation. 103 The newer AED have not been

studied for their effects on cognitive function in patients with TBI. These negative conse

quences of treatment with AED on cognitive functioning are not surprising when one

considers anticonvulsant drugs can adversely affect cognitive function in nonbrain-injured

individuals 120,125,126 and that drug sensitivity is greater after brain injury.

Animal studies addressing these issues paint a similarly negative picture (Table 2.2).

For example, if diazepam is administered during the first 3 weeks after unilateral anter

omedial cortex damage, recovery from somatosensory deficits is delayed indefinitely. 98

Even if diazepam is administered only for the first 7 days after brain damage, recovery

is significantly delayed. 127,128 Phenobarbital also appears to interfere with somatosensory

and motor recovery following brain damage in rats and nonhuman primates. 129,130 Not all

anticonvulsant drugs have been found to be detrimental after brain damage in animals:

carbamazepine 131 and vigabatrin 132 had no impact on recovery from somatosensory

deficits. As a caveat, however, when an anticonvulsant dose of vigabatrin was coadmin

TABLE 2.2

Postinjury Factors and Their Impact on Neurobehavioral

Function Seizure Type Effect Reference

Animal studies

Kindled (early Stage 0/subclinical;

ipsilateral or contralateral focus)

Kindled (early Stage 1/clinically evident;

ipsilateral focus only)

Kindled (late Stage 1/clinically evident;

ipsilateral or contralateral focus)

Pentylenetetrazol (clinically evident)

Electroconvulsive shock (generalized)

Human studies

Early posttraumatic seizures (subclinical)

Late posttraumatic seizures

Posttraumatic epilepsy

Posttraumatic epilepsy (controlling for

injury severity) 0 ⇓ 0 ⇑ ⇑ 0 0 ⇓ 0 (Hernández and Warner, 1995; Kline et al., 2000) (Hernández and Warner, 1995; Kline et al., 2000) (Hernández and Warner, 1995; Kline et al., 2000) (Hamm et al., 1995; Hernández and Schallert, 1988) (Feeney et al., 1987) (Vespa et al., 1999) (Haltiner et al., 1996) (Armstrong et al., 1990; Dikmen and Reitan, 1978) (Haltiner et al., 1996) Anticonvulsant Drug Effect Reference

Animal studies

Diazepam

Phenytoin

Carbamazepine

Phenobarbital

Vigabatrin

Human Studies

Phenytoin

Carbamazepine

Benzodiazepines ⇓ ⇓ 0 ⇓ 0 ⇓ ⇓ ⇓ (Hernández et al., 1989a; Schallert et al., 1986) (Brailowsky et al., 1986) (Schallert et al., 1992) (Hernández and Holling, 1994; Watson and Kennard, 1945) (Wallace et al., 1999) (Dikmen et al., 1991; Smith et al., 1994) (Smith et al., 1994) (Goldstein, 1995) Anticonvulsant Drug + Seizures Effect Reference

Animal studies

Phenobarbital + Kindled (early Stage 0)

Vigabatrin + Kindled (early Stage 0) ⇓ ⇓ (Montañez et al., 2000) (Montañez et al., 2001)

Note: 0 = no effect; ⇓ = hindered; ⇑ = improved; “early” = occurring within the first week postinjury; “late” = occurring after the first week postinjury.

istered against subconvulsive kindled seizures, recovery was impeded. 133 Similarly detri

mental to functional recovery was phenobarbital administration prior to evoked

subconvulsive seizures. 134 These data suggest that the interaction between anticonvulsant

drugs and subclinical seizures after brain insult are detrimental to functional recovery and

the net effect is greater than either factor alone. This further supports the value of EEG

monitoring after traumatic brain injury, 15,26 however, not only as a means of detecting

subclinical seizures, but also to influence treatment strategies that optimize neurobehav

ioral outcome.

There are several potential mechanisms by which

anticonvulsants may adversely affect

the recovering brain. First, these drugs suppress repetitive firing, which is important for

long-term potentiation (LTP), a phenomenon associated with learning. LTP is discussed

in the chapter by Lehr in this volume. Second, barbiturates and benzodiazepines directly

modulate the GABA A receptor and increase neuronal inhibition. That there is a link

between enhanced postsynaptic GABA-mediated inhibition and impaired functional

recovery is well established. 98,127–130,135–137 Likely mechanisms include toxicity of excessive

intracellular Cl– 138,139 and Ca++ 64,65 associated with GABA postinjury, GABA receptor

dependent excitotoxicity, 140 and decreases in growth factor production attributed to GABA

augmentation. 141 Finally, suppression of repetitive firing or general CNS depression could

be counterproductive following brain injury, especially since neuronal depression already

occurs as a consequence of brain injury. This condition of postinjury neuronal depression

has been referred to as diaschisis, 142 which is the temporary disruption of neuronal activity

in undamaged areas functionally related to injured areas.

Evidence that diaschisis occurs after brain injury has been well established with mea

sures of blood flow, metabolism, electrical activity, and neurotransmitter levels. 143–146 More

over, this depression of neuronal activity after brain injury has been correlated with

behavioral deficits, and restoration of normal neuronal

activity correlates with behavioral

recovery. 147–149 The use of positron emission tomography (PET) has made it possible to

measure posttraumatic neural depression after brain injury in humans. Measures of cere

bral glucose metabolism clearly show a state of metabolic depression postinjury, though

there is not a clear relationship between this and functional level (e.g., consciousness). 150

Based on the brain's functionally-depressed state after trauma, it has been hypothesized 98

that posttraumatic seizures may be the result of adaptive mechanisms initiated by the

injured brain in its attempt to restore normal neuronal activity. For this to be the case, the

neurobehavioral consequences of seizures would need to be associated with improved

recovery or no deleterious effect (e.g., neutral). Experimental data in animal studies sug

gest the effects of seizures are not uniform, and greatly depend on seizure type, severity,

and frequency (Table 2.2). For example, mild or infrequent seizures have been found to

improve the recovery process. 151–153

At first blush, these data may seem counterintuitive. However, when the entire array

of neural and functional consequences of seizures are considered, a complex yet fairly

clear picture emerges that is dependent on the timing, type, and severity of postinjury

seizures. For example, using an animal model of posttraumatic epilepsy (described above),

it appears that the impact of seizures is bimodal;

convulsive seizures (Stage 1) during the

6-day postlesion, critical period are detrimental to the recovery process, whereas subcon

vulsive seizures have no functional impact. 95,154 This effect is time dependent and hemi

sphere specific in that Stage 1 kindled seizures occurring on postlesion Day 7 or later have

no impact on the recovery process. Moreover, contralaterally kindled seizures exert no

impact on recovery regardless of when they occur. Potential mechanisms for these effects

stem from the fact that Stage 0 seizures exert no impact on peak basic fibroblast growth

factor (bFGF) expression, whereas Stage 1 seizures block this important neurotrophic

contributor to functional recovery. 155 Interestingly, kindled seizures in nonbrain-injured

animals have been associated with neurogenesis, 156,157 which may contribute, in a positive

or negative way, to the recovery process, depending upon whether these new cells replace

lost ones, make functionally relevant connections, or contribute to aberrant plasticity (e.g.,

excitability that might contribute to epileptogenesis). It would be interesting to assess the

impact of postinjury seizures, with or without anticonvulsant drug administration, on

neurogenesis in traumatically brain-injured animals.

There is other evidence that seizure effects vary. Clinical studies have shown that simple

abnormal EEG activity is associated with impaired cognition 158 and that response time is

impaired even during single focal interictal spikes in

humans. 159 Learning is also impaired

in young rodents undergoing repetitive and frequent audiogenic seizures. 160 In contrast,

repetitive kindled seizures do not appear to affect most aspects of learning and mem

ory, 161,162 though some (e.g., acquisition) are impacted by the transition from partial to

generalized seizures. 161 Taken together, these data suggest that, at least in some situations,

seizures may inhibit learning. Finally, brief seizures do not necessarily cause brain dam

age, 88 yet prolonged seizures cause neuronal death via excitotoxicity. 75,163 This latter type

of seizure activity following trauma would likely contribute to further cell death or

interfere with the plasticity underlying recovery processes.

While seizures, per se, may not be detrimental to functional outcome, there is significant

evidence suggesting that posttraumatic epilepsy poses significant problems for rehabilitation

of the TBI patient. The uncertainty caused by randomly occurring loss of consciousness

places yet an additional barrier to independence. At the most, uncontrolled epilepsy may

necessitate placement in specialized care facilities and, at the least, may prohibit driving

privileges. Uncontrolled seizures are also associated with a significant risk of trauma and

unexpected death (SUDEP). 164 Some data suggest the impact of posttraumatic epilepsy on

neurorehabilitation may extend beyond these social aspects and could actually impede

brain recovery. World War II veterans with head injury who

developed posttraumatic

epilepsy had a lower survival rate than veterans without epilepsy. 165 The incidence and

severity of cognitive deficit in hemiplegic children is highly correlated with the presence

of seizure activity, independent of the amount of cerebral damage. 166 A retrospective study

on head-injured patients demonstrated that functional measures were lower in patients

that developed posttraumatic epilepsy upon entry into rehabilitation than those who did

not. Although both groups improved significantly, functional outcome remained lower in

the epileptic group. 167 Importantly, these studies could not address the question of whether

the results were due to seizures, injury severity, or anticonvulsant drug administration.

Haltiner and colleagues 168 were able to tease apart some of these issues: when injury

severity is controlled, neither late posttraumatic seizures nor posttraumatic epilepsy had

an influence on neuropsychological outcome measures.

To effectively delineate the neurobehavioral impact of seizures vs. epilepsy following

traumatic brain injury in humans, it is necessary to know when, and if, the patient is

having seizures. To this end, Vespa and colleagues 26 continuously monitored patients after

TBI for up to 14 days. Of these individuals, 22% had clinically-evident or nonclinically

evident seizures. When comparing outcome between these individuals and those in the

nonseizure group, it appears that seizures are not

necessarily detrimental. For example,

both groups exhibited increased intracranial pressure (ICP) after brain injury, but the

overall ICP was actually greatest in the nonseizure group. Cerebral perfusion pressure

(CPP) was slightly, though significantly, lower in the nonseizure group. There was no

difference between the groups in terms of length of stay, nor in outcome (Glasgow Out

come Score [GOS]); both good and poor outcomes were equally likely regardless of

whether there had been seizures or not. A caveat, however, is that there was a greater

mortality rate within the seizure group, which could be fully accounted for by those

individuals with status epilepticus. If these individuals were removed from the analysis,

it appeared that the seizure group had a lower mortality rate than the nonseizure group.

It is also worth noting that Vespa and colleagues 169 have shown postinjury seizures can

be correlated with elevated glutamate levels as assessed by intracerebral microdialysis.

Such an elevation could contribute to further seizures and/or damage, though it remains

unclear in this type of study as to the exact level of glutamate that would be toxic.

In summary, experimental data suggest the effect of seizures on functional recovery of

the injured brain is not uniform and depends on seizure type, timing, and severity.

Specifically, recurrent and/or severe seizures may have a negative impact on recovery,

while mild, infrequent seizures may be associated with improved behavioral recovery or

be without neurobehavioral consequence. Thus, it is only when the seizures are severe

enough to cause further brain damage, or frequent enough to develop into epilepsy, that

they appear to be detrimental to the behavioral recovery and quality of life.

Conclusions

The accurate diagnosis of episodic behaviors is crucial to providing the most appropriate

therapy for TBI patients. Although posttraumatic epilepsy is a common entity, it may be

difficult to recognize. Posttraumatic epilepsy must be carefully distinguished from other

types of behavioral spells because either unnecessary antiepileptic drug therapy or uncon

trolled seizures may potentially impair neurologic recovery. At present, there is little

evidence to support prophylactic use of anticonvulsants in TBI patients. Their use in this

way does not prevent epileptogenesis clinically and much data implicates negative effects

on cognition and recovery of brain function. Thus, antiepileptic drug therapy should be

withheld until there is a bona fide diagnosis of epilepsy — that is, at least two separate

seizure events that are not due to transient metabolic derangements. Once the diagnosis

of epilepsy is secure, effective therapy should be initiated promptly to prevent the dele

terious effects of uncontrolled seizures on brain recovery. Future research will need to

address whether control of posttraumatic epilepsy improves functional outcome and if

these gains outweigh the adverse effects of antiepileptic drug therapy. In addition, the

mechanisms of posttraumatic seizures will need to be better understood so that therapies

that prevent epileptogenesis may be achieved.

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3

Neurotransmitters and Pharmacology

Ronald A. Browning

CONTENTS

and Various Neurotransmitters

Editor’s Note

Pharmacological treatment of traumatic brain injury (TBI) is complex and still in its infancy as

a field of clinical investigation. Patients with TBI have a wide variety of central nervous system

(CNS) problems, as well as numerous peripheral disorders (e.g., hypertension, reduced bowel

function) that can be addressed pharmacologically. One of the major difficulties in identifying

useful medications for TBI patients is the diversity of brain injury encountered in this population.

The non-CNS medical problems in TBI patients often require the use of drugs to control hyper

tension or increase bowel function and drugs that affect the autonomic nervous system are com

monly used for such disorders. While this chapter focuses on the medications that are used to alter

neurological or behavioral functions (i.e., those that act on the CNS), neurotransmission in the

autonomic nervous system and the drugs that modify it are also described.

Introduction

Most drugs that are used for an action on the central nervous system (CNS), such as those

employed in neurology and psychiatry, exert their action by acting at the site where

neurons communicate with one another, namely, the synapse. These drugs, therefore, exert

their effect by modifying the process of neurotransmission. The exceptions to this rule are

those classes of drugs known as: (1) the local anesthetics,

which prevent nerve conduction

by blocking sodium channels and, thereby, alleviating pain, (2) general anesthetics, which

produce a reversible loss of consciousness by unknown means, although recent evidence

suggests these agents can also modify neurotransmission, and (3) some antiepileptic agents,

which prevent seizures by acting directly on voltage-gated ion channels to alter nerve

conduction. It should be noted that some antiepileptic drugs do produce their beneficial

effects by altering neurotransmission (e.g., tiagabine).

Drug classes whose mechanism of action involves a modification of synaptic neurotrans

mission include narcotic analgesics (used to alleviate pain), antipsychotic agents (used to

treat schizophrenia), antidepressants, antianxiety agents (e.g., diazepam or Valium ®), some

antiepileptic drugs, antispasmodics, and muscle relaxants. In addition, due to the ubiqui

tous role of the peripheral autonomic nervous system in the regulation of organ-system

function such as cardiovascular, respiratory, gastrointestinal, nasal congestion, and the

like, it is not surprising to find that drugs altering peripheral neurotransmission are used

to treat a wide variety of disorders such as hypertension, heart disease, gastrointestinal

disorders, hiccups, asthma, hay fever, etc.

The question of whether or not a substance functions as a neurotransmitter is not an

easy one to answer and requires extensive experimental testing by neuroscientists. Neu

robiologists have set specific criteria that must be fulfilled before a substance is accepted

as a neurotransmitter. These criteria were established in the mid-1960s by Werman 1 and,

while the original criteria were extremely useful for over 25 years, they may not be entirely

adequate because knowledge of how neurons communicate with one another and with

target organs in the periphery has expanded. Indeed, some of the recently discovered

signaling molecules, such as the gases nitric oxide and carbon monoxide, do not fulfill

the previously established criteria, yet clearly function as important neural messengers. 2–4

Nevertheless, there are about seven chemicals that have been well-established as neu

rotransmitters and another 20 to 30 substances that are highly suspected as neurotrans

mitters or neuromodulators in the nervous system. The seven well-established or classical

neurotransmitters include:

1. Acetylcholine

2. Norepinephrine

3. Dopamine

4. 5-Hydroxytryptamine (5-HT, serotonin)

5. Gamma-aminobutyric acid (GABA)

6. Glycine

7. Glutamate/aspartate

All of these have been associated with the action of drugs that exert an effect on the

nervous system. In addition, there are several neuropeptides which serve as neurotrans

mitters or neuromodulators (i.e., modify the action of the classical neurotransmitters) that

have been associated with the action of drugs and these will be discussed.

In order to appreciate the physiological and/or biochemical mechanisms by which drugs

alter neurotransmission, one must have an understanding of the events involved in syn

aptic neurotransmission. Thus, we will begin with a description of the physiology of

chemical neurotransmission and, then, proceed to discuss the individual neurotransmitters

and the drugs that mediate their effects through such neurotransmitters. It should be kept

in mind that synaptic transmission is not only important for understanding the action of

drugs, but it is vital for all functions of the nervous system, and it appears to be the site

at which learning and memory take place in the CNS (see Chapter 10).

Chemical Neurotransmission

In the mammalian nervous system (both central and peripheral), the predominant form

of communication between two nerves and between nerve and muscle (or nerves and

glands) is chemical. Electrical transmission between nerve cells can also occur, but is not

easily modified by drugs and will not be considered here. The site at which this chemical

transmission occurs is called the synapse. From Figure 3.1, it can be seen that the synapse

consists of several cellular and subcellular structures. Although synapses can occur at

several locations on a neuron which is receiving information from another neuron, the

more typical arrangement is that described in Figure 3.1. Thus, the axon terminal of one

neuron generally synapses on the cell body (soma or perikaryon called axosomatic synapses)

or dendrites of another neuron (called axodendritic synapses). Axons may also synapse on

other axons, especially at the nerve terminals (called axo-axonic synapses) and, under

unusual circumstances, dendrites may synapse with other dendrites (dendrodendritic syn

apses) or cell bodies may synapse with one another (soma-somatic synapses). At the proto

typical synapse, the neurotransmitter, which is usually a small water soluble organic

amine, is synthesized from precursors within the axon terminal, taken up into and stored

in a small round or ovoid vesicle, and released from the nerve terminal in a calcium

dependent process when an action potential or nerve impulse reaches the nerve terminal.

Indeed, the steps associated with neurotransmission at a chemical synapse are as follows:

Step 1: The first step is the release of the neurotransmitter from its storage site in a

vesicle due to the arrival of an action potential which, in turn, opens voltage-dependent

calcium channels and allows the influx of calcium from the extracellular fluid. The calcium

then triggers a release process called exocytosis. Exocytosis involves fusion of the vesicle

membrane with the nerve membrane and the opening of the vesicle into the synaptic cleft

(Figure 3.1). Thus, the vesicle extrudes its contents into the synaptic cleft. The release

process can be regulated by receptors found on the nerve terminal (called presynaptic

receptors or autoreceptors). Exocytosis is described in more detail below.

Step 2: The next step in neurotransmission involves binding of the neurotransmitter to

receptors in the postsynaptic membrane and the initiation of postsynaptic events, i.e., a

depolarization or a hyperpolarization. Receptors give both neurotransmitters and drugs

their selectivity and specificity. The receptors, which are typically membrane proteins or

glycoproteins, only recognize and bind chemicals of the “correct” chemical structure. Thus,

just as only one key opens a lock, only one chemical structure can initiate postsynaptic

events via the receptor. The receptors for neurotransmitters come in two varieties: (1) those

that actually form an ion channel in the membrane (such as the nicotinic cholinergic

receptor) and mediate rapid events when the transmitter binds and are called ligand-gated

ion channels, or (2) those that are connected to ion channels indirectly via “second mes

senger” molecules that become activated inside the cell when the transmitter binds to the

receptor. In the latter case, the receptor is linked to a guanine nucleotide binding protein

(called a G-protein) which functions as the link between

the receptor protein and the

enzyme(s) that synthesize the “second messenger.” This class of receptors is referred to

as G-protein linked receptors or metabotropic receptors.

The potentials that develop in the postsynaptic cell either move the membrane potential

further from the threshold for triggering an action potential (hyperpolarization) or move

it closer to the threshold (depolarization). Hyperpolarization (inhibitory postsynaptic

potentials or IPSPs) results from the opening of chloride or potassium channels in the

membrane, allowing chloride to flow in or potassium to flow out. Hyperpolarization, then,

inhibits postsynaptic firing. Depolarization (excitatory postsynaptic potentials or EPSPs)

results from the opening of channels that allow both sodium and potassium to flow down

their concentration gradients through the same channel. This is different from the sodium

selective channel that is involved in the propagation of the action potential down the axon.

If the depolarization is great enough, the threshold for an action potential is reached and

an action potential (regenerative, sodium current) is propagated down the axon to initiate

more synaptic transmission.

In the central nervous system, a neuron can only respond in one of two ways: (1) it

either reaches threshold and fires an action potential, which, in turn, propagates informa

tion to the next neuron via synaptic transmission or (2) it is inhibited and does not fire

an action potential.

Step 3: The third step of the neurotransmission process consists of the postsynaptic

response. The postsynaptic response can consist of an action potential in the neuron, the

contraction of muscle or the secretion of a gland.

Step 4: This step consists of inactivation of the neurotransmitter in the synaptic cleft.

The transmitter must be removed from the synaptic cleft in order for the postsynaptic cell

to repolarize, which is necessary for the synapse to remain responsive to incoming infor

mation. The two most important mechanisms for removing the neurotransmitter from the

cleft are: (1) reuptake into the neuron from which it was released, and (2) enzymatic

degradation. In addition, other mechanisms include diffusion away from the cleft and

uptake (transport) into other cells (e.g., glial cells, muscle cells in the periphery, or other

FIGURE 3.1

Drawing of an axosomatic (typical) synapse between two neurons. The neuron synapsing on another neuron is

referred to as the presynaptic neuron, while the neuron receiving the input is called the postsynaptic neuron. Various

subcellular structures associated with the synapse are labeled. The active zone is the site at which vesicles attach

to the docking sites just prior to release. Dendrites Synaptic Cleft Postsynaptic Receptor Neurotransmitters Vesicles Nucleus Cell Body or Soma Axon Terminal Mitochondrion Active Zone Presynaptic Neuron Postsynaptic Neuron Axon

neurons). Just as the neurotransmitter can be taken up and reused by the cell that released

it, the vesicle membrane can be retrieved from the nerve terminal where it fused. Thus,

vesicles are also recycled.

Sites Where Drugs Act

Drugs may either facilitate (enhance) or inhibit neurotransmission. Some of the mecha

nisms by which drugs can facilitate neurotransmission include:

• Stimulation of the release of the neurotransmitter into the cleft

• Increased synthesis of the neurotransmitter in the presynaptic terminal

• Prevention of inactivation of the transmitter following release (e.g., blocking reuptake or blocking enzymes of degradation)

• Stimulation of the postsynaptic receptors directly to produce a response. A drug that does this is called an agonist

Some of the mechanisms by which drugs inhibit neurotransmission include:

FIGURE 3.2

Drawing of a cholinergic synapse showing the fate of ACh after release into the synaptic cleft. Note that the

neuron utilizes choline from two sources: (1) the blood and (2) that which is recycled from the breakdown of

released ACh in the synaptic cleft. Acetylcholinesterase associated with the postsynaptic membrane terminates

the action of released ACh. Mitochondrion Nicotinic or Muscarinic Receptor ACh ACh ACh Presynaptic Neuron Terminal Postsynaptic Neuron Nucleus Dendrite Choline Axon Acetylcholinesterase Fused Vesicle Releasing ACh Acetyl CoA + Choline Acetic Acid Choline

- Inhibition of the synthesis of the transmitter
- Prevention of transmitter release
- Interference with neurotransmitter storage in the vesicle
- Blocking the neurotransmitter receptor

A drug which binds to a receptor, blocking the neurotransmitter action but producing no

effect, is called an antagonist.

In the sections that follow, we will consider the individual neurotransmitters and the

drugs that produce clinical effects by altering chemical neurotransmission.

Acetylcholine (ACh)

Acetylcholine is one of the most widely studied neurotransmitters and one of the oldest,

phylogenetically. It was, in fact, the neurotransmitter for which chemical neurotransmis

sion was originally demonstrated, when it was found to be released from nerves inner

vating the frog heart by Loewi in 1921. 5 It has been most thoroughly studied in the

peripheral nervous system where it functions as a neurotransmitter of the motoneurons

innervating skeletal muscle (involved in the voluntary control of movement). ACh is also

the neurotransmitter of the preganglionic sympathetic and parasympathetic fibers as well

as the postganglionic parasympathetic fibers. 5 The response to stimulating parasympa

thetic nerves innervating various organs in the body is shown in Table 3.1. As you can

see, these nerves affect every organ in the body. Drugs

which alter neurotransmission at

these synapses can have very profound effects.

ACh is also a neurotransmitter in the central nervous system where specific pathways

have been identified in the brains of primates and other species. Basically, there are two

groups of ACh pathways: 6 (1) those innervating the forebrain (cell bodies in the basal

forebrain around the medial septum and nucleus basalis of Meynert), as well as the

interneurons in the striatum (basal ganglia) and (2) those innervating the brainstem and

diencephalon (cell bodies in the laterodorsal tegmental nucleus and the pedunculopon

tine tegmental nucleus). Some of the proposed functions of ACh in these CNS pathways

are given in Table 3.2, but it is clear that there is much to learn about the intricate details

of how ACh regulates such things as learning and memory, sleep, seizures, and emotional

states.

Synthesis, Storage, Release, and Inactivation of ACh

Neurons that utilize ACh as a neurotransmitter are referred to as cholinergic neurons and

a schematic diagram of such a neuron is shown in Figure 3.2. Acetylcholine is synthesized

within cholinergic neurons from the precursor, choline, which comes from the diet, and/

or the breakdown of phospholipids, primarily in the liver. 7 Some of the choline that is

taken up into cholinergic neurons for synthesis of ACh comes from the enzymatic degra

dation of released ACh (Figure 3.2). In fact, about 50% of the choline released as ACh is

recaptured by the neuron for the synthesis of more ACh. 8

Choline is transported into the nerve by a transporter or “carrier” protein in the mem

brane. This transporter or carrier has a high affinity for choline, which means that it avidly

picks up choline from the surrounding area. It has, however, a limited number of transport

sites, meaning that it can get filled up or saturated. Increasing the concentration of choline

up to the point at which the sites become filled results in a proportional increase in the

rate of choline transport. However, once all the transporters are occupied, the rate of

transport becomes constant.

Theoretically, one should be able to increase the synthesis of ACh by increasing the

availability of choline, especially since the enzyme that converts choline to ACh, choline

acetyltransferase, is not saturated with substrate (choline).

A cosubstrate to choline is utilized in the synthesis of ACh. This cosubstrate is called

acetylcoenzyme A (acetylCoA). AcetylCoA derives from pyruvate via the breakdown of

glucose and is, therefore, plentiful inside the neuron.

Experimental studies have established that the rate-limiting factor in the overall ACh

synthesis is the uptake of choline by the neuron. 8,9 Since ACh neurons are lost in Alz

heimer’s disease, it has been of interest to attempt to increase ACh synthesis in brains

of Alzheimer’s patients. Although some studies have suggested that this is possible, TABLE 3.1 Organ Response to Parasympathetic Nerve Stimulation Organ Receiving Innervation Response to Stimulation Receptor Type Eye Iris, sphincter Ciliary muscle Pupillary constriction (miosis) Contraction — near vision Muscarinic Muscarinic Heart SA node Atrium AV node Ventricles Decrease in heart rate Shortens refractory period Slows conduction No response — poor innervation Muscarinic Muscarinic Muscarinic Vasculature No parasympathetic innervation (has muscarinic receptors which can respond with vasodilation) Muscarinic Trachea and bronchioles Constriction Muscarinic Stomach and intestine Increase in motility, tone, and secretions; relaxation of sphincters Muscarinic Urinary bladder Detrusor muscle Trigone and sphincter Contraction, bladder emptying Relaxation Muscarinic Muscarinic Sex organs, male Erection Muscarinic Sweat glands Secretion Muscarinic Lacrimal glands Secretion Muscarinic Nasopharyngeal glands Secretion Muscarinic Source: Hoffman, B. B. and Taylor, P., Neurotransmission: The autonomic and somatic motor nervous systems, in The Pharmacological Basis of Therapeutics, Hardman, J. G., Limbird, L. E., and Gilman, A. G., Eds., McGraw-Hill Medical Publishing, New York, 2001, 115. TABLE 3.2 Some Proposed Functions of ACh in the CNS Learning and memory (cholinergic neurons lost in Alzheimer’s disease) Sleep and arousal states Body temperature Susceptibility to seizures Affective states (mood) Cardiovascular function via hypothalamus Motor disorders (Parkinson’s disease)

choline has not been found terribly useful for improving memory in this or other pop

ulations. 10 The reason for this may be that the choline uptake transporter saturates and

that the intracellular or cytoplasmic choline concentration can only be increased to a

limited extent. There are no known drugs to increase the uptake of choline, though there

are experimental drugs which inhibit the uptake of choline and interfere with the syn

thesis of ACh, such as hemicholinium and triethylcholine, both of which are competitive

inhibitors of choline uptake.

Choline can also get into neurons by another mechanism, called “low-affinity” uptake,

which may account for the increase in synthesis of ACh that is seen in some peripheral

organs following the administration of high doses of choline. Much higher concentrations

of choline are required to saturate the transport proteins involved in low-affinity transport.

It has recently been hypothesized that the selective vulnerability of cholinergic neurons

in Alzheimer’s disease may be due to the double role of choline in forming membrane

phospholipids and ACh in these neurons and the selective breakdown of cell membrane

to shunt choline into the neurotransmitter leading to cell membrane damage. 11 If the latter

hypothesis is true, treatment with choline may be beneficial. There is evidence that giving

choline to rats can increase the release of ACh in the striatum 12 and this effect can appar

ently be enhanced by caffeine. 13

The enzyme that catalyzes the synthesis of ACh is choline acetyltransferase (ChAT),

which is a soluble enzyme (nonmembrane bound) found in the cytoplasm of cholinergic

neurons. The gene responsible for forming ChAT is expressed only in cholinergic neurons

and this enzyme, therefore, serves as a phenotypic marker for cholinergic neurons. The

overall synthetic scheme is given in Figure 3.3.

Once ACh is synthesized, it is stored in small spherical (synaptic) vesicles along with

several other constituents, including adenosine

triphosphate (ATP) and a protein called

vesiculin. The sequestration of the ACh within these tiny vesicles serves to protect it from

destruction by the enzyme, acetylcholinesterase. Although there appears to be some ACh

in the cytoplasm of the neuron, the vast majority is found within the vesicles from which

it is released directly into the synaptic cleft. This is accomplished by the complex process

called exocytosis.

Exocytosis requires that the vesicle membrane fuse with the neuron membrane and

“dump” its contents into the cleft in an all-or-none process. Some of the ACh that is free

within the cytoplasm of the neuron may have just been synthesized en route to being

taken up by the vesicle membrane transporters for storage within the vesicle. ACh is

believed to be transported into the vesicle by an ATPase that pumps protons (hydrogen

ions) into the vesicle so the inside does not become charged and also maintains an isotonic

state, in spite of the high concentration of ACh in the vesicle. 14 The only drug currently

FIGURE 3.3

Synthesis and enzymatic degradation of acetylcholine (ACh). ACh is synthesized in the cytoplasm of the nerve

terminal where choline acetyltransferase (synthetic enzyme) is found. Acetylcholinesterase (degradative enzyme)

is associated with the postsynaptic membrane. Choline + Acetyl CoA Choline + Acetic Acid (Cytoplasm) Choline acetyltransferase (Inhibited by Physostigmine, Neostigmine, etc.) Acetylcholine (Ach) + Coenzyme A Acetylcholinesterase

known to interfere with the storage of ACh is vesamicol, which blocks the uptake of ACh

into the vesicle and prevents the release of newly synthesized ACh. 14,15

The latter findings greatly strengthened the hypothesis that ACh is released from the

neuron by exocytosis. Exocytosis is a calcium-dependent process and calcium is necessary

for fusion to occur between the vesicle membrane and the cell membrane. The voltage

change that occurs in the nerve terminal with the arrival of the action potential opens

calcium ion channels, allowing calcium to enter the nerve terminal and initiate the exo

cytotic process. Considerable electrophysiological and morphological evidence indicates

that ACh is released from neurons by exocytosis. 8,14 Although no clinically used drugs

inhibit ACh release, some toxins are known to inhibit its release, including botulinum

toxin A. 5 Botulinum toxin A (Botox ®) is commercially available and can be injected directly

into muscles to block ACh release and relax the muscle. It is approved for the treatment

of blepharospasm and facial wrinkles. 16

Once ACh has been released from the neuron, it can diffuse to the postsynaptic receptor

to mediate a response in the postsynaptic neuron. However, it must then be inactivated

if the synapse is to remain functional. In the case of ACh, inactivation occurs by enzymatic

destruction of the neurotransmitter. Almost all other neurotransmitters (except for the

peptides) are inactivated by reuptake into a neuron. Thus, ACh is unique among neu

rotransmitters in terms of the mechanism of inactivation following release into the syn

aptic cleft.

The enzyme that degrades ACh is called acetylcholinesterase. However, several cholinest

erases have been found in the body. One of them circulates in plasma and is known as

pseudocholinesterase or butyrylcholinesterase, which hydrolyzes butyrylcholine faster than

ACh. 8 Acetylcholinesterase is associated with the synaptic cleft and is attached both to

the presynaptic and postsynaptic membranes. This enzyme has been shown to exist in

several molecular forms that differ in their lipid solubility and in the way they attach to

membranes. Several inhibitors of acetylcholinesterase are available and these produce a

dramatic increase in the concentration of ACh in the body. Such drugs are widely used

in medicine and are discussed below.

Acetylcholine Receptors

Like other neurotransmitters, ACh produces its effects and obtains its selectivity by bind

ing to specific receptors in the postsynaptic cell membrane. These receptors chemically

recognize ACh and allow it to interact with specific functional groups in the receptor.

Based on the studies of Dale, 17 it has long been known that there are two major types of

ACh receptors, which were first identified in the

peripheral nervous system: (1) ACh

receptors at which nicotine can mimic the action of ACh that were termed nicotinic by

Dale and (2) ACh receptors that are activated by the alkaloid muscarine (from mushrooms)

and were called muscarinic receptors. The nicotinic receptors were found to be localized

at the neuromuscular junction (voluntary nerves to skeletal muscle), the autonomic gan

glia, and the adrenal medulla, while muscarinic receptors were found at the effector organs

innervated by the postganglionic parasympathetic fibers. Both types of ACh receptors

have been found in the brain.

Nicotinic Receptors

Nicotinic receptors have been widely studied, and most of our knowledge about nicotinic

receptors comes from work on electric fish such as the Torpedo, which uses its electric

organs to kill prey. It turns out that the high voltage in these fish is generated by ACh

receptors, which are highly concentrated in the electric organ. Thus, the electric fish has

served as a rich source of nicotinic receptor protein for the biochemists to study.

The nicotinic receptor was found to be a ligand-gated ion channel composed of four

subunits (termed alpha, beta, gamma, and delta). However, it takes five subunits to form

the ion channel, so the channel is formed by two alphas, one beta, one gamma, and one

delta subunit. 18 The ACh binds to the alpha subunit of the receptor and, since there are

two alpha subunits, it takes two molecules of ACh to open the channel. The techniques

of molecular biology (genetic engineering) have contributed greatly to our knowledge of

the nicotinic receptor, as well as to our knowledge of the molecular structure of other

receptors. These studies have led to a widely accepted model of the nicotinic receptor at

the neuromuscular junction of mammals.

However, the nicotinic receptor associated with neurons (e.g., the autonomic ganglia

and in the brain) appear to be slightly different. For example, it has long been known that

they are not blocked by the classical neuromuscular nicotinic antagonist, d-tubocurarine,

but are blocked by hexamethonium, another nicotinic antagonist. Research on neuronal

nicotinic receptors is still quite active and has important bearing on nicotine addiction

and Alzheimer’s disease since nicotine has been shown to increase the release of ACh in

the cerebral cortex. 19,20 A greater understanding of the different subtypes of neuronal

nicotinic receptors (which is now unfolding) is certain to have a big impact on the future

treatment of CNS disorders. There is now some evidence that nicotinic receptor agonists

may be beneficial in restoring memory that has been impaired due to Alzheimer’s disease.

Muscarinic Receptors

Muscarinic receptors are thought to make up the majority of the ACh receptors in the

mammalian brain. Unlike nicotinic receptors, the muscarinic receptors are linked to G

proteins and second messengers that carry the signal to ultimately produce a response or

change in the cell. Based on molecular cloning technology, five subtypes of muscarinic

receptor have been identified. The basic chemical structure (i.e., the amino acid sequence)

of these muscarinic receptors has been determined. 21 The best described of the muscarinic

receptors are the so-called M1, M2, and M3 which correspond to the m1, m2, and m3

cloned receptors. 22 Inasmuch as the muscarinic receptors are G-protein linked, they medi

ate their effects through second messengers. Muscarinic receptors may be involved in

mediating either excitation or inhibition in the brain, which is usually produced by the

opening (inhibition) or closing (excitation) of K + channels (i.e., potassium channels).

All G-protein coupled receptors consist of a polypeptide chain (protein) with seven

hydrophobic regions (i.e., areas containing amino acids that are more lipid than water

soluble). It has been found that these hydrophobic regions of the molecule correspond to

positions where the protein loops (crosses) through the cell membrane. So, these receptors

loop back and forth through the membrane seven times and are said to contain seven

membrane-spanning regions. Other G-protein coupled receptors (GCPRs) with seven mem

brane-spanning regions include the adrenergic, dopaminergic, and serotonergic receptors

(see the following text).

The M2 receptor found in the heart is the one most often involved in inhibition. The

M1, M3, and cloned m5 subtypes increase phospholipase C activity via a G protein called

Gq. The activation of phospholipase C by the latter muscarinic receptors and Gq leads to

the hydrolysis of phosphatidyl inositol and the formation of diacylglycerol (DAG) or

inositol triphosphate (IP 3), which, in turn, function as second messengers to activate

protein kinase C and increase intracellular calcium levels, respectively. M2 and M4 recep

tors result in the inhibition of adenylate cyclase by acting through a Gi protein and, in

addition, may activate (open) K + channels directly. These effects can lead to a slowing of

the heart as shown in Table 3.1. 23

Atropine is a nonselective antagonist for all muscarinic receptors while pirenzepine is

selective for the M1 receptor and AFDX 116 and methoctramine are antagonists for the

M2 receptor. The release of ACh and other neurotransmitters may be partially regulated

by the activation of M2 receptors located on presynaptic nerve terminals. 24

Clinically Useful Drugs That Alter Cholinergic Neurotransmission

Facilitators of Cholinergic Neurotransmission

Cholinergic Agonists

There are a number of cholinergic agonists (drugs which bind to the receptor and produce

a response or mimic the action of ACh), but only the muscarinic agonists find significant

clinical usefulness. These drugs are primarily used in ophthalmology to treat glaucoma

or to treat bowel and bladder retention postoperatively.

Muscarinic agonists include acetylcholine, which is not used because it is rapidly

destroyed by acetylcholinesterase or butyrylcholinesterase; methacholine, which is only

partially sensitive to the action of acetylcholinesterase and is available as a diagnostic tool;

bethanechol (Urecholine ®), which is used for bowel and bladder retention; carbachol,

which is used to treat glaucoma and has some nicotinic agonist activity as well; and

pilocarpine, a naturally occurring alkaloid found in plants, which is a potent muscarinic

agonist used to treat glaucoma. Pilocarpine is generally given in eye drops applied topi

cally to the eye.

All of these drugs are used for their effect on the peripheral autonomic nervous system

rather than the CNS. Presumably, some of these agonists have some difficulty crossing the

blood–brain barrier. However, when given in high doses, pilocarpine gets into the brain

and causes seizures in experimental animals. 25 Another muscarinic agonist, oxotremorine,

seems to produce marked effects on the brain at low doses in that it produces many of the

symptoms of Parkinson’s disease. Based on the apparent role of the ascending cholinergic

neurons in the brain in regulating states of consciousness, it seems possible that cholinergic

agonists that enter the brain produce arousal and insomnia. Indeed, even small doses of

pilocarpine, given intravenously in cats, have been shown to produce arousal. 23

There are no therapeutically useful nicotinic agonists except nicotine, itself, which is

used in patches or gum to treat smokers' dependence. However, clinical trials are being

conducted to test the efficacy of nicotine in the treatment of Alzheimer's disease. Given

the fact that the neuronal nicotinic receptor is different from the muscle receptor and that

there are several subtypes of neuronal nicotinic receptors, it is likely that we will soon see

some new nicotinic drugs that are useful in various neurological disorders.

Cholinesterase Inhibitors

Other than agonists, the only drugs used clinically to facilitate cholinergic neurotransmis

sion are the inhibitors of acetylcholinesterase. These include the reversible cholinesterase

inhibitors such as physostigmine (Antilirium ®), neostigmine (Prostigmin ®), pyridostig

mine (Mestinon ®), and edrophonium (Tensilon ®) that are used to treat myasthenia gravis.

Physostigmine crosses the blood-brain barrier while others do not, due to the fact that

they are highly charged molecules. Tacrine (Cognex ®), donepezil (Aricept ®), rivastigmine

(Exelon ®), and galantamine (Reminyl ®) are lipid soluble reversible cholinesterase inhibi

tors that easily reach the brain. These drugs are approved for the treatment of memory

and cognitive impairment associated with Alzheimer's disease. There are also several

irreversible inhibitors of cholinesterase, such as the organophosphates (e.g., diisopropyl

fluorophosphate or DFP), which irreversibly inhibit the enzyme and are used, primarily,

as insecticides. However, some of these are present in eye drops for the treatment of

glaucoma. Obviously, the irreversible cholinesterase inhibitors are extremely toxic and are

of interest because of their toxicological effects. They are too dangerous for systemic use.

Inhibitors of Cholinergic Neurotransmission

Muscarinic Antagonist

Alkaloids present in the belladonna plant have long been used as muscarinic antagonists.

These include atropine and scopolamine (hyoscine), both of which are nonselective mus

carinic antagonists. These drugs readily enter the brain after systemic administration and

some antimuscarinic agents, like benztropine (Cogentin ®), are used exclusively for their

effect on the brain. The latter compound has been used to prevent the Parkinsonian-like

side effects associated with antipsychotic drugs like Haldol ® . In the days before H 2 hista

mine receptor antagonists (e.g., cimetidine), which are among the most commonly used

ulcer drugs, atropine and other belladonna alkaloids were used to treat gastric ulcers and

other conditions associated with increased gastrointestinal

(GI) activity. However, piren

zepine, the M1 selective antagonist, has been found to be better at reducing gastric

secretion. A new muscarinic antagonist, ipratropium (Atrovent ®), is delivered in an aerosol

in the treatment of bronchial asthma. Anticholinergic drugs reduce bronchial secretions

and cause bronchodilatation, while decreasing GI activity and dilating the pupils. Hence,

they are also used by ophthalmologists to dilate the pupils for examination of the retina.

When there is hypersecretion of saliva or bronchiolar secretions, as there is during general

anesthesia, atropine or other antimuscarinic drugs are also used to reduce secretions and

to dilate bronchiolar passages.

Nicotinic Antagonists

Nicotinic antagonists, at the present time, may be divided into two general categories: (1)

those that are muscle nicotinic receptor antagonists or, so-called neuromuscular blockers, such

as d-tubocurarine (curare, the South American arrow poison), and (2) the neuronal nicotinic

antagonists, or so-called ganglionic blockers, such as hexamethonium or mecamylamine

(Inversine ®). Neuromuscular and ganglionic blockers interfere with neurotransmission by

acting on the postsynaptic nicotinic receptor (ion channel) and binding to it, in a competitive

or noncompetitive manner, to prevent the binding of ACh to the receptor. The drugs that

act at the neuromuscular junction to produce muscle paralysis bind directly to the nicotinic

receptor, preventing access of ACh. This is also how some of the ganglionic blocking agents

work (e.g., mecamylamine, trimethaphan). However, some of the ganglionic blockers (e.g.,

hexamethonium) enter the ion channel and form a plug, which also effectively interferes

with neurotransmission by preventing influx of sodium ions. 26

The neuromuscular blocking agents are also classified into two types: (1) depolarizing

blockers and (2) nondepolarizing blockers. Succinylcholine (Anectine ®) is the most com

monly used and best-known depolarizing blocker. It binds to the nicotinic receptor at the

neuromuscular junction and produces a depolarization of the membrane, which remains

in persistent depolarization for a long time, rendering the synapse nonfunctional. After a

period of time, the neuromuscular block actually converts to a competitive-type block,

which is called Phase II. Giving a cholinesterase inhibitor will not antagonize the action

of a depolarizing blocker, and, in fact, may make the block worse. On the other hand, d

tubocurarine, gallamine, vecuronium, and pancuronium are competitive neuromuscular

blockers which compete with ACh for the receptor. Thus, administering a cholinesterase

inhibitor (e.g., physostigmine or neostigmine) can reverse the block produced by compet

itive antagonists such as d-tubocurarine. All neuromuscular blockers and most ganglionic

blockers have a charged nitrogen atom and, therefore, do

not get into the brain when

injected systemically. In fact, if they are injected into the cerebrospinal fluid, they typically

cause seizures. Mecamylamine, on the other hand, is a secondary amine which can enter

the brain. Ganglionic blockers are used to lower blood pressure during removal of tumors

of the adrenal gland and neuromuscular blockers are used to relax muscles during endo

scopic examinations, surgery, and electroconvulsive shock therapy.

Cholinergic Drugs in the TBI Patient

There is evidence of changes in ACh neurotransmission following TBI. Immediately fol

lowing injury, there appears to be a hyperfunction of the cholinergic system, which lasts

15 minutes to 4 hours. During this time, administration of antimuscarinic drugs has been

shown in animal studies to enhance the recovery of function. 27 This is followed by a period

of cholinergic hypofunction where administration of cholinergic agonists can reduce cog

nitive deficits. Thus, cholinesterase inhibitors such as those used in Alzheimer’s disease

(e.g., tacrine, donepezil, rivastigmine, or galantamine) may be beneficial for improving

memory in TBI patients. Indeed, donepezil was found to improve memory in two TBI

patients. 28 Clearly, more extensive clinical trials are warranted and should be undertaken.

Norepinephrine

Norepinephrine (NE) is one of three endogenous chemicals known as catecholamines that

function as neurotransmitters in the mammalian nervous system. The other two are

epinephrine, which is a neurotransmitter in brain but a hormone in the periphery, and

dopamine, which is a neurotransmitter in brain. NE is the neurotransmitter of the sym

pathetic postganglionic fibers of the autonomic nervous system where it is involved in

such things as increasing heart rate, constricting blood vessels or raising blood pressure,

reducing gastrointestinal motility, and dilating pupils (see Table 3.3 for the response of

various organs to sympathetic nerve stimulation). There are some exceptions to the rule

that all postganglionic sympathetic nerves are “adrenergic” (i.e., use NE as a transmitter),

namely, those postganglionic fibers going to sweat glands and those going to certain blood

vessels in lower mammals. These both use ACh as a transmitter.

The finding that catecholamines form fluorescent compounds in tissue exposed to form

aldehyde gas greatly facilitated the mapping of such neurons in the brain. The technique

known as fluorescence histochemistry was developed by Falk and Hillarp in Sweden in the

early 1960s. 29

The noradrenergic neurons in the brain are found in one of two systems: (1) the locus

coeruleus system and (2) the lateral tegmental system. A description of these two systems

is beyond the scope of this chapter, but can be found in an excellent review by Moore and

Bloom. 30 Histochemical studies showed that the noradrenergic axons have a very wide

spread distribution, reaching essentially all levels of the neuraxis. For example, neurons

in the nucleus locus coeruleus of the pons innervate everything from the cerebral cortex

to the spinal cord. The diffuse nature of the noradrenergic innervation allows this system

to have global influences on brain function. The NE system in the brain has been implicated

in a wide variety of functions including anxiety, affective states (mood), arousal, REM

sleep, aggression, pain perception, pleasure experience, seizures, and endocrine function.

Synthesis, Storage, Release, and Inactivation of NE

Neurons which synthesize and use NE as a neurotransmitter are referred to as adrenergic

neurons or noradrenergic neurons. NE is synthesized in postganglionic sympathetic neu

rons and in neurons of the brain from tyrosine, an amino acid which is formed from

phenylalanine in the liver. Phenylalanine is referred to as an essential amino acid because

it must be supplied in the diet. Tyrosine is transported into adrenergic neurons by a high

affinity uptake transporter. 31 Once inside the neuron, tyrosine is converted to NE by the

reactions shown in Figure 3.4.

The rate-limiting enzyme in the overall synthesis of catecholamines (both NE and

dopamine) is tyrosine hydroxylase, which is found in the cytoplasm of the neuron. This

enzyme utilizes molecular oxygen and tyrosine as substrates and requires iron and tet

rahydrobiopterin as cofactors. Under most conditions, the concentration of tyrosine in the

neuron saturates the enzyme. Thus, increasing the tyrosine concentration will not enhance

the rate of NE synthesis. 32 However, under conditions of increased utilization (e.g., stress),

it may be possible to increase the rate of NE synthesis by administering tyrosine. 32

The second step in the pathway, the conversion of DOPA (dihydroxyphenylalanine) to

dopamine requires aromatic-L-amino acid decarboxylase, which uses pyridoxal phosphate

(vitamin B 6) as a cofactor (Figure 3.4). TABLE 3.3 Organ Response to Sympathetic Nerve Stimulation Organ Receiving Innervation Response to Stimulation Receptor Type Eye Iris, radial muscle Iris, ciliary muscle Dilation (mydriasis) Relaxation of far vision Alpha 1 Beta 2 Heart SA node Atrium AV node Ventricle Increase in heart rate Increase in contractility Increased conduction velocity Increased contractility Beta 1 Beta 1 Beta 1 Beta 1 Vasculature Skin and mucosa Skeletal muscle Cerebral Abdominal viscera Constriction Constriction, dilatation Constriction Mostly constriction, some dilation Alpha 1 Alpha 1 , Beta 2 Alpha 1 Alpha 1 , Beta 2 for dilation Trachea and bronchioles Relaxation Beta 2 Stomach and intestine Decrease in motility and tone and secretion; contraction of sphincters Alpha 1 , Alpha 2 Beta 2 Urinary bladder Detrusor muscle Trigone and sphincter Relaxation Contraction Beta 2 Alpha 1 Sex organ, male Ejaculation Alpha 1 Sweat glands Localized secretion (palms of hands) Alpha 1 Lacrimal glands Slight secretion Alpha 1 Nasopharyngeal glands No direct innervation — Source: Hoffman, B. B. and Taylor, P., Neurotransmission: The autonomic and somatic motor nervous systems, in The Pharmacological Basis of Therapeutics, Hardman, J. G., Limbird, L. E., and Gilman, A. G., Eds., McGraw-Hill Medical Publishing, New York, 2001, 115.

The third step in the pathway utilizes dopamine-β-hydroxylase (DBH) to convert

dopamine to NE. DBH is a copper-containing enzyme which

uses ascorbic acid as a

cofactor and is located in the membrane of the storage vesicle. Thus, as dopamine is

actively transported into the vesicle, it gets converted to NE. 8 Apparently, there is some

soluble DBH inside the vesicle which is coreleased with NE. Inhibition of DBH should

reduce the levels of NE without affecting the levels of dopamine. In the adrenal medulla

and in some neurons of the brain, NE is converted to epinephrine by the enzyme phe

nylethanolamine-N-methyltransferase (PNMT), which is found in the cytoplasm of cells. 5

Synthesis of NE within a neuron is regulated by a wide variety of factors, including the

intracellular concentration of NE and the firing rate of the neuron.

Once synthesized, the catecholamines (NE, dopamine, and epinephrine in the brain) are

stored in both small (200 to 300 Å) or large (500 to 1200 Å) membrane-bound vesicles.

Inside the vesicle, NE is stored in a complex with ATP (adenosine triphosphate), as shown

in Figure 3.5. NE is actively transported into the vesicle from the surrounding cytoplasm

by an ATP-Mg ++ dependent process. 33 Uptake of NE into the vesicle, as well as the storage

inside the vesicle, is inhibited by the drug reserpine, which ultimately leads to the deple

tion of the tissue content of NE.

The release of NE from nerve terminals occurs when the terminal is depolarized by the

incoming action potential. This results in the opening of

voltage-dependent Ca 2+ channels

and triggers the process of exocytosis, similar to the release of ACh described above. The

sites at which drugs can act to alter neurotransmission at a noradrenergic synapse are

shown in Figure 3.5.

Many drugs can facilitate the release of NE from nerve endings to increase the concen

tration in the synaptic cleft and the postsynaptic receptors. These include the amphet

amines (Adderall ®) and methylphenidate (Ritalin ®), which stimulate the release of NE

and dopamine by a Ca 2+ -independent mechanism that does not involve exocytosis.

Following release of NE into the synaptic cleft and interaction with the postsynaptic

receptors, the neurotransmitter action is terminated primarily by reuptake into the pre

synaptic terminal from which it was released. 8,32 The reuptake process for NE involves a

sodium-dependent process which is inhibited by antidepressants and cocaine, but not by

drugs like reserpine, which inhibit the vesicular uptake. The molecular characteristics of

the uptake transporter protein have been studied in great detail and the chemical structure

of this protein has been determined from cloning experiments. 34 Although reuptake has

been shown to be the major process responsible for terminating the action of NE, enzymatic

degradation also takes place via the enzymes monoamine oxidase (MAO) and catechol

O-methyltransferase (COMT).

MAO, which is present in the outer membrane of the mitochondrion, is involved in the

intraneuronal degradation of free NE that is present in the cytoplasm of neurons. The

FIGURE 3.4

Synthesis of norepinephrine (NE) in the adrenergic nerve terminal. Shows the enzymes and cofactors required

for synthesis, as well as their location (see parentheses) within the neuron. Tyrosine Rate Limiting Step (Cytoplasm) Dopa (Cytoplasm) Dopamine Norepinephrine (NE) (Storage Vesicle) Dopamine- β-Hydroxylase Ascorbic Acid O 2 L-Aromatic Amino Acid Decarboxylase Pyridoxal Phosphate O 2 Fe 2+ Tyrosine Hydroxylase Tetrahydrobiopterin

MAO that is found in human and rat brain is present in two forms that are referred to as

Type A and Type B, based on the fact that they have different substrate specificity and

different sensitivity to specific inhibitors. For further discussion of the different types of

MAO, the reader is referred to Cooper et al. 8 COMT is present in most cells of the body

and takes care of the extraneuronal metabolism of catecholamines (NE and dopamine)

before they reach the urine. 8,32

Drugs which act as inhibitors of MAO cause elevations in the intraneuronal content of

catecholamines (NE and dopamine) and eventually enhance the concentration of

FIGURE 3.5

Drawing of an adrenergic (sympathetic) neuron terminal synapsing on an effector organ in the peripheral

autonomic nervous system. This also serves as a model for adrenergic synapses in the central nervous system

(CNS). The numbers shown indicate the sites where drugs are known to act to modify neurotransmission. These

are as follows: (1) some drugs (e.g., guanethidine and bretylium) inhibit release by blocking the propagation of

the action potential (essential for release) into the nerve terminal; (2) under conditions of stress, it may be possible

to increase NE synthesis by increasing the concentration of circulating tyrosine (i.e., by administering tyrosine);

(3) a more effective way to increase dopamine and NE synthesis is to administer L-DOPA because it bypasses

the rate-limiting step involving tyrosine hydroxylase; (4) inhibitors of monoamine oxidase (MAO) (e.g., tranyl

cypromine) act at Site 4 to prevent the degradation of NE; (5) inhibitors of tyrosine hydroxylase (e.g., alpha

methyltyrosine) act here to block synthesis of NE; (6) drugs which interfere with the storage of NE (e.g., reserpine)

act on the vesicle and eventually deplete the neuron of NE; (7) drugs which block reuptake (e.g., cocaine and

tricyclic antidepressants) act to increase the concentration of NE in the synapse; (8) NE in the synaptic cleft can

act as an agonist on the postsynaptic receptors, as can other agonists for alpha or beta receptors; (9) inhibitors

of COMT can increase the availability of NE for agonist action; (10) NE, as well as other directly acting agonists,

initiate a response; however, antagonists can also act here to block the response; (11) presynaptic alpha 2 receptors

decrease the release of NE when these receptors are activated by NE or drugs such as clonidine. NE Dopamine DOPA TYR Circulating Tyrosine XXXXXXXXXXXXXXXXXXX Effector Tissue Postsynaptic cell Free NE NE NE • ATP complex COMT M A O Metabolites (DOMA) O-Methylated Metabolites r e l e a s e d b y N . i m p l u l s e α 2 3 5 2 6 11 8 10 A c t i o n P o t e n t i a l o f P o s t G a n g l i o n i c F i b e r 4 7 9 1

neurotransmitter reaching the receptors. MAO inhibitors are employed as antidepressant

drugs. COMT inhibitors are used in the treatment of Parkinson's disease to reduce the

metabolism of levodopa and enhance its action. The metabolic products resulting from

the action of COMT and MAO on NE and dopamine are shown in Figure 3.6. These

products represent clinically important metabolites that can be measured in cerebrospinal

fluid (CSF) or urine to provide an index of how the catecholamine systems have been

altered by disease or drug treatment. 32

Norepinephrine Receptors

Norepinephrine receptors (adrenoceptors) mediate the effects of NE. Adrenoceptor sub

types that respond to NE include alpha 1 , alpha 2 , and beta 1 . Beta 2 receptors have a lower

affinity for NE, but have a high affinity for epinephrine and are involved in mediating

some of the effects of the latter neurotransmitter or hormone. Specific agonists and antag

onists exist for each receptor and some of these are described later in this chapter.

In recent years, a great deal of information has been gained about the molecular nature

of the adrenoceptors, both in terms of their coupling to second messenger systems (so

called signal transduction mechanisms) and their chemical structure. Each receptor is known

to be an integral membrane protein with seven trans-membrane-spanning regions and a

molecular weight of 64,000 to 80,000 Da. 35

Unlike the nicotinic cholinergic receptor, which is intimately associated with an ion

channel and produces ultra-rapid effects, the adrenoceptors mediate their effects through

G-protein coupled receptors (GPCRs) like the muscarinic ACh receptor. 5,32 Both beta 1 and

beta 2 adrenoceptors are linked to adenylate cyclase in the membrane by a G s (stimulatory

FIGURE 3.6

Enzymatic degradation of NE by monoamine oxidase (MAO) and catecholamine-O-methyltransferase (COMT). COMT MAO MAO COMT Normetanephrine NE 3, 4-Dihydroxyphenylglycoaldehyde (DOPGAL) 3-Methoxy-4-hydroxymandelic Acid "Vanillylmandelic Acid" 3-Methoxy-4-hydroxyphenylglycoaldehyde 3, 4-Dihydroxyphenylglycol (DOPEG) 3, 4-Dihydroxymandelic Acid (DOMA) 3-Methoxy-4-hydroxyphenylglycol (MHPG) Aldehyde Reductase Aldehyde Reductase Aldehyde Dehydrogenase COMT Aldehyde Dehydrogenase

G) protein which is activated by a combination between the receptor protein and an

adrenergic agonist. The alpha subunit of the G s protein with GTP bound to it can then

interact with adenylate cyclase and activate it, leading to the conversion of ATP to cyclic

AMP. The latter can, in turn, activate various protein kinases which are involved the

phosphorylation (i.e., the addition of a phosphate group or PO 4 –) of various proteins that

regulate membrane ion transport to alter membrane potentials (Figure 3.7).

The alpha 2 adrenoceptors, which are usually located presynaptically (Figure 3.5), also

mediate their effect on membrane potential through a G-protein and adenylate cyclase

activity, but unlike the beta receptors, the alpha 2 receptor is linked to a G i protein which

causes an inhibition of adenylate cyclase and a reduction in the amount of cyclic AMP

(and, presumably, a reduction in protein phosphorylation) in the neuron.

The alpha 1 adrenergic receptor mediates its action through another second messenger

system which is linked to the receptor by a G q protein. The second messengers produced

when an agonist binds to the alpha 1 receptor are actually metabolites of phosphoinositide

breakdown mediated by phospholipase C and include inositoltriphosphate (IP3) and

diacylglycerol (DAG), as was the case for certain muscarinic receptors described above.

IP3 causes the release of Ca 2+ from intracellular storage sites and the Ca 2+ can then activate

protein kinases to produce phosphorylation of membrane proteins (Figure 3.7). The DAG

activates protein kinase C which, in turn, phosphorylates various proteins to mediate

various cellular responses of alpha 1 agonists. 8,36

FIGURE 3.7

Diagram of second messenger (signaling) system linked to alpha- and beta-adrenergic receptors in a cell (neuron

or effector cell) containing such receptors. The α 1 receptor is linked by a G-protein (G q) to phospholipase C (PLC)

which, when activated (by agonist binding to the α 1 receptor), leads to the breakdown of phosphatidylinositol

4,5-bisphosphate (PIP 2) to form two second messengers (diacylglycerol, or DAG, and inositol triphosphate, or

IP3). The DAG activates protein kinase C which can, in turn, phosphorylate proteins including those in ion

channels, while IP3 causes an increase in intracellular calcium by releasing it from various stores. The calcium

can activate calcium/calmodulin-dependent protein kinase which can phosphorylate other proteins. Beta 1 and

beta 2 receptors act through a G s protein to stimulate adenylyl cyclase (AC), leading to an increase in the formation

of cyclic adenosine monophosphate (cAMP) which can activate protein kinase A to increase the phosphorylation

of various proteins. Note that the α 2 receptor acts through a G i protein (inhibitory G-protein) which leads to

inhibition of adenylyl cyclase and a decrease in the intracellular concentration of cAMP. As can be seen here,

protein phosphorylation is the major mechanism by which receptors act through signal transduction to alter

cell function. (–) (+) PLC DAG IP 3 Protein Kinase C G q α 1 α 2 G i β 1 o r β 2 G s AC Protein Phosphorylation Change in Cell Function ATP Protein Kinase A cAMP M e m b r a n e P I P 3 Ca 2 +

Three subtypes of alpha 1 receptors (e.g., α 1a , α 1b , α 1d) and three subtypes of alpha 2

receptors (α 2a , α 2b , and α 2c) have been identified. 37 There are also three subtypes of beta

receptor (β 1 , β 2 , and β 3). Selective agonists and antagonists are available for alpha 1 , alpha 2 ,

beta 1 , and beta 2 receptors, and these drugs are primarily used for their effects on the

peripheral autonomic nervous system, especially in the area of cardiovascular disease.

Chronic treatment with agonists or antagonists can result in compensatory changes in the

sensitivity and/or receptor number of adrenergic receptors.

Such changes appear to be

carried out by enzymes that phosphorylate the receptor (i.e., receptor kinases). 37

Clinically Useful Drugs That Alter Noradrenergic Neurotransmission

Facilitators of Noradrenergic Neurotransmission

Adrenergic Agonists

These are also referred to as direct-acting sympathomimetic amines and they are classified

as either alpha or beta agonists. There are both alpha 1 and alpha 2 agonists available, but

many are nonselective. Norepinephrine (Levophed ®), itself, is available and is an agonist

for alpha 1 , alpha 2 , and beta 1 receptors, while epinephrine is an agonist for all adrenergic

receptors. Phenylephrine is an alpha 1 agonist that is used in nose drops (Neo-Synephrine ®)

as a nasal decongestant where it acts to vasoconstrict the mucosal blood vessels and reduce

congestion. Other alpha agonists that are predominantly alpha 1 selective include meth

oxamine and metaraminol. Clonidine (Catapres ®) is an alpha 2 agonist used as an antihy

pertensive agent because of its action on the brain where stimulation of alpha 2 receptors

presumably decrease the activity of the peripheral sympathetic nervous system. Other

alpha 2 agonists include guanfacine and guanabenz.

Isoproterenol (Isuprel ®) is a beta agonist that stimulates both beta 1 and beta 2 receptors

and has been used as a bronchodilator because of the beta 2 receptors in the bronchioles

that mediate bronchiolar relaxation (Table 3.3). Indeed, most of the beta agonists are

used for the treatment of diseases that are associated with bronchoconstriction such as

asthma. Selective beta 2 agonists are also available and have the advantage of not causing

cardiac stimulation when used in asthma. These include metaproterenol (Metaprel ®),

terbutaline (Brethine ®), and albuterol (Proventil ®). There are no highly selective beta 1

agonists available. However, dopamine and dobutamine (Dobutrex ®) are used for their

ability to stimulate beta 1 receptors in the heart to increase cardiac output in states of

shock or heart failure.

Drugs Which Block NE Reuptake

Inasmuch as reuptake is the major mechanism for inactivating released NE, drugs which

block this process have a marked ability to facilitate noradrenergic neurotransmission.

The classical example of a drug that does this is cocaine. Cocaine, however, also blocks

dopamine and serotonin reuptake. Many of the antidepressant drugs (so-called tricyclic

antidepressants) are potent and selective inhibitors of NE uptake and, presumably, mediate

some of their beneficial effects in depression via this mechanism. 38 Selective NE uptake

inhibitors include desipramine (Norpramin ®), protriptyline (Vivactil ®), nortriptyline

(Aventyl ®), and maprotiline (Ludiomil ®). All of these are used to treat depression. Side

effects of these drugs include their ability to increase

heart rate and blood pressure due

to peripheral effects on the cardiovascular system. At plasma concentrations that exceed

the recommended level, these drugs can also lower the seizure threshold and may pre

cipitate seizures. However, therapeutic plasma levels have been shown to exert anticon

vulsant effects in experimental animals.

Drugs Which Increase NE Release

Several drugs are available to increase the release of NE (as well as dopamine in CNS)

from nerve endings. The mechanism by which this is accomplished is not entirely clear.

However, it appears to involve the release of NE from a nonvesicular pool which does

not require calcium and does not involve exocytosis. The current hypothesis is that these

drugs are taken up by the uptake transporter for NE, bringing the carrier to the inside of

the neuron where NE can bind to it for exchange transport. Such drugs also interfere with

the uptake of NE by vesicles, increasing the cytoplasmic concentration of NE and making

more available for reverse transport. 5 Drugs that facilitate the release of NE include

amphetamine, dextroamphetamine (Dexedrine ®), methamphetamine (Desoxyn ®), and

methylphenidate (Ritalin ®). These drugs also increase the release of dopamine from nerve

terminals, which is believed to be responsible for many of their effects and will be dis

cussed later.

Amphetamine is the racemic mixture of D- and L-amphetamine. Dextroamphetamine is

three to four times more potent in stimulating the CNS than is L-amphetamine. One

commercial product contains a mixture of amphetamine and dextroamphetamine (Adder

all ®). All amphetamine analogues have powerful cardiovascular stimulating effects leading

to an increase in blood pressure and the work of the heart. The CNS stimulating effects

of amphetamine on arousal and locomotor activity are dependent on newly synthesized

NE or dopamine since these effects are blocked by alpha methyltyrosine, a tyrosine

hydroxylase inhibitor used to block NE synthesis. 26

The amphetamines, as a group, are used to suppress appetite in the treatment of obesity

and to treat narcolepsy (a sleep disorder) and attention deficit hyperactivity disorder

(ADHD). These drugs are regulated as controlled substances because of their abuse poten

tial. High doses can produce a psychosis that is indistinguishable from an acute paranoid

schizophrenic syndrome. Moreover, it has been shown, in both rats and nonhuman pri

mates, that repeated injections of methamphetamine can produce neurotoxicity leading

to the loss of both dopamine and serotonin containing neurons in the brain. 39–42 The

mechanism responsible for this neurotoxicity remains unknown, although several hypoth

eses have been proposed.

Drugs That Decrease the Enzymatic Degradation of NE

NE is degraded intraneuronally by the enzyme monoamine oxidase (MAO) as indicated

above. Inhibiting this enzyme should eventually increase the concentration of NE in the

synaptic cleft. Several MAO inhibitors are used clinically as antidepressants. These include

tranylcypromine (Parnate ®), phenelzine (Nardil ®), and isocarboxazid (Marplan ®). Some

MAO inhibitors are being used to prevent further deterioration of Parkinson’s disease.

One drug in the latter category is selegiline (deprenyl, Eldepryl ®), which is selective for

MAO-B. Patients on MAO-inhibitors cannot eat foods containing tyramine (a potent NE

releaser). Normally, tyramine is metabolized by MAO in the intestine, but this enzyme is

inactive in patients on an MAO inhibitor. Tyramine reaching the circulation causes a

hypertensive crisis with very dangerous consequences. Thus, individuals taking MAO

inhibitors must avoid foods containing tyramine, such as wine, beer, cheese, and other

fermented products.

Inhibitors of Noradrenergic Neurotransmission

Adrenoceptor Antagonists

There have long been available drugs that are selective antagonists of either alpha or beta

adrenergic receptors. Now, we have drugs that are even selective for a specific subtype

of alpha or beta receptor. The main advantage of a subtype selective antagonist is that it

will have fewer side effects. Nonselective alpha

antagonists include phenoxybenzamine

and phentolamine, while nonselective beta-antagonists include propranolol (Inderal ®),

sotalol, and pindolol. Of interest for the treatment of hypertension are the alpha 1 selective

antagonists, prazosin (Minipress ®) and terazosin (Hytrin ®). Beta 1 selective antagonists are

useful because they can be used to reduce blood pressure, stop cardiac arrhythmias, or

prevent subsequent heart attacks with minimal effects on bronchiolar smooth muscle.

Metoprolol (Lopressor ®), atenolol (Tenormin ®), acebutolol (Sectral ®), and esmolol

(Brevibloc ®) are all currently marketed beta 1 selective antagonists used to treat cardiovas

cular disorders.

Inhibitors of NE Release

Some drugs are selectively taken up into noradrenergic nerve terminals and then prevent

the release of NE, apparently by blocking the invasion of the action potential into the

terminal (i.e., a local anesthetic-like effect). Drugs in this category are referred to as

adrenergic neuronal blocking agents and include guanethidine (Ismelin ®), guanadrel

(Hylorel ®), and bretylium. Initially, these drugs cause a transient release of NE, prior to

the inhibition of release. When used chronically, guanethidine also has a reserpine-like

effect (see below) by interfering with NE storage and depleting the neurons of NE. Such

drugs are primarily used as antihypertensive agents. However, bretylium is now used

exclusively to treat cardiac arrhythmias.

Inhibitors of Storage

Reserpine is the classical drug for inhibiting the storage of catecholamines (NE, epinephrine,

and dopamine) and serotonin (see the following text). Reserpine binds to the vesicle mem

brane and interferes with the uptake of monoamines into the vesicle, rendering the vesicle

nonfunctional. When NE cannot be stored in the vesicle, it leaks out into the cytoplasm and

is degraded by MAO. Thus, reserpine leads to a depletion of the NE from the nerve terminals.

It is primarily used in combination with other drugs as an antihypertensive agent. 43

Inhibitors of NE Synthesis

There are two sites within the NE synthetic pathway where drugs can be used to block

synthesis: (1) the tyrosine hydroxylase step (which is the rate-limiting enzyme) and (2)

the dopamine β hydroxylase step. The latter is more selective and can be accomplished

with the drug disulfiram (Antabuse ®) or its active metabolite diethyldithiocarbamate

(DDTC). Unfortunately, these drugs inhibit many other enzymes and have many side

effects. The most common way to interfere with synthesis of NE is to inhibit tyrosine

hydroxylase with α-methyltyrosine (metyrosine, Demser ®). However, this drug also

blocks the synthesis of epinephrine and dopamine and is, therefore, not very selective.

Noradrenergic Drugs in the TBI Patient

There is considerable evidence that enhancing noradrenergic neurotransmission in the

CNS has beneficial effects on recovery of function after TBI in animal studies. 44–48 Moreover,

interference with noradrenergic neurotransmission (e.g., using alpha adrenoceptor antag

onists) was found to retard the recovery of motor function in rats after head injury. 49

Because of these findings, Feeney and coworkers 49 have put forth the NE hypothesis of

recovery. Consistent with this hypothesis is the finding that amphetamines, when paired

with physical therapy, have been shown to enhance recovery following stroke. 50,51

The above findings indicate that drugs which enhance NE neurotransmission (e.g., d

amphetamine, tricyclic antidepressants) facilitate recovery following TBI. However, more

clinical studies are needed since most of the data has been obtained in animals.

Dopamine

Although dopamine can be found in the peripheral nervous system in such places as the

carotid body and sympathetic ganglia, it is of interest primarily for its neurotransmitter

role in the CNS where it is involved in a wide variety of functions from regulating motor

function (basal ganglia) to inhibiting the release of prolactin from the pituitary gland.

Most of the dopamine neurons in the brain have their cell bodies either in the midbrain

(e.g., substantia nigra) where they are involved in the regulation of emotional states or

motor activity (e.g., substantia nigra dopamine is lost in Parkinson's disease) or the

hypothalamus where it is involved in regulating endocrine function. 8 Thus, there are three

major dopaminergic pathways in the CNS: (1) the nigrostriatal pathway (which projects

from substantia nigra to the striatum and is important in Parkinson's disease), (2) the

mesocortical/mesolimbic system (which projects from the ventromedial aspects of the

midbrain to the limbic system and the cerebral cortex, playing a role in psychiatric

disorders), and (3) the tuberoinfundibular pathway (which projects from the arcuate

nucleus of the hypothalamus to the median eminence of the pituitary stalk and regulates

endocrine function).

Synthesis, Storage, Release, and Inactivation of Dopamine

Dopamine is an intermediate compound in the synthesis of NE and is, in fact, the imme

diate precursor of NE (see Figure 3.4 and Figure 3.8). Thus, the synthesis is identical to

that of NE up through the formation of dopamine, but does not proceed to NE because

dopaminergic neurons lack the enzyme dopamine-β-hydroxylase. As was the case with

NE synthesis, tyrosine hydroxylase is the rate-limiting enzyme in the synthetic pathway

and, if one wants to block synthesis, this is the enzyme to block.

Dopamine synthesis is regulated somewhat differently than is NE synthesis. This is

largely because dopaminergic neurons have autoreceptors on the dopamine nerve terminal

that regulate both synthesis and release, whereas NE neurons have autoreceptors (which

are α 2) that regulate release only. 8 However, like NE, the intracellular concentration of

dopamine can regulate synthesis through end-product inhibition. Again, tyrosine hydrox

ylase is normally saturated with tyrosine, so that administering tyrosine is not an effective

way to enhance the synthesis of dopamine. However, DOPA decarboxylase is not saturated

with substrate and synthesis of dopamine can be increased by the administration of DOPA,

given as levodopa, which is now the drug of choice in the treatment of Parkinson’s disease.

In Parkinson’s disease, the nigrostriatal dopaminergic pathway degenerates and the

administration of levodopa helps replace the dopamine in the striatum.

Dopamine is stored in vesicles in a manner similar to that of NE in a complex with ATP.

Several soluble proteins called chromogranins are also present in the dopamine storage

vesicle. The release of dopamine from nerve terminals, like that of NE, is triggered by the

arrival of an action potential. Release occurs by a process of exocytosis and, therefore, is

calcium-dependent. The release of dopamine is apparently reduced by a negative feedback

mechanism when excess dopamine in the synaptic cleft interacts with presynaptic

receptors (autoreceptors). Activation of autoreceptors on the cell body reduces the firing

rates of dopaminergic neurons. 8 All dopaminergic autoreceptors are believed to be of the

D 2 or D 3 subtype (see Dopamine Receptors section).

Dopamine is inactivated following release by a high-affinity uptake transporter

(reuptake), which transports it back into the neuron from which it was released. This is

an energy requiring process that is dependent on sodium and is similar to the NE reuptake.

As is the case with NE and most other neurotransmitters, the dopamine transporter has

been cloned and found to be a member of a large family of transporter proteins that have

12 membrane-spanning regions. Indeed, much is known about the molecular character

istics of the dopamine transporter. 52

Although reuptake into the neuron from which it was released is the primary mechanism

for terminating the physiological effects of released dopamine, it may also undergo enzy

matic metabolism similar to NE. Thus, both MAO and COMT can convert dopamine to

inactive compounds according to the schema shown in Figure 3.8. Moreover, the resulting

metabolites DOPAC and HVA (Figure 3.8) are often used as indices of the rate of dopamine

turnover in the CNS. Antipsychotic drugs (neuroleptics) which block dopamine receptors

increase the concentration of dopamine metabolites in cerebrospinal fluid (CSF) and in

brain. 8

Dopamine Receptors

Two subtypes of dopamine receptors (D-1 and D-2) have been identified and described

in great detail using receptor binding techniques. 53 However, using molecular cloning

techniques, five dopamine receptors have been identified and all of them, including the

FIGURE 3.8

Synthesis and degradation of dopamine. Note that HVA is the major metabolite. COMT: catechol-O-methyl

transferase; DOPA: dihydroxyphenylalanine; MAO: monoamine oxidase. Dopa Tyrosine Dopamine 3, 4, Dihydroxyphenylacetic Acid (DOPAC) 3-Methoxytyramine 3, 4, Dihydroxyphenylacetaldehyde Homovanillic Acid (HVA) Tyrosine Hydroxylase Aldehyde Reductase COMT MAO L-Aromatic Amino Acid Decarboxylase MAO Aldehyde Dehydrogenase Aldehyde Dehydrogenase COMT 3, 4-Dihydroxyphenylethanol (DOPET)

3-Methoxy-4-hydroxyphenylacetaldehyde

new ones (D-3, D-4, and D-5), are now classified as either D-1-like or D-2-like receptors. 54–57

The D-1-like include the D-1 and D-5 receptors, while the D-2-like include D-2, D-3, and

D-4 receptors. The D-1-like receptors appear to mediate their effects through a G s protein

which activates adenylate cyclase and increases cyclic AMP, while the D-2-like receptors

appear to be negatively coupled to adenylate cyclase, producing an inhibition of the latter

through a G i protein. All of the dopamine receptors (D-1, D-2, D-3, D-4, and D-5) have

seven hydrophobic regions corresponding to the predicted seven membrane-spanning

regions of the other G-protein linked receptors in this family.

There is considerable sequence homology (similar sequence of amino acids in the pro

tein) between the various dopamine receptors as well as between these receptors and

other members of this family such as the beta 1 and muscarinic receptors. 54 The D-3 receptor

appears to represent both an autoreceptor and postsynaptic receptor and is found in limbic

areas of brain. 54 The D-4 receptor is of great interest because it has been implicated in the

effects of clozapine (an atypical antipsychotic agent) and may account for the atypical

effects of clozapine (Clozaril ®). For most antipsychotic drugs, there is a high correlation

between their clinical potency and their D-2 receptor blocking action. However, clozapine

is much more potent at blocking D-4 receptors and has fewer motor side effects than the

other antipsychotic drugs. Moreover, clozapine is effective at alleviating the symptoms of

schizophrenia in some patients who are refractory to other antipsychotic drugs. Because

of these differences, clozapine and newer antipsychotic drugs are referred to as atypical

antipsychotics. The D-4 receptor is largely found in the limbic system and there is some

evidence that the D-4 receptor is markedly increased in the brains of schizophrenic

patients. 57 In general, the functions of most subtypes of dopamine receptor are unknown;

D-1 receptors have only been found postsynaptically, but D-2 receptors occur either pre

or postsynaptically and autoreceptors are usually of the D-2 subtype. The use of D-1 and

D-2 agonists has shown that activation of both receptors may be necessary for expression

of certain dopamine functions.

The dopamine neurons have been implicated in the abuse of stimulants such as cocaine

and amphetamine. Mesolimbic dopaminergic neurons have also been implicated in addic

tion to alcohol, opioids, and nicotine. It has been proposed that variations in the gene for

the D-2 receptor may contribute to inter-individual differences in vulnerability to alcohol

ism and polysubstance abuse. 58

Clinically Useful Drugs That Alter Dopamine Neurotransmission

Facilitators of Dopaminergic Neurotransmission

Dopamine Agonists

Dopamine, itself, does not cross the blood-brain barrier and, therefore, cannot be used

for effects on the CNS. However, dopamine is used intravenously for its effects on the

cardiovascular system where it acts on beta 1 receptors in the heart to increase contractility

and on dopamine receptors in the renal vasculature to cause vasodilation. Because of the

latter two actions, dopamine is used to treat various forms of shock. Apomorphine is a

nonselective dopamine agonist that does get into the brain and has been used to treat

such things as Parkinson’s disease. However, it is poorly absorbed from the gut and must

be administered parenterally. Apomorphine achieves high concentrations in the chemore

ceptor trigger zone (CTZ) in the area postrema of the medulla oblongata, which regulates

vomiting. Because of its effects here, apomorphine produces nausea and vomiting, limiting

its usefulness in the treatment of dopamine deficiency syndromes. Other nonselective

dopamine agonists include bromocriptine (Parlodel ®) which has long been used to treat

endocrine disorders, such as hyperprolactinemia, where it acts in the anterior pituitary

gland to inhibit the release of prolactin. Bromocriptine is also now recommended for the

treatment of Parkinson’s disease. Lisuride and pergolide (Permax ®) are two other dopam

ine agonists that, along with bromocriptine, have been used in Parkinson’s disease.

Several new selective D-1 or D-2 agonists are now being examined experimentally. For

example, SKF 38393 is a D-1 agonist while LY 17155 is a D-2 agonist. These are being used

as tools to learn more about the function of D-1 an D-2 receptors, but they could become

clinically useful in the future. Drugs selective for the D-3, D-4, or D-5 receptor have not

yet been developed.

Drugs That Increase the Synaptic Concentration of Dopamine by Acting Indirectly

These include the indirectly acting agents, such as amphetamine and methylphenidate

(Ritalin ®), which increase the release of dopamine into the synaptic cleft, the dopamine

reuptake inhibitors (GBR 12909, amphetamine, nomifensine, benztropine, amantadine),

and the drugs which increase dopamine synthesis (levodopa, amantadine). The reader

will note that some drugs have more than one action. For example, amphetamine and

amantadine increase the release of dopamine from nerve endings as well as prevent the

inactivation by reuptake.

Drugs That Block Enzymatic Degradation of Dopamine

Like other catecholamines, dopamine is degraded by MAO and COMT (see Figure 3.8).

Therefore, MAO inhibitors can increase the synaptic concentration of dopamine. Selegiline

(Eldepryl ®) (described previously) is now being used to treat Parkinson’s disease because

it may prevent the formation of neurotoxins that destroy dopaminergic neurons and arrest

the progression of the disease. All of the MAO inhibitors described above under NE will

also prevent the enzymatic degradation of dopamine. Two COMT inhibitors have recently

become available for the treatment of Parkinson’s disease. These include tolcapone (Tas

mar ®) and entacapone (Comtan ®), which block the conversion of levodopa to 3-O-meth

yldopa and increase the amount of levodopa that gets converted to dopamine in the brain. 59

The COMT inhibitors can reduce the “wearing off” symptoms in patients treated with

levodopa/carbidopa. However, caution should be exercised in the use of tolcapone

because of potential liver toxicity.

Inhibitors of Dopaminergic Neurotransmission

Drugs That Interfere with Dopaminergic Neurotransmission

In this category, we have just two groups of drugs: (1) the receptor antagonists or blockers

and (2) the drugs which interfere with storage (e.g., reserpine). As would be expected, the

only ones that provide selective effects on dopaminergic neurotransmission are the recep

tor blockers, since reserpine-like drugs interfere with the storage of all monoamines. We

will, therefore, consider only the dopamine antagonists here.

Antagonists of dopamine receptors are primarily used as antipsychotic drugs (also called

neuroleptics) to treat schizophrenia. The fact that essentially all of the drugs effective in

schizophrenia are dopaminergic antagonists has led to the hypothesis that schizophrenia

is caused by too much dopamine at certain synapses — a hypothesis that has been difficult

to prove. Essentially, all of the dopamine antagonists block D-2 receptors, but D-1 and D

4 receptors may be affected by certain drugs. The atypical antipsychotic drugs, unlike the

older (typical) drugs, appear to have a low affinity for the D-2 receptor and have a higher

affinity for the D-3 or D-4 receptor. The latter drugs are also effective antagonists at the

5-HT 2A receptor. 60 A list of the dopamine antagonists is given in Table 3.4.

Dopamine antagonists have many side effects because they block dopamine receptors

not only in the limbic system, which regulates emotion, but also in the basal ganglia,

where loss of dopamine function causes Parkinsonian-like symptoms, and in the pituitary

where they cause endocrine-related side effects. Metoclopramide (Reglan ®) is a dopamine

antagonist used for its peripheral effects and its effects on the chemoreceptor trigger zone

(which is outside the blood–brain barrier) to prevent nausea and vomiting. Although it

penetrates the brain poorly, some does reach the basal ganglia which can cause some

Parkinsonian-like side effects. All of the D-2 dopamine receptor antagonists have anti

emetic properties, but only some (e.g., metoclopramide and prochlorperazine [Com

pazine ®]) are approved for such use.

Dopaminergic Drugs in the TBI Patient

Several reports in recent years suggest that enhancing dopaminergic neurotransmission

may be beneficial to patients with traumatic brain injury. Improving dopaminergic func

tion appears to be useful for two types of deficits in these patients. First, some TBI patients

display Parkinsonian-like symptoms; and second, dopaminergic agents may improve

arousal and the ability to focus attention on the task at hand, including rehabilitation

therapy. Just as L-DOPA (levodopa) is effective in Parkinson’s disease, it may help similar

symptoms in patients with TBI. The combination of L-DOPA with a peripheral decarbox

ylase inhibitor will reduce the metabolism of L-DOPA in the periphery and increase the

amount that actually reaches the brain. Thus, the combination of levodopa and carbidopa

(a decarboxylase inhibitor) is often used. Sinemet ® (a mixture of L-DOPA and Carbidopa)

has, in fact, been used successfully in some patients with TBI. 61,62 There is also some

evidence from animal studies that treatment with dopamine agonists (e.g., ropinirole) can

either reduce or reverse the motor and cognitive deficits produced by brain injury. 63

Dopamine agonists are also available and may have an advantage because they do not

depend on intact dopaminergic neurons. The dopaminergic agonists include such things

as the ergot derivatives (e.g., bromocriptine, pergolide, and lisuride), nonergot agonists

such as ropinirole (Requip ®) and pramipexole (Mirapex ®), and the antiviral drug with

dopaminergic agonist activity, amantadine. There is some evidence that these drugs can

reduce fatigue, distractibility, and bradykinesia, and improve attention, concentration, and

purposeful movement in TBI patients. 64,65 TABLE 3.4 Dopamine Receptor Antagonists (Blockers) Chemical Class Examples of Drugs Receptor Type Phenothiazines Chlorpromazine Thioridazine Perphenazine D-1 and D-2 Thioxanthenes Chlorprothixene D-2 Butyrophenones Haloperidol (Haldol ®) Some selectivity for D-2 Dihydroindoles Molindone D-2 Dibenzodiazepines Clozapine (Clozaril ®) D-4(?) Substituted benzamides Metoclopramide (Reglan ®) SCH23390 D-2 Selective for D-1 Atypical Antipsychotics Clozapine (Clozaril ®) D-2, D-4, 5-HT 2A Risperidone (Risperdal ®) D-2, D-4, 5-HT 2A Olanzapine (Zyprexa ®) D-2, D-4, 5-HT 2A Quetiapine (Seroquel ®) D-2, D-4, 5-HT 2A Ziprasidone (Geodon ®) D-2, D-4, 5-HT 2A Source: Baldessarini, R. J. and Tarazi, F. I., Drugs and the treatment of psychiatric disorders: Psychosis and mania, in The Pharmacological Basis of Therapeutics, Hardman, J. G., Limbird, L. E., and Gilman, A. G., Eds.,

McGraw-Hill, New York, 2001, 485.

The use of dopamine antagonists can be advantageous in controlling the symptoms of

psychosis, but could impair motivation. The role of dopamine neurons in motivation and

reward, as well as in addiction, is well established. 6 Thus, blocking dopamine receptors

could reduce motivation. Perhaps it would be possible to enhance motivation with a

dopamine reuptake inhibitor like bupropion (Wellbutrin ® , Zyban ®). There is one report

showing that bupropion improved restlessness in a TBI patient. 66

5-Hydroxytryptamine (Serotonin)

5-Hydroxytryptamine or serotonin (5-HT) is an indolamine that is found both in the periph

ery and in the CNS. About 90% of the 5-HT in the body is found in the gastrointestinal

tract (in enterochromaffin cells and neurons of the myenteric plexus), while 8% of the 5

HT of the body is found in platelets, and only 2% is found in the brain. 8 It is, however, the

2% in the brain that receives most of the attention and this is the fraction we will focus on.

Within the brain, 5-HT is localized in neurons that express the gene for tryptophan

hydroxylase (Trp-OH). Extensive mapping of serotonergic neurons in the CNS of the rat

has been performed using fluorescence histochemistry and immunocytochemistry. In gen

eral, the cell bodies of the serotonergic neurons are located along the midline of the

brainstem in what are called raphe nuclei. Originally, nine

separate groups of 5-HT cell

bodies were described by Dahlstrom and Fuxe, 67 but more recently, other cell groups have

been detected in the area postrema (vomiting area) and in the caudal locus coeruleus, as

well as in the interpeduncular nucleus. 8 Like the noradrenergic neurons, the serotonergic

neurons have a widespread distribution innervating essentially all areas of the CNS from

the cerebral cortex to the spinal cord. The more caudal cell groups (B-1 to B-3) primarily

innervate the brainstem and spinal cord, while the rostral cell groups (B-6 to B-9) innervate

the forebrain. A detailed description of the neuroanatomy of serotonergic neurons has

been provided by Molliver. 68

Synthesis, Storage, Release, and Inactivation of Serotonin

The amino acid precursor for 5-HT synthesis is tryptophan, which is an essential amino

acid supplied in the diet. Tryptophan, like tyrosine, is a neutral amino acid that also gains

entry into the brain by the large neutral amino acid transporter. Thus, plasma tryptophan

will compete with other neutral amino acids, such as tyrosine and phenylalanine, for

transport into the brain, which means that the concentration of brain tryptophan will be

determined not only by the concentration of tryptophan in plasma but also by the plasma

concentration of other neutral amino acids. 8,69 Once in the extracellular fluid of the brain,

tryptophan is transported into the serotonergic neurons by a high-affinity and a low

affinity transport system where it can then be converted to 5-HT by a two-step reaction

(Figure 3.9) with each step being catalyzed by a different enzyme. 70

The rate-limiting step in the overall conversion of tryptophan to serotonin is the first

step which is catalyzed by tryptophan hydroxylase (Figure 3.9) and results in the conver

sion of tryptophan to 5-hydroxytryptophan (5-HTP). Like tyrosine hydroxylase, tryp

tophan hydroxylase is a cytoplasmic mixed-function oxidase which requires molecular

oxygen and a reduced pteridine as cofactors. It should also be noted that a membrane

associated form of tryptophan hydroxylase has been found, indicating that some of the

enzyme may be membrane bound. Various inhibitors of tryptophan hydroxylase have

been identified, the best known of which is parachlorophenylalanine (PCPA), which has

been used experimentally to study the function of 5-HT.

Inasmuch as the K m of tryptophan hydroxylase (50 to 120 μM) is higher than the con

centration of brain tryptophan (30 μM), the enzyme is not saturated with tryptophan,

which means that increasing the concentration of brain tryptophan can increase the syn

thesis of 5-HT and lead to higher brain levels of serotonin. 70,71 Thus, it has been found

that dietary manipulations of tryptophan can change the brain concentration of serotonin.

The 5-HTP formed by the action of tryptophan hydroxylase on tryptophan is immediately

converted to 5-HT (serotonin) by the action of L-aromatic amino acid decarboxylase, the

same enzyme that converts DOPA to dopamine in catecholaminergic neurons. The decar

boxylation of 5-HTP, like that of DOPA, requires pyridoxal phosphate as a cofactor. Inas

much as the decarboxylation takes place in the cytoplasm, the resulting 5-HT must then

be transported into vesicles for storage (see text below).

The rate of 5-HT synthesis appears to be regulated by the rate of neuronal firing. The

latter control over 5-HT synthesis appears to be exerted on tryptophan hydroxylase by a

Ca 2+ -dependent phosphorylation of the rate limiting enzyme. 71

The available evidence suggests that serotonin, like the catecholamines, is stored in mem

brane-bound synaptic vesicles inside nerve terminals. 72 A substantial portion of the serotonin

in brain is found in isolated vesicles and these vesicles have been shown to take up seroto

nin. 73,74 Release of 5-HT, like that of other neurotransmitters, appears to occur by exocytosis

in a calcium-dependent manner. 72 However, certain drugs such as p-chloroamphetamine

are believed to release serotonin from the cytoplasmic pool rather than the vesicular pool 75

and there is some evidence that the depolarization mediated release by neurons can involve

either vesicular or cytoplasmic pools. 76 The available evidence suggests that 5-HT is stored

in the vesicles in a complex with ATP and perhaps a serotonin-binding protein. 72

The release of 5-HT from nerve endings is also believed to be regulated via a negative

feedback mechanism through serotonin autoreceptors located on the presynaptic (sero

tonergic) nerve terminals. The evidence indicates that these 5-HT autoreceptors are of the

5-HT 1B subtype (see following text). 71 Most of the postsynaptic effects of 5-HT are believed

to be inhibitory, although it has been shown to facilitate excitatory neurotransmitters at

some sites in the brain. 71

Mechanisms similar to those of catecholamine inactivation (see above) have been shown

to occur for serotonin inactivation. Thus, both reuptake into the neuron from which it was

FIGURE 3.9

Synthesis and degradation of 5-hydroxytryptamine (serotonin) in the CNS. Note that 5-HIAA is the major

metabolite. MAO: monoamine oxidase. 5-Hydroxytryptophan 5-Hydroxyindoleacetaldehyde Tryptophan Tryptophan Hydroxylase Tetrahydrobiopterin O 2 L-Aromatic Amino Acid Decarboxylase Pyridoxal Phosphate MAO Aldehyde Reductase Aldehyde Dehydrogenase 5-Hydroxytryptamine (Serotonin) 5-Hydroxytryptaphol 5-Hydroxyindoleacetic Acid (5-HIAA) rate limiting step

released and monoamine oxidase may be involved in the inactivation of 5-HT following

its action in the synaptic cleft. A high-affinity, sodium-dependent, energy-dependent

(requires ATP) uptake of 5-HT has been demonstrated in experimental studies, 69 and

reuptake into serotonergic terminals appears to function as the primary inactivation mech

anism for removing released serotonin from the synaptic

cleft. This concept is supported

by studies showing that inhibitors of serotonin uptake such as fluoxetine (Prozac ®), ser

traline (Zoloft ®), or paroxetine (Paxil ®) enhance the action of serotonin. However, others 77

believe that the primary fate of released 5-HT is uptake by nonserotonergic cells, followed

by degradation by monoamine oxidase to form 5-hydroxyindoleacetic acid (5-HIAA). The

latter investigators have suggested that brain or CSF levels of 5-HIAA can be used as an

index of serotonin turnover and utilization. 77 From Figure 3.8, it can be seen that 5

hydroxytryptophol can also be formed by the action of monoamine oxidase on serotonin

in brain, although the major metabolite is 5-HIAA. 71

Serotonin Receptors

In the last 10 years, there has been an explosion of information about the 5-HT receptor.

The 5-HT receptor family has become very large with at least 14 distinct receptors, all of

which have been cloned. These include the 5-HT 1 subfamily (including 5-HT 1A , 5-HT 1B , 5

HT 1D , 5-ht 1E , 5-ht 1F), the 5-HT 2 subfamily (including 5-HT 2A , 5-HT 2B , and 5-HT 2C), the 5

HT 3 subfamily, as well as the individual 5-HT 4 ,5-ht 5 , 5-HT 6 , and 5-HT 7 receptors. The

lower-case designation (e.g., 5-ht) is used for receptors in which no known function has

yet been established. 78

The 5-HT 1 subfamily is negatively coupled to adenylate cyclase through a G i protein

similar to the alpha 2 adrenergic receptor and, when activated, produces a decrease in the

adenylate cyclase activity. The 5-HT 2 subfamily, consisting of 5-HT 2A , 2B , and 2C , is linked

to phospholipase C and the phosphoinositide second messenger system through a G q

protein similar to the alpha 1 adrenergic receptor. The 5-HT 4 , 5-HT 6 , and 5-HT 7 are positively

coupled with adenylate cyclase through a G s protein similar to the beta adrenergic recep

tors. 78 The intracellular signaling system for the 5-ht 5 (5-ht 5A , 5-ht 5B) receptors has not been

determined. There are no clinically used drugs that act on the 5-HT 5 , 5-HT 6 or 5-HT 7

receptors. However, we are likely to see such drugs in the future.

The 5-HT 3 family was originally identified in the periphery. 79 These receptors are unique

among the monoamine receptors in that, instead of being G-protein linked receptors, they

are ligand-gated ion channels similar to the nicotinic ACh receptor. The 5-HT 3 receptor is

a nonselective cation channel that allows Na + and K + to enter the cell when 5-HT is bound

to it. Thus, the 5-HT 3 receptors result in excitation. Originally, the 5-HT 3 receptors were

identified primarily by their affinity for specific agonists and antagonists, 79,80 but they have

now been cloned. 81 The 5-HT 3 receptors appear to be present in the area postrema where

they play a role in regulating vomiting. Indeed, the 5-HT 3 antagonists ondansetron (Zof

ran ®) and granisetron (Kytril ®) are widely used to treat the nausea and vomiting associated

with cancer chemotherapy.

Clinically Useful Drugs That Alter Serotonergic Neurotransmission

Facilitators of Serotonergic Neurotransmission

Drugs That Increase the Synthesis and/or Release of 5-HT

Since the rate-limiting enzyme, Trp-OH, is not saturated with tryptophan, it is possible

to increase the synthesis of 5-HT by administering tryptophan. However, a number of

factors affect the amount of tryptophan that actually gets into the brain, such as the ratio

of tryptophan to other neutral amino acids in the plasma that compete with tryptophan

for transport into the brain, and the concentration of free fatty acids in the plasma which

compete with tryptophan for binding to plasma proteins.

Tryptophan administration has apparently been used in the treatment of depression,

but its effectiveness has been questioned. It is also possible to increase the release of 5

HT from nerve terminals with fenfluramine, a drug that was marketed as an appetite

suppressant (anorexiant) to treat obesity. Fenfluramine is no longer on the market in the

United States because of toxicities associated with pulmonary hypertension and damaged

heart valves. It was one of the ingredients in Fen-Phen used to treat obesity.

Drugs That Are 5-HT Agonists

The availability of agonists highly selective for specific subtypes of 5-HT receptors is low.

Serotonin, itself, does not cross the blood-brain barrier and many of the other agonists

are hallucinogenic. However, there are three partial agonists for 5-HT 1A receptors (ipsa

pirone, gepirone, and buspirone) that are being used for the treatment of anxiety. Of

these, buspirone (Buspar ®) is the only one approved for use in the United States in the

treatment of anxiety. Sumatriptan (Imitrex ®), zolmitriptan (Zomig ®), naratriptan

(Amerge ®), and rizatriptan (Maxalt ®) are agonist for the 5-HT 1D and 5-HT 1B receptors and

are used widely for the treatment of migraine headache. The latter are believed to act by

increasing cerebral vascular constriction during the vasodilatory phase of a migraine

headache. 82,83

Drugs That Block the Reuptake or Prevent Enzymatic Degradation of 5-HT

It is clear that the most common way to increase serotonergic neurotransmission, clinically,

is to use a reuptake blocker. The ones approved for clinical use include fluoxetine

(Prozac ®), sertraline (Zoloft ®), paroxetine (Paxil ®), fluvoxamine (Luvox ®), and clomi

pramine (Anafranil ®) — the first three of which are used as antidepressants, while the

last two (fluvoxamine and clomipramine) are used for obsessive-compulsive disorder. In

addition to their use in obsessive-compulsive disorder, the 5-HT reuptake inhibitors can

be used to suppress appetite, although they are not approved for this use. Monoamine

oxidase inhibitors, described above under norepinephrine, can also be used to enhance

serotonergic neurotransmission since they will prevent the degradation of this amine as

well. 8 However, the MAO inhibitors are not selective and could result in an increase in

the synaptic content of NE, dopamine, and 5-HT.

Inhibitors of Serotonergic Neurotransmission

There are few drugs clinically available for interfering with serotonergic neurotransmis

sion, and these fall into one of two categories: (1) drugs that interfere with storage of 5

HT and (2) drugs that block 5-HT receptors. The drugs that interfere with the storage of

5-HT are the same drugs that do this to NE and dopamine — namely, reserpine or

tetrabenazine. The only one used clinically is reserpine, which is used to treat hyperten

sion. A side effect of reserpine is depression with suicidal tendency, which apparently

results from the depletion of brain NE and 5-HT.

There are a whole host of experimental drugs that block 5-HT receptors, but only a

few are available for clinical use at the present time. These include methysergide (San

sert ®), a nonselective (broad spectrum) 5-HT antagonist, which is used to prevent the

onset of migraine headaches, and selective 5-HT 3 antagonists ondansetron (Zofran ®) and

granisetron (Kytril ®) which are used to treat nausea and vomiting. Given the plethora of

5-HT receptors and the rate at which new ones are being discovered, it is clear that the

drug companies have a difficult road ahead; however, it is also clear that a wide variety

of new and, it is hoped, selective 5-HT antagonists will be available in the near future.

Serotonin has been implicated in a wide variety of functions including anxiety, sleep

states, pain perception, affective states (depression), food intake, thermoregulation, sei

zures, vomiting, neuroendocrine functions, and blood pressure. New drugs to treat dis

orders of these functions may well come from selective agents for modifying serotonergic

neurotransmission.

Serotonergic Drugs in the TBI Patient

The role of 5-HT in brain injury and the recovery of function after injury is not clear.

Studies done in animal models of TBI suggest that 5-HT synthesis increases after TBI

and that this is associated with a decrease in local cerebral glucose utilization in the

cerebral cortex. 84 Moreover, inhibition of 5-HT synthesis with p-chlorophenylalanine

was found to reduce cerebral blood flow changes, cerebral edema, and cell injury

following TBI in animals. 85 Such findings suggest that 5-HT contributes to the damage

after TBI. However, several studies show that drugs that increase the concentration of

5-HT at its receptors in brain enhance recovery of function after TBI. For example, an

agonist for the 5-HT 1A receptor has been shown to reduce learning deficits in rats

following TBI. 86 The antidepressant fluoxetine has also been shown to facilitate cognitive

function in rats following TBI. 87 Fluoxetine has also been found to reduce OCD in TBI

patients. 88 The antidepressant effects of SSRIs are also seen in TBI patients, just as they

are in the noninjured population. Thus, it would appear that enhancing serotonergic

neurotransmission is beneficial in TBI patients. However, more studies are needed

before definitive conclusions can be reached regarding the use of serotonergic drugs

for TBI patients.

Gamma Aminobutyric Acid (GABA)

GABA is one of two amino acids (the other being glycine) that function as major inhibitory

neurotransmitters in the mammalian brain. GABA is present in essentially all areas of the

brain and has been implicated in the mechanism of action of several antiepileptic drugs,

as well as in the action of hypnotics (sleeping aids) and antianxiety drugs. The concen

tration of GABA in the brain is much higher than that of the monoamine neurotransmitters.

Studying the neurotransmitter role of GABA and other amino acids has not been easy for

researchers because these amino acids also play a metabolic role and are structural com

ponents of proteins. Thus, within the neuron, there is both a metabolic and a neurotrans

mitter pool of GABA. Determining whether one is dealing with the metabolic pool or the

neurotransmitter pool of GABA is crucial, but not always

easy.

GABAergic neurons are widely distributed throughout the brain and spinal cord. In

most areas of the brain, GABAergic neurons are short interneurons (inhibitory interneu

rons) rather than long projection cells. However, some GABAergic pathways have been

mapped and these include the pathway from the striatum (caudate) to the substantia nigra

and another from the globus pallidus to the substantia nigra. The purkinje cells of the

cerebellum are also GABAergic and some of these project to the lateral vestibular nucleus

in the medulla oblongata. 89

Synthesis, Storage, Release, and Inactivation of GABA

GABA is synthesized from glutamic acid by the enzyme glutamic acid decarboxylase (L

glutamate decarboxylase, GAD), which serves as a biochemical marker for GABAergic

neurons. 90 The glutamate is formed from glucose via the glycolytic pathway and the Krebs

cycle. 90,91 Pyruvate, formed from glucose, enters the Krebs cycle as acetyl CoA and is

converted to alpha ketoglutarate, the first component of the “GABA shunt,” which leads

to the synthesis of GABA (Figure 3.10). 91

The GABA shunt represents an alternative pathway between two intermediates of the

Krebs cycle. In this shunt, alpha ketoglutarate is converted to glutamic acid in a transam

ination reaction involving GABA-alpha ketoglutarate transaminase. Some authorities

have suggested the transamination of alpha ketoglutarate to glutamate may involve the

enzyme aspartate amino transferase which is coupled to the conversion of aspartic acid

to oxaloacetic acid. 92,93 The glutamate is then converted to GABA by glutamate decarbox

ylase (GAD).

GABA is degraded by GABA-transaminase (GABA-T) which converts it to succinic

semialdehyde. In this process, a molecule of GABA can be broken down only if a molecule

of precursor is formed (Figure 3.10). 90 The succinic semialdehyde is then converted to

succinic acid by the enzyme succinic semialdehyde dehydrogenase (SSADH), returning

the shunt to the Krebs cycle (Figure 3.10).

Released GABA may also enter the glutamine loop. In the latter case, the GABA is taken

up by glial cells where it is converted back to glutamate by a reverse transamination

involving GABA-T. The glia cannot convert glutamate to GABA because they lack GAD,

but they convert the glutamate to glutamine with glutamine synthetase. The newly formed

glutamine can diffuse out of the glial cells and into the GABAergic nerve endings where

it can be converted back to glutamate by glutaminase. This provides another mechanism

by which neurons can conserve GABA. 90

GAD and GABA-T can be manipulated pharmacologically. Both enzymes require pyri

doxal phosphate (vitamin B6) as a cofactor, but the subcellular location of the enzymes

FIGURE 3.10

Synthesis and degradation of GABA via the GABA “shunt” of the tricarboxylic acid (Krebs) cycle. Note that

glutamate is a precursor of GABA. Fumaric Acid Malic Acid Succinic Acid Succinyl CoA

Isocitric Acid TRICARBOXYLIC ACID CYCLE

Citric Acid Oxaloacetic Acid Glutamine Glutamic Acid GABA Glutaminase GAD GABA α- Ketoglutaric Acid Transaminase (GABA-T) NADH NAD SSADH NAD NADH α-Ketoglutaric Acid Aldehyde reductase γ-Hydroxybutyrate Succinic Semialdehyde

differs for the two. GAD is a soluble enzyme found in cytoplasm and GABA-T is a

mitochondrial enzyme.

Based on recent findings, it appears that there are two types of GAD, each of which is

formed from a different gene. The two types of GAD are referred to as GAD 65 and

GAD 67 . 81,94 These forms differ in molecular weight, amino acid sequence, interaction with

pyridoxal phosphate, and expression in different parts of the brain. GAD 65 appears to be

localized to nerve terminals to a greater extent than GAD 67 .

There is some controversy over whether or not GAD is saturated with glutamate. Some

authorities suggest that it is 90 while others 94 suggest that it is not. However, all investigators

agree that there is no evidence that GABA synthesis is controlled by the availability of

glutamate, which should be the case if GAD is unsaturated with substrate. Of interest is

the finding that GAD is the target of antibodies present in people who later develop

insulin-dependent diabetes mellitus (Type 1 diabetes). In these patients, the antibody

which destroys the beta islet cells of the pancreas is directed at GAD. 95,96

GABA-T is also a pyridoxal phosphate-dependent enzyme which has been purified to

homogeneity and was shown to have a molecular weight of about 109,000. The availability

of alpha ketoglutarate may regulate the tissue levels of GABA. Variations in the concen

tration of alpha ketoglutarate could be responsible for the postmortem changes in GABA

levels that are known to occur. For example, when respiration stops, the dependence of

the Krebs cycle on respiration results in a marked decline in the availability of alpha

ketoglutarate and the consequent reduction in GABA-T activity, which depends on alpha

ketoglutarate for transamination. However, GABA synthesis can still occur from glutamate

via GAD, which is an anaerobic enzyme. 90

Whether GABA and other amino acid neurotransmitters are stored in and released from

synaptic vesicles remains somewhat controversial. Both a vesicular and a cytoplasmic pool

of GABA exist within the neuron and release occurs in both a Ca 2+ -dependent and Ca 2+

independent manner. 97 However, synaptic vesicles isolated from the pig cortex contain a

high concentration of GABA. 98 Based on differences in the rate of equilibration of 3 H-GABA

between cytoplasmic and vesicular fractions, it has been concluded that the calcium

dependent release is from the vesicular fraction rather than the cytoplasmic fraction. 99

As has been demonstrated for the uptake of NE and 5-HT into synaptic vesicles, GABA

may be taken up into synaptic vesicles by a Na + -independent mechanism that is driven

by a proton gradient maintained by a Mg ++ -ATPase. 100 Evidence also suggests that GABA

is released from a cytoplasmic fraction, 101 both in a Ca 2+ -dependent and Ca 2+ -independent

manner. The cytoplasmic release may involve an exchange transporter between cytoplas

mic and extracellular compartments. The latter exchange system seems to be coupled to

a Na + transporter. 97

It has recently been suggested that the amino acidergic exchange transporter is respon

sible for the Ca 2+ -independent release of GABA that is known to coexist with the Ca +2

dependent release. 102 Thus, the available evidence suggests that the release of GABA (and

other amino acid neurotransmitters) can occur by either of two Ca 2+ -dependent mecha

nisms, vesicular or cytoplasmic, and also by a Ca 2+ -independent mechanism. How these

three systems interact with each other and which system, if any, predominates is yet to

be determined. (See detailed review by Nicholls.) 97

Following release from nerve endings, high-affinity uptake by neurons and glial cells

is believed to be responsible for terminating the neurotransmitter action of GABA since

no rapid enzymatic destruction system similar to that for ACh has been identified. The

plasma membrane transporter responsible for GABA uptake requires extracellular sodium

and chloride ions. Two sodiums and one chloride ion are cotransported with each mole

cule of GABA. 81,103,104 The high-affinity uptake transporter of GABA is capable of moving

GABA against a concentration gradient and, generally, concentrates the amino acid three

to four orders of magnitude higher in the intracellular compartment than in the extracel

lular compartment.

High affinity uptake of GABA and excitant amino acid into neurons and glial cells has

also been demonstrated by several laboratories. 105 The operation of the glial transporter

is similar to the neuronal transporter and is in the direction of net uptake.

Four distinct plasma membrane GABA transporters have been cloned. These are referred

to as GAT-1, GAT-2, GAT-3, and BGT-1. 106 Such findings suggest a much greater heteroge

neity of GABA transporters than was expected, and the significance of this heterogeneity

is still unknown. Although it was hoped that these could be localized to either neurons or

glia, this is not the case. However, some regions of the brain appear to contain a predom

inance of one type of transporter over another. 106 Of interest is the finding that certain drugs

(e.g., hydroxynipecotic acid) appear to preferentially inhibit the glial vs. the neuronal

transporter, 81 although the pharmacology of these transporters is still being determined.

GABA Receptors

Two subtypes of GABA receptor have been described in detail and are referred to as

GABA A and GABA B receptors. The GABA A receptor has been more thoroughly investi

gated and is ligand-gated ion channel that functions as a channel for the chloride ion. 107,108

This receptor is usually placed in a gene family that also includes the nicotinic acetylcho

line receptor and the glycine receptor. GABA A receptors are stimulated by GABA, mus

cimol, and isoguvacine and are blocked by the convulsants bicuculline (competitive

antagonist) and picrotoxin (noncompetitive antagonist). The GABA A receptor has long

been described as a macromolecular complex which consists of the GABA recognition

site, the chloride channel, and the benzodiazepine binding site. Benzodiazepine anxiolytics

(e.g., diazepam) and sedative-hypnotics (e.g., barbiturates) modulate the GABA A receptor

by enhancing the action of GABA. Activation of the GABA A due to the binding of GABA

to the receptor causes the chloride channel to open, which usually results in hyperpolar

ization unless the membrane potential is already greater than the chloride equilibrium

potential, in which case GABA produces depolarization. In the adult nervous system,

GABA almost always produces hyperpolarization (inhibition). However, in the developing

brain, it can be excitatory.

Molecular cloning has indicated that there are five major types of polypeptide subunits

for the GABA A receptor, which range in weight from 50 to 60 kDa (alpha, beta, gamma,

delta, and rho). Like the nicotinic ACh receptor, each subunit has four membrane-spanning

regions, one of which is believed to contribute to the walls of the ion channel. Molecular

cloning studies have provided evidence for the existence of six alpha, four beta, three

gamma, one delta, and three rho subunits. Scientists often use cells that do not normally

express (contain) GABA receptors, like the Xenopus oocyte. By adding the genes for the

GABA receptor to these cells, they can cause them to express GABA receptors, the function

of which can then be studied. By examining recombinant receptors in Xenopus oocytes,

it is possible to determine the importance of each subunit. It appears that while GABA

regulated chloride conductance, which is inhibited by bicuculline and picrotoxin, can be

obtained with the expression of alpha and beta subunits only, full benzodiazepine sensi

tivity is only obtained if the neurons contain the alpha, beta, and the gamma 2 subunits. 109

Thus, recombinant receptors containing α, β, and γ 2 subunits most closely resemble GABA A

receptors found in brain and the subtype of α and β subunits expressed determines the

various affinities for benzodiazepines found in different parts of the brain. 109 As was the

case with the ACh receptor, it is believed that five subunits (e.g., two alphas, two betas,

and a gamma 2) form the ion channel.

The GABA B receptor is insensitive to bicuculline, 3-aminopropanesulfonic acid, and

isoguvacine, but has a weak sensitivity to muscimol and is stereospecifically sensitive to

(-)baclofen (Lioresal ®). The GABA B receptor, unlike the GABA A receptor, is not a ligand

gated ion channel, but is, instead, linked through G-proteins to a second messenger system

like the muscarinic cholinergic and the adrenergic receptors. Most of the early studies

suggested that GABA B receptors were primarily presynaptic receptors involved in inhib

iting the release of neurotransmitters; however, it is now clear that they may also mediate

postsynaptic inhibition as well. 110,111 Basically, two membrane effects have been attributed

to the GABA B receptors: (1) a decrease in Ca 2+ conductance (usually a presynaptic effect

leading to decreased neurotransmitter release) and (2) an increase in K + conductance

(usually leading to postsynaptic hyperpolarization) as occurs in hippocampal pyramidal

cells following the application of baclofen. It has been suggested that the reason for the

different effects may be related to the fact that GABA B receptors are linked to different

channels in different locations. Thus, they are probably linked via second messengers to

Ca 2+ channels on presynaptic terminals and to K + channels at postsynaptic sites. 111 The

second messengers to which GABA B receptors have been suggested to be linked are cAMP

(decreased) and phosphatidyl inositols.

The classical agonist for GABA B receptors is (-)baclofen. A number of studies have been

carried out with baclofen to assess the function of GABA B receptors. However, one diffi

culty with the use of baclofen is that it crosses the blood-brain barrier rather poorly. 111

A third subtype of GABA receptor called the GABA C receptor has recently been iden

tified on the basis of its lack of sensitivity to bicuculline and baclofen and its sensitivity

to cis-4-aminocrotonic acid (agonist). These receptors were first discovered in the retina,

but have now been found in retina, cerebellum, optic tectum, hippocampus, and spinal

cord. GABA C receptors form a chloride channel from five rho subunits and are, therefore,

referred to as homomeric channels. 81,112 While many known drugs act on GABA A and

GABA B receptors, we have no useful pharmacological agents for the GABA C receptor.

Clinically Useful Drugs That Alter GABAergic Neurotransmission

Facilitators of GABAergic Neurotransmission

GABA Agonists

Several experimental drugs are used as agonists for the GABA A receptor including mus

cimol, THIP, and isoguvacine. In fact, there are no clinically approved drugs that act as

GABA A agonists per se. However, the benzodiazepines are allosteric modulators of the

GABA A receptor which, when bound to their high-affinity site on the GABA A receptor,

enhance the binding of GABA to its binding site and increase the frequency of chloride

channel opening. The benzodiazepines are, by far, the most popular clinically used drugs

whose mechanism of action involves the GABA A receptor. The latter compounds have a

wide variety of uses, including the treatment of anxiety, seizures, insomnia, and muscle

spasms. The benzodiazepines bind with high affinity to a site on the chloride channel and

enhance the inhibitory action of GABA.

Benzodiazepines used to treat anxiety include diazepam (Valium ®), oxazepam (Serax ®),

alprazolam (Xanax ®), and lorazepam (Ativan ®). Those used as antiepileptic drugs include

diazepam, clonazepam (Klonopin ®), and nitrazepam. Benzodiazepines used as hypnotics

include flurazepam (Dalmane ®), temazepam (Restoril ®), triazolam (Halcion ®), and

quazepam (Doral ®). Additionally, all of these drugs have muscle relaxant properties, but

diazepam is, probably, most commonly used for this purpose.

There is another major class of drugs that act as positive allosteric modulators of the

GABA A chloride channel. These are the barbiturates such as phenobarbital, pentobarbital,

and secobarbital. The barbiturates are widely used as hypnotic agents (sleeping pills) and

as adjuncts to anesthetics during surgery. Moreover, some barbiturates find important use

as antiepileptic drugs (e.g., phenobarbital and primidone [Mysoline ®]). Barbiturates bind

to a different site on the chloride channel than do the benzodiazepines, and they increase

the duration of channel open time, rather than the frequency of opening.

GABA B receptors also mediate inhibition in the nervous system through the action of

G-proteins and second messengers. Baclofen (Lioresal ®) is a GABA B receptor agonist that

has long been used to treat spasticity in patients with multiple sclerosis or other neuro

logical diseases.

Drugs That Block GABA Degradation

There are a whole host of compounds used experimentally to block GABA-T, but only

one of these is used clinically and that is gamma vinyl-GABA or vigabatrin, which is used

as an antiepileptic drug in Europe but has not been approved for use in the United

States. 113,114 Vigabatrin is an irreversible GABA transaminase inhibitor that has been shown

to be of value in some drug-refractory epileptic patients. Valproic acid (Depakene ®) has

also been shown to elevate brain GABA levels by inhibiting GABA-T. 115 Valproic acid is

used to treat a variety of seizure types including absence and generalized tonic-clonic.

Whether the action of valproic acid in epilepsy is due primarily to an enhancement of the

action of GABA is not known because it has another important effect that is probably

responsible for its effect in tonic-clonic seizures —

namely, it blocks sodium channels in

a frequency- and voltage-dependent fashion. 113

Drugs That Inhibit GABAergic Neurotransmission

Drugs That Block GABA Receptors

There are several GABA antagonists available for experimental use. However, because all

the GABA A antagonists are convulsants, they have no clinical use, at the present time. The

classical GABA A antagonist is bicuculline, but picrotoxin is also an antagonist. Saclofen

and phaclofen are GABA B antagonists that are being used in experimental animals to help

deduce the functional importance of the GABA B receptor. There are also a group of exper

imental compounds that bind to the benzodiazepine binding site on the chloride channel

and cause a reduction in the effectiveness of GABA. The latter compounds, of which beta

carboline-3-carboxylic acid (and other beta carbolines) is an example, are called inverse

agonists. Clearly, the GABA antagonists and the inverse benzodiazepine agonists are pro

convulsant and have no clinical use in medicine.

GABAergic Drugs in the TBI Patient

GABA is the major inhibitory neurotransmitter in brain and, therefore, changes in

GABAergic neurotransmission can have major consequences. In general, anything that

reduces GABA neurotransmission can cause seizures and would be detrimental to the

patient. Indeed, loss of GABAergic neurons following TBI may be responsible for post

traumatic epilepsy. However, immediately following TBI in animals, it appears that GABA

release is increased. 116

The increase in GABA release may represent a compensatory attempt to reduce seizures

in the injured region. However, other studies have found a decrease in benzodiazepine

receptor binding which may also reflect a reduction in GABA receptor function since the

benzodiazepine binding site is on the same chloride channel as the GABA binding site

(see text on GABA receptors). 117

Drugs that facilitate GABAergic neurotransmission are widely used in TBI patients. For

example, GABA B agonists, such as baclofen, are used to treat spasticity, while benzodiaz

epines, such as clonazepam and diazepam, are used to suppress seizures and anxiety. In

general, however, drugs that facilitate neurotransmission at GABA A receptors (e.g., ben

zodiazepines, barbiturates, and some antiepileptics) may impair memory and cognition

and could ultimately retard recovery of intellectual function in TBI patients.

Glycine

Glycine has the simplest chemical structure of any amino acid and it is not an essential

component of the diet. It is believed to function as a neurotransmitter in spinal cord

interneurons (e.g., Renshaw cell, which mediates recurrent inhibition) and in the brain

stem. 8 Like GABAergic synapses, all of the glycinergic

synapses appear to be inhibitory.

The inhibition also seems to be mediated through a ligand-gated chloride channel which,

as indicated above, places these receptors in a common family with the nicotinic ACh,

GABA A , 5-HT 3 , and glutamate receptors.

The anatomical distribution of glycinergic neurons have not been extensively mapped.

However, the concentrations of glycine found in the spinal cord (dorsal and ventral horn),

medulla, and pons are higher than in other CNS regions. Neuronal pathways suggested

to be glycinergic include spinal interneurons, a corticohypothalamic pathway, reticulospi

nal projections from the raphe and reticular formation, brainstem afferents to the substan

tia nigra, cerebellar golgi cells, and retinal amacrine cells. 89,118

Synthesis, Storage, Release, and Inactivation of Glycine

Glycine is synthesized from glucose via the glycolytic pathway to produce 3-phospho

glycerate and 3-phosphoserine, which forms serine. Serine (the immediate precursor of

glycine) is converted to glycine by the enzyme serine hydroxymethyltransferase (SHMT),

which is found in the mitochondria. Radioactive tracer studies show that most of the

glycine in brain is made from serine. 119 Serine hydroxymethyltransferase requires tetrahy

drofolate, pyridoxal phosphate, and manganese ion for activity. 90

Glycine appears to be abundant in the CNS and it is not clear what factors, if any, are

rate limiting in the overall synthesis. Moreover, it is not clear whether neurons utilizing

glycine as a neurotransmitter must synthesize it de novo or whether they accumulate

existing glycine. 8 SHMT is inhibited by pyridoxal phosphate inhibitors, which also inter

fere with GABA synthesis and degradation. Enzymatic degradation of glycine can occur

via a glycine cleavage pathway, which is also located in the mitochondria. Genetic muta

tions in the proteins of this pathway can cause metabolic disorders known as nonketotic

hyperglycinemias. 120

Whether glycine is stored in, and released from, vesicles has been somewhat controver

sial. Nevertheless, the evidence indicates that glycine (like GABA and glutamate) is taken

up into synaptic vesicles by a Na + -independent mechanism involving a low-affinity uptake

system. 121

The evidence suggests that glycine uptake (like that of GABA and glutamate) is driven

by an electrochemical proton gradient, generated by an ATP-dependent proton pump

(ATPase) located in the synaptic vesicle membrane. Kish et al. 121 have found that the

glycine vesicle transporter has a different substrate specificity from that of the GABA

uptake system and a different regional distribution in the brain, suggesting they are in

separate neurons. The likelihood that there is both vesicular and cytoplasmic release of

glycine, as there appears to be for GABA (see text on synthesis and storage of GABA),

remains very high.

After its release into the synaptic cleft, glycine is primarily inactivated by reuptake into

the terminal of the releasing neuron or by uptake into glial cells. Glycine reuptake is

carried out by a glycine transporter in the membrane. The Na + and Cl _ electrochemical

gradients assist in the movement of glycine against its concentration gradient. 120 Two

glycine membrane transporters have been identified by molecular cloning: GLYT-1 and

GLYT-2. It appears that GLYT-1 is found in both neurons and glial cells, while GLYT-2 is

localized to neurons. Both transporters are expressed in the hindbrain, whereas GLYT-1

can also be found in forebrain areas even though there are few, if any, glycinergic terminals.

Since glycine also functions as a coagonist with glutamate at NMDA receptors (see text

on glycine receptors and EAA), there is speculation that the GLYT-1 transporter might

regulate glutamate receptor function in forebrain areas. 120 Selective inhibitors of the glycine

transporter are not yet available, but could become useful drugs in the future. It has been

suggested that GLYT-1 is the glial transporter, while GLYT-2 is the neuronal transporter,

but this remains somewhat controversial. 8

Glycine Receptors

As indicated above, the glycine receptor is a member of a super family of ligand-gated

ion channels where the ligand binding site and the ion channel are in the same molecule.

In this regard, the glycine receptor, like that of the nicotinic ACh and GABA A receptors,

has been classified as an ionotropic receptor. 89 The glycine receptor has been purified using

affinity chromatography 122 and cloned. 123 It is a glycoprotein with two polypeptide sub

units called alpha (48 kDa) and beta (58 kDa).

These polypeptides have four membrane-spanning hydrophobic regions (like the nico

tinic ACh and GABA receptors) and it is believed that three alpha and two beta subunits

are responsible for forming the ion channel. 122 One hydrophobic region of each subunit

(probably M2) is believed to contribute to the walls of the chloride channel. The compo

sition of the receptor appears to depend on development. In embryonic tissue, the recep

tors consist entirely of alpha-2 subunits, but in adults, glycine receptors are composed of

3α and 2β subunits. 120

The glycine receptor is associated with, a 93 kD protein called gephyrin, which associates

with the intracellular domain of the beta subunit. Gephyrin is believed to function as an

anchoring protein that connects the membrane receptor protein with the protein tubulin

in the cytoplasm.

Strychnine is the classical glycine antagonist, and radioactive strychnine was originally

used to map the distribution of glycine receptors in the

CNS. The strychnine binding site

is on the 48-kDa subunit which is where glycine also binds. 122

Glycine also has an action at a strychnine-insensitive receptor that has been linked to

the NMDA excitatory amino acid receptor. 90 This is a high-affinity site that appears to

increase the action of glutamate at its NMDA receptor. 124 This strychnine-insensitive gly

cine binding site has a widespread distribution in brain and seems to be similar to that

of the NMDA receptors. Thus, glycine, in submicromolar concentrations, appears to

enhance the action of excitant amino acid neurotransmitters and may even be necessary. 124

It appears to enhance excitant amino acid action by binding to a site within the channel

and producing an allosteric modification. In this regard, it appears to be analogous to the

interaction between the GABA receptor and the benzodiazepine binding site. The strych

nine-insensitive glycine binding site also appears to have an endogenous antagonist. The

tryptophan metabolite, kynurenic acid, is an antagonist of the glycine binding site on the

NMDA receptor. However, 7-cholorkynurenic acid is a more selective and more potent

antagonist and is now being widely used to study this glycine receptor. 124

Clinically Useful Drugs That Alter Glycinergic Neurotransmission

At the present time, there are no clinically available drugs whose mechanism of action is

mediated through glycinergic neurotransmission. However, there is an experimental drug

called milacemide that is believed to increase glycine levels in the brain and is being tested

as an anticonvulsant agent in experimental animals. Thus, we may have drugs available

to enhance glycinergic neurotransmission in the future.

As far as antagonists are concerned, strychnine, which is a convulsant drug, was once

used to treat a variety of disorders, as well as being a potent poison. This agent no longer

finds any medical use. As indicated above, glycine appears to also bind to a site on the

NMDA receptor (the so-called strychnine-insensitive receptor) to enhance the excitatory

effects of glutamate or aspartate. Thus, at this site, glycine is proconvulsant. At the present

time, there is considerable interest among drug companies to explore the use of strychnine

insensitive glycine antagonists (e.g., 7-chlorokynurenic acid) as potential antiepileptic

drugs and it is conceivable that we will see such agents available in the future. The ability

of glycine to enhance the excitatory effects of glutamate may stem from its ability to block

NMDA receptor desensitization. 8

Glycinergic Drugs in the TBI Patient

As indicated above, there are no drugs currently available that modulate glycine neu

rotransmission. However, the drug milacemide, which increases glycine levels in brain,

may eventually be useful as an anticonvulsant. The antagonist at the strychnine-insensitive

glycine receptor (7-chlorokynurenic acid) may also prove to be useful in the future. At

present, there is no information on whether or not glycinergic drugs would be useful in

the TBI patient.

L-Glutamic Acid

The major excitatory neurotransmitter in the CNS is glutamic acid or glutamate. Aspartate

is also plentiful and may function as an amino acid neurotransmitter, but glutamate has

been more widely studied and is considered to be the most important excitatory trans

mitter. Glutamate and aspartate are sometimes referred to as the excitant amino acids

(EAAs). Glutamate is found in higher concentrations than any other free amino acid in

the CNS, being three or four times higher than aspartate and six times higher than

GABA. 125 The role of glutamate as an excitatory neurotransmitter is the subject of intense

current investigation, in part, because of glutamate's abundance and importance in so

many neural pathways and, in part, because of studies implicating it in such pathological

conditions as epilepsy, postanoxic cell loss, and neurotoxicity. It has been suggested that

the vast majority of the synapses in the mammalian brain use an excitatory amino acid

(EAA) as their neurotransmitter. 126

So, glutamatergic neurons are found throughout the CNS. There are, however, some

specific pathways that have been mapped using lesion and

biochemical analyses. These

include the well-known corticostriate pathway from the cerebral cortex to the striatum,

as well as many other corticofugal pathways. 89 In addition, the perforant pathway, from

the entorhinal cortex to the dentate gyrus of the hippocampus, contains a heavy

glutamatergic component, as do the Schaffer collaterals from CA3 to CA1 of hippocam

pus. 89 The dorsal horn of the spinal cord has a high concentration of glutamate, which

disappears after cutting the primary sensory afferents, indicating that glutamate is an

important neurotransmitter of the primary afferents.

Synthesis, Storage, Release, and Inactivation of Glutamate

Glutamate is a nonessential amino acid that does not cross the blood-brain barrier. There

fore, it must be synthesized in the brain. 89 However, unlike most other neurotransmitters,

the synthesis of glutamate is far from straightforward. This problem arises, in part, because

glutamate plays many roles in the brain and is available from many sources. For example,

in addition to its neurotransmitter role, it is an important component of protein and

peptide (e.g., glutathione) synthesis. 127 It also functions as an amino group acceptor to

detoxify ammonia in the brain, and it is the immediate precursor of GABA for GABA

synthesis. Glutamate can be synthesized from several sources, but it is not always clear

which one contributes most to the neurotransmitter pool. 8

Some investigators have suggested that the main pathways contributing to the trans

mitter pool of glutamate are from glucose via the Krebs cycle intermediates or from

glutamine by the enzyme glutaminase (in the mitochondria). Although both glucose and

glutamine are readily converted to glutamate, the pool derived from glutamine is prefer

entially released, 119 suggesting that this may be more important. However, in vivo studies

using 14 C-glucose and 14 C-glutamine showed that released glutamate was derived equally

from glucose and glutamine. 128

The various routes of synthesis are shown in Figure 3.11. Some authors have suggested

that the transmitter pool may utilize glutamate from several sources and that the critical

factor is the transmitter-storing vesicle that can take it up irrespective of its source. 125 Glial

cells probably also play a role in the synthesis of glutamate. 129 The latter cells can actively

accumulate glutamate by a sodium-dependent process and convert the glutamate to

glutamine by the enzyme glutamine synthetase. The glutamine can diffuse out of glial

cells and into glutamatergic terminals where it is converted back to glutamate by glutam

inase. This appears to be one of the mechanisms by which the neurotransmitter is recycled.

There has been some controversy over whether or not glutamate is stored in, and

released from, synaptic vesicles. However, several lines of evidence indicate that vesicles

do serve as storage organelles for glutamate, just as they do for other transmitters. 127, 130

Indeed, the protein (i.e., transporter) that moves glutamate from the cytoplasm into the

vesicle was recently identified, after many decades of searching, by a team at the Univer

sity of California at San Francisco. This vesicular glutamate transporter protein is appar

ently the same transporter that moves inorganic phosphate ions across the cell membrane,

but the one found in synaptic vesicles of glutamatergic neurons has been called

VGLUT1. 131 Glutamate is released from synaptosomes in a Ca 2+ -dependent manner and

is derived from a noncytosolic compartment. 97 Thus, the finding that glutamate can be

taken up and stored in synaptic vesicles and that its calcium-dependent release from

synaptosomes is from a noncytoplasmic compartment has led to the view that release

occurs by exocytosis. At present, the view that glutamate is released from neurons by

exocytosis is widely accepted. 120

High affinity uptake is believed to be responsible for terminating the synaptic actions

of glutamate and aspartate. The transporter(s) involved in terminating the actions of EAAs

is a sodium-dependent, high-affinity transporter that has been studied in synaptosomes

and brain slices. It does not distinguish between L-glutamate, L-aspartate, and D-aspar

tate. 127,132,133 This transporter has an uneven brain regional distribution consistent with a

role in neurotransmission. However, glial cells also possess a high-affinity uptake for

glutamate and aspartate which is believed to play an important role in terminating the

action of the EAA neurotransmitters following their release from nerve endings, as was

discussed above for GABA. Indeed, it has been shown that some glial cells possess

receptors for glutamate which, when activated, lead to a transient increase in intracellular

calcium (i.e., a Ca 2+ wave) which may pass from one glial cell to another and function as

a form of intercellular communication. 134 Molecular cloning studies have revealed at least

four different high-affinity Na + -dependent glutamate transporters, three of which are

found in mammals. 120 These are referred to as GLAST (glutamate-aspartate transporter),

GLT-1 (glutamate transporter-1), and EAAC1 (excitatory amino acid carrier-1). GLAT and

GLT-1 are expressed in glial cells and are believed to be responsible for the majority of

the glutamate inactivation in the CNS. 120

Excitatory Amino Acid Neurotransmitter Receptors

The EAA receptors (i.e., receptors for glutamate and aspartate) have been actively inves

tigated over the last 15 years and are still among the most vigorously targeted areas of

research by drug companies seeking new compounds for epilepsy, stroke, psychiatric

disorders, and degenerative brain disease.

FIGURE 3.11

Three pathways that can synthesize glutamic acid in brain. The glutamine and α-ketoglutarate pathways are

primarily responsible for synthesizing glutamate in nerve terminals Glutaminase Ornithine Aminotransferase Aspartate Aminotransferase Glutamine(1) (2) (3) Ornithine α-Ketoglutarate Glutamic Acid Glutamic Acid - Pyrroline - 5 - carboxylate Δ 1 (P5C) (P5C) Dehydrogenase Glutamic Acid Glutamate Semialdehyde

These receptors have been found to occur in two large families referred to as (1) ionotropic

receptors and (2) metabotropic receptors.

The ionotropic glutamate receptors are ion channels for sodium, potassium, and calcium

similar to the nicotinic ACh, GABA, and glycine receptors. These channels are opened by

glutamate and various synthetic chemicals with a similar structure. Three subtypes of

ionotropic glutamate receptors have been identified, originally based on the chemicals

that activate them: (1) N-methyl-D-aspartate or NMDA, receptor, (2) α-amino-3-hydroxy

5-methyl-4-isoxazole propionic acid, or AMPA, receptor, and (3) kainate receptor. Separate

families of genes have been identified for each of these ionotropic receptor subtypes. 120 In

the past, these receptors were separated into NMDA and nonNMDA because of the

antagonists that blocked either the NMDA or nonNMDA (AMPA, kainate) receptors. A

variety of protein subunits that comprise the excitant amino acid (EAA) receptors have

been identified through molecular cloning. The subunits for the NMDA receptor are

referred to as NR1, NR2A, NR2B, NR2C, and NR2D, while those for the AMPA receptor

are designated as GluR1-4. The protein subunits that form the kainate receptor include

GluR5-GluR7 and a KA1 and KA2. 120

Of the ligand-gated EAA receptor channels, the NMDA receptor is unique in that it is

voltage-dependent (as well as ligand-dependent), requiring some depolarization of the

membrane to remove an Mg ++ block within the ion channel. 125 The NMDA receptor also

has several functional subcomponents with discrete binding domains, which make it

similar to the GABA A -benzodiazepine receptor complex. 126 In this regard, glycine has a

binding site on the NMDA receptor and has been shown to facilitate the excitatory action

of NMDA receptor agonists. 120,126,135 The latter has often been referred to as a strychnine

insensitive glycine binding site. Thus, glycine appears to be a coagonist at the NMDA

receptor and there are now some selective antagonists for this glycine site (e.g., 7-Chlo

rokynurinate). The NMDA receptor is also unique in that it conducts calcium, as well as

sodium, into the cell.

The agonist binding site on the NMDA receptor has several selective competitive antag

onists (e.g., 2-amino-5-phosphonovalerate or AP5, 2-amino-7-heptanoate or AP7, and 2

carboxypiperazin propyl-1-phosphonic acid or CPP). In addition, some noncompetitive

antagonists of the NMDA receptor have been discovered. These apparently bind to a site

within the ion channel to inhibit neurotransmission. The latter compounds include such

drugs as phencyclidine (PCP), ketamine (Ketalar ®), and MK-801 (dizocilpine). 120,126 The

EAA receptors (especially the NMDA receptor) are believed to be important in learning

and memory (see Chapter 10), which is believed to be mediated through their role in long

term potentiation (LTP). 125 Indeed, the NMDA receptor may be the primary receptor

responsible for LTP. The distribution of the NMDA and nonNMDA glutamate (AMPA

and kainate) receptors has been extensively mapped in the rat brain using radioactive

ligands and autoradiography. 126

However, excessive amounts of EAAs in the brain are believed to be responsible for

excitotoxicity (leading to neuronal death) and seizures mediated through the ionotropic

EAA receptors. The latter effect has led to the interest in EAA antagonists in neuropatho

logical states such as those following stroke. 126 The excitatory amino acids have also been

shown to play a role in posttraumatic brain injury, 136 and the neuropathology may be due

to the excitotoxic effects of EAAs released after injury.

AMPA receptors can be blocked selectively by the quinoxaline diones such as 6-nitro

7-sulphamobenzo-quinoxaline 2,3-dione (NBQX). There are no selective antagonists at the

kainate receptor except, perhaps, the experimental drug LY294486.

Eight different metabotropic glutamate receptors have now

been cloned, which are

designated as mGluR1 through mGluR8. Like other G-protein-coupled receptors, these

have seven membrane-spanning regions, but are larger (i.e., contain more amino acids)

than most other G-protein coupled receptors. The mGluRs are classified into three groups,

based on amino acid sequence homology, signal transduction mechanisms, and pharma

cology: Group I includes mGluR1 and mGluR5; Group II includes mGluR2 and mGluR3;

and Group III includes mGluR4, mGluR6, mGluR7, and mGluR8. 137 Several of the mGluRs

are located on presynaptic nerve terminals and seem to decrease neurotransmitter release.

Depending on the transmitter release, an agonist for the mGluR can produce either exci

tation or inhibition. 120 At present, there are no clinically approved drugs that act on the

mGluRs, but selective antagonists for Group I, Group II, and Group III have been identified

and it is likely that some of these drugs will be available for clinical use in the future.

Group I mGluRs are linked to a Gq protein, leading to activation of the phosphatidyli

nositol pathway (described above), while Groups II and III appear to signal through the

Gi/Go proteins leading to a decrease in cAMP. 137

Clinically Useful Drugs That Alter Excitant Amino Acid Neurotransmission

Drugs That Enhance the Action of Glutamate

Basically, there are no clinically useful drugs that are known to enhance the action of

excitant amino acids. Indeed, those that are available for experimental studies in animals

(e.g., glutamate, kainate, ibotenic acid, etc.) are all convulsants which also cause excito

toxic lesions of neuronal cell bodies. Cycloserine and drugs developed for the treatment

of tuberculosis are weak partial agonists at the NMDA receptor and there is some evidence

that these drugs have antipsychotic effects that can be used to treat schizophrenia. Whether

agents that selectively enhance LTP in the hippocampus can be developed without the

dangers of killing neurons remains to be determined.

Drugs That Inhibit the Action of Glutamate

Several glutamate receptor antagonists are available for experimental work in animals

and some of these have been described above, but again, none are available for clinical

use at the present time. These drugs are of interest for treating such disorders as epilepsy,

postischemic brain syndrome, and posttraumatic brain injury. Moreover, such drugs are

believed to have some potential in various neurodegenerative diseases such as Hunting

ton’s chorea, Alzheimer’s disease, Fredrick’s ataxia, and stroke. Thus, a great deal of

research time and money has been, and continues to be, invested in developing effective

EAA antagonists. One disappointing aspect of this work has been the psychotic-like side

effects that have accompanied the testing of some NMDA antagonists in humans.

It is of interest to note that the widely used drug dextromethorphan (marketed as a

cough suppressant) has been shown to antagonize experimental seizures in animals and

has been found to be an NMDA antagonist. 138–140 Because of all the modulatory sites on

the NMDA receptors, several drugs are known to have some antagonist effects on this

receptor. For example, phencyclidine (PCP, angel dust) and ketamine act as noncompeti

tive antagonists of the NMDA receptor and have psychotomimetic effects at low doses

and function as dissociative anesthetics at higher doses. While both are still used in

veterinary medicine, only ketamine is used in humans, at the present time, where it is

mainly used as a pediatric anesthetic. Both are considered drugs of abuse in humans. 120

Glutamatergic Drugs in the TBI Patient

Glutamate and other excitatory amino acids have long been known to produce excitotoxic

damage to neurons and glial cells, and are believed to play a role in producing brain

damage in the hours immediately following TBI. 141,142 Indeed, it has been suggested that

the EAAs contribute to CNS damage in a variety of neurological disorders such as epilepsy,

stroke, and other neurodegenerative diseases. 143 Moreover, animal and human studies

using microdialysis have shown the extracellular levels of glutamate are increased imme

diately following TBI. 143 Therefore, treatment with glutamate antagonists in the early hours

following TBI should limit the damage and facilitate recovery.

Most of the evidence suggests that the NMDA subtype of glutamate receptor is respon

sible for the neuronal damage because of the increase in intracellular calcium that follows

the opening of this channel. Calcium, in high concentrations, can damage and kill cells. 6

Thus, administration of NMDA antagonists immediately following injury has been shown

to improve recovery in rats. The hallucinogen, phencyclidine (PCP), an NMDA antagonist,

was found to attenuate long-term neurobehavioral deficits in rats receiving TBI. 143 Clearly,

more studies are needed in this area.

Since glutamate is involved in normal cognitive processing and in learning and memory,

it seems reasonable that NMDA agonists might improve cognitive function after TBI.

Because too much glutamate receptor activation can lead to seizures and neuron cell death,

moderate or controlled activation of NMDA receptors would seem to be more useful. In

this regard, the chronic administration of D-cycloserine, an NMDA partial agonist acting

at the glycine site, has been shown to improve cognitive function in rats following TBI. 144

Thus, weeks or months after the injury, it may be beneficial to augment glutamate neu

rotransmission and metabotropic glutamate agonists may turn out to be useful in this

regard. On the other hand, the Group I metabotropic glutamate receptor agonists are

known to potentiate excitation, and antagonists of these receptors have been shown to

reduce brain damage and improve recovery of motor function after TBI. 145 Clearly, drugs

acting on glutamate receptors can have profound effects in TBI patients and should

provide some new therapeutic tools in the future.

Peptide Neurotransmitters

Until 1960, acetylcholine and the monoamines were the only well-recognized neurotrans

mitters. Then came the GABA and the amino acids in the 1960s and 1970s. The amine and

amino acid neurotransmitters are sometimes referred to as the classical neurotransmitters.

However, within the last 20 years, there has been an explosion in the number of candidate

neurotransmitters due largely to the discovery of various peptides that may function as

neurotransmitters or neuromodulators. Many of the neuroactive peptides were first dis

covered as hormones and were then found to also be present in neurons within the CNS.

Another common finding was that many of the neuroactive peptides were also found in

the gut where they served as gastrointestinal hormones (e.g., cholecystokinin).

Although one finds that the peptide neurotransmitters are not classified in any consistent

manner, a common approach used by authors is based on localization. For example,

peptide neurotransmitters have been grouped into the following categories: (1) the gut

brain peptides, (2) the pituitary peptides, and (3) the

hypothalamic-releasing hormones. 146

There are far too many candidate peptide neurotransmitters to cover here. Moreover, there

are no clinically useful drugs to affect their action, except in the case of the opioid peptides,

which mediate their effects through the receptors on which morphine and other potent

narcotic analgesics act. Therefore, we will restrict this discussion to the opioid peptides.

However, substance P is also of interest because it was the first peptide neurotransmitter

isolated from horse gut and brain by Euler and Gaddam, 147 although it was 40 years later

before its structure was determined. Substance P is of interest because, while there are no

clinically available drugs to modify its action, it appears to be the neurotransmitter of

primary sensory afferent fibers carrying pain sensation (i.e., C-fibers) and it can be released

from such nerve terminals by the active ingredient in chili peppers (i.e., capsaicin). 148,149

Moreover, neurons containing opioid peptides appear to synapse on the terminals of

substance P containing neurons in the dorsal horn of the spinal cord. Substance P is one

of a group of interesting peptides known as tachykinins for which three receptors have

been cloned and new antagonists are being developed. Cooper, Bloom and Roth 8 provide

a review of further information on this subject.

Opioid Peptides as Neurotransmitters

The first discovered opioid peptides were the pentapeptides (containing five amino acids),

leucine-enkephalin, and methionine-enkephalin, which were isolated by Hughes et al. 150

We now have three separate families of opioid peptides, each derived from a separate

gene family. 151 These include (1) the enkephalins (pentapeptides derived from a proen

kephalin precursor), (2) the endorphins (e.g., β-endorphin, a 31 amino acid containing

peptide derived from proopiomelanocortin or POMC), and (3) the dynorphins (8–13 amino

acid containing peptides derived from a prodynorphin precursor).

Extensive maps of the enkephalin, endorphin, and dynorphin containing neurons in the

rat brain have been obtained using immunocytochemistry, but these will be only briefly

described here (see Khachaturian, Lewis, Schafer, and Watgson 152 for more detail). In

general, the enkephalinergic neurons are short interneurons widely distributed throughout

the neuraxis. A high density of enkephalinergic neurons is found in the basal ganglia,

cerebral cortex, amygdala, hippocampus, and in such brainstem areas as the periaqueduc

tal gray, interpeduncular nucleus, parabrachial nucleus (concerned with respiration), and

the nucleus tractus solitarius, as well as in the dorsal horn of the spinal cord.

The dynorphin-like immunoreactivity follows the distribution of the enkephalinergic

neurons fairly closely and also appears to be found mostly in short local neurons rather

than in long projection fibers. Thus, the enkephalin and

dynorphin systems appear to be

anatomically contiguous. The endorphin-containing neurons are, however, different in

that they tend to be long projection neurons which arise from the arcuate nucleus of the

hypothalamus. Another area containing a high density of endorphin (POMC) containing

cell bodies is the pituitary gland from which β-endorphin is presumably released into the

blood. However, the precursor of β-endorphin, POMC, is also the precursor for adreno

corticotrophic hormone (ACTH) and melanocyte stimulating hormone (α-MSH). Thus,

depending on where in its structure POMC is cleaved by enzymes, one gets different

biologically active peptides. It is little wonder, then, that the endorphins are intimately

related to the endocrine system and are apparently released during stress.

Synthesis, Storage, Release, and Inactivation of Opioid Peptides

The synthesis of any peptide involves transcription of the information in the genetic code

of DNA (the gene) into messenger RNA (mRNA), and the translation of the message in

mRNA into the appropriate sequence of amino acids in the peptide chain to form a

functionally important peptide or protein. A detailed description of protein synthesis is

clearly beyond the scope of this chapter and the reader is referred to a basic textbook of

biochemistry for more detail.

As indicated above, there are three families of opioid

peptides derived from different

genes which lead to the synthesis of precursor proteins from which the neuroactive peptide

is cleaved by the action of enzymes. Thus, proenkephalin, prodynorphin, or proopiomel

anocortin (POMC) can be synthesized in the cell body of a cell that expresses these genes.

After the peptide precursors are formed, they are usually sent to the golgi apparatus

where they are packaged into membrane-bound vesicles and then transported to the nerve

terminals by axoplasmic transport. At the axon terminal, the opioid peptides are stored

in vesicles from which they are released by exocytosis. 89 However, the mechanisms of

peptide packaging, storage, and release are poorly understood at the present time. It is

important to note that peptides cannot be synthesized at nerve terminals and must be

made in the cell body and transported to the terminal for release, making them much

more expensive in terms of energy expenditure.

Once the opioid or any other neuroactive peptide is released from a neuron, it is

apparently degraded by peptidases (enzymes) and cannot be recaptured by reuptake.

Thus, utilization of peptides is less efficient than that for the classical neurotransmitters

and is, again, a more energy-expensive process. Moreover, once they are used, it will take

a significantly longer time to replace them at the nerve terminal than it does for the classical

transmitters. 89,153

Another interesting aspect of peptide neurotransmitters is that they appear to be

costored in neurons with other neurotransmitters, either other peptides or the classical

neurotransmitters. Examples of a classical transmitter coexisting in a neuron with a peptide

include (1) serotonin and substance P, (2) dopamine and cholecystokinin, and (3) acetyl

choline together with vasoactive intestinal polypeptide (VIP). In some neurons, the clas

sical transmitter and the peptide may even be stored within the same vesicle (e.g., 5-HT

and substance P). 153

Opioid Receptors

Opioid receptors were known to exist long before the discovery of the opioid peptides.

Indeed, it was the discovery of opioid receptors using radioactive ligands that led to the

search for the endogenous peptides by Hughes and Kosterlitz. 146 The distribution of opioid

receptors was mapped before the distribution of the peptides. The opioid receptors are

now divided into three main subtypes: (1) mu (μ) receptors, (2) delta (δ) receptors, and

(3) kappa (κ) receptors, although some authors include the sigma (σ) receptors as a fourth

subtype.

Mu receptors appear to be the primary receptors involved in mediating analgesia and,

therefore, have a high affinity for morphine and related drugs. The endorphins have a

higher affinity for μ receptors than for any other opiate

receptor. Indeed, the rank-order

potency of agonists for opioids binding to the mu receptor is β-endorphin > morphine >

met-enkephalin > leu-enkephalin.

The mu receptor is believed to be a 65 kDa protein with a widespread distribution in

the CNS. 154 The density of μ receptors is high in striatum, amygdala, cortex, periaque

ductal gray regions of midbrain, and thalamus. 155 Mu receptors are also found in the

periphery. The mu receptor appears to be a G-protein linked receptor that is negatively

coupled with cAMP (i.e., a Gi protein) and is involved in mediating hyperpolarization

by opening K + channels. 155

The use of mu agonists can alleviate the opiate withdrawal syndrome. Beta-endorphin

is probably the naturally occurring ligand for the mu receptor, although morphine and

its analogs appears to mediate most of their effects through the mu receptor. Naloxone

(Narcan ®) is a potent antagonist of the mu opioid receptor.

The delta receptor binds leu-enkephalin with a greater affinity than met-enkephalin, β

endorphin, or morphine. Thus, the enkephalins are believed to be the natural ligands for

the delta receptor. 154 The distribution of δ receptors corresponds closely to the distribution

of enkephalin neurons and, like the mu receptors, are linked to adenylate cyclase in a

negative fashion via a Gi protein. 154 Naloxone is a less potent antagonist at delta receptors

than it is at mu receptors so that higher concentrations of naloxone are required.

The kappa opioid receptors bind ketocyclazocine with high affinity. The latter com

pound, along with pentazocine, bremazocine, and butorphanol, is a kappa receptor

agonists. The density of kappa receptors is highest in the spinal cord and brainstem and

the dynorphins are believed to be the naturally occurring agonists for these receptors.

Naloxone can act as an antagonist at kappa receptors, but it is less potent than at mu

receptors. Kappa agonists cannot alleviate the symptoms of opioid withdrawal. However,

stimulation of kappa receptors can alleviate pain, especially viscerally mediated chemical

pain. 154 Dynorphin is believed to be the natural agonist for the kappa receptor and

dynorphin levels are increased immediately following TBI. Indeed, kappa agonists may

increase neurological deficits when administered following TBI (see Opioids in the TBI

Patient section).

More recently, a new receptor related to the opioid receptors was cloned. Because it had

a high degree of homology (similarity) to other opioid receptors, but was unresponsive

to endogenous opioid peptides (enkephalins, endorphins, dynorphins), it was referred to

as an orphan receptor. More recently, a novel endogenous peptide for the orphan receptor

was isolated and sequenced. This peptide appeared to have antiopioid effects (i.e., cause

pain) when bound to the orphan receptor. Thus, it was named nociceptin/orphanin FQ.

Now, there appears to be a family of these peptides and they all bind to G-protein coupled

receptors (i.e., Gi/Go). 156,157 The functional significance of the nociceptin/orphanin FQ

system is not known, but there is interest in developing antagonists for these receptors

because they could be useful in the treatment of pain.

Clinically Useful Drugs That Alter Opioid Neurotransmission

Drugs That Enhance Opioideragic Neurotransmission

Opioid Agonists

A comprehensive discussion of the pharmacology of opioid agonists and antagonists has

been provided by Gutstein and Akil 158 and is beyond the scope of this chapter. The agonists

are the only available drugs for enhancing opioidergic neurotransmission. These are the

narcotic analgesics used to treat severe pain, such as that occurring postoperatively. Mor

phine is the prototypical drug in this class and has been around since 1806. It is a natural

constituent of opium powder, but can now be made in the chemistry laboratory. Meperi

dine (Demerol ®) is a synthetic analog of morphine widely used in hospitals for postop

erative pain. Both of these are primarily mu agonists, but also have some agonist activity

at delta and kappa receptors. Codeine, the o-methyl analog of morphine, has similar

properties, but is a weaker agonist. Indeed, codeine is metabolized to morphine in the

body. Pentazocine (Talwin ®) is a kappa agonist and a mu antagonist and butorphanol

(Stadol ®) has similar properties. Pentazocine was originally marketed as a nonnarcotic

analgesic, but this error was eventually corrected. Buprenorphine (Buprenex ®) is a partial

mu agonist and a kappa antagonist. The latter drugs are sometimes referred to as mixed

agonist-antagonists.

Opioid analgesics have many side effects, not the least of which is respiratory depression,

which can kill the patient in overdose. These drugs are also very useful to suppress the

cough reflex and are commonly added to cough mixtures (syrups).

Drugs That Inhibit Opioidergic Neurotransmission

Opioid Antagonists

Naloxone (Narcan ®) is a pure opioid antagonist that is used to treat life-threatening

overdoses of opioid analgesics. It functions as an antagonist at mu, delta, and kappa

receptors, but must be given by injection. The administration of 0.4 to 0.8 mg intravenously

or intramuscularly can reverse the effects of mu opioid agonists in humans and will

precipitate a withdrawal syndrome in addicted individuals. 158 Naltrexone (Trexan ®) is also

a pure narcotic antagonist with greater oral efficacy and a longer duration of action

allowing it to be administered orally.

Opioids in the TBI Patient

An increase in dynorphin has been demonstrated following TBI in an animal model of

brain injury 159 and kappa receptor agonists have been shown to increase neurologic deficits

after experimentally induced spinal cord injury in rats. Moreover, kappa antagonists have

been found to reverse deficits associated with spinal cord injury. 160 Kappa agonists may,

in fact, facilitate neuronal damage via an action through glutamate, since NMDA antag

onists were found to reverse the neurotoxicity associated with dynorphin in the spinal

cord injury model. 161

While activation of kappa receptors appears to enhance neurologic damage, activation

of mu and delta opioid receptors may be neuroprotective rather than neurotoxic. 162 Thus,

it appears that, immediately following injury, administering a kappa antagonist or a mu

agonist could be beneficial in reducing neurological damage associated with TBI. However,

more research is needed to determine the appropriate timing and dose needed to reduce

neurological deficits.

Other uses of opioids in the TBI patient obviously includes their use as analgesics to

alleviate pain while recovering from multiple injuries. However, when using opioids as

analgesics, it is important for practitioners to be cognizant of possible detrimental effects

that can also occur. Knowledge of the specific receptors on which the drugs act and the

selection of specific mu or delta agonists may prevent such

detrimental effects.

Summary

The preceding pages provide considerable detail concerning the process of neurotrans

mission in the nervous system. It is clear that this is a major form of communication

between neurons and the principal site of controlling neuronal function. It is also clear

that neurotransmission is the principal target for drugs that affect the nervous system.

Although it is impossible to provide a concise summary of the broad array of topics

covered in this chapter, the editor felt that some type of summary of the clinically relevant

drugs showing the neurotransmitters through which they exert their action would be

useful for the busy practitioner and, I fully agree. Therefore, an appendix (see Appendix

3A) has been provided at the end of this chapter to summarize these relationships and to

give the reader a quick mechanism for linking the drugs to the neurotransmitters. It should

be noted, however, that, in the interest of space, we have only included those drugs

discussed in this chapter. Although they represent some of the more popular ones in use

today, they are by no means the only ones available. Practitioners of rehabilitation, as well

as other specialties in medicine, must be aware that pharmacology is a constantly changing

field with new drugs being introduced every day. It is hoped that this chapter also provides

a foundation that will allow the reader to appreciate and

understand the mechanism of

action of new (undiscovered) drugs that will be introduced in the future.

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Appendix 3A Summary of Relationship between Therapeutically Used Drugs and Various Neurotransmitters

Drug Name	Brand Name*	Neurotransmitter Receptor Drug Action
Alphamethyltyrosine (metyrosine)	Demser	Dopamine; NE—Blocks synthesis of dopamine and NE
Acebutolol	Sectral	NE Beta 1 Beta 1 receptor blocker
Acetylcholine	Miochol (Ophthalmic)	ACh Nicotinic and muscarinic cholinergic Agonist for muscarinic and nicotinic receptors
Albuterol	Proventil	Epinephrine (hormone) Beta 2 Beta 2 receptor agonist
Alprazolam	Xanax	GABA Benzodiazepine GABA A complex Agonist for benzodiazepine receptor
Amantadine	Symmetrel	Dopamine—Increases release and blocks reuptake of dopamine
Amphetamine	Obetrol	Dopamine

;NE–IncreasesreleaseandblocksreuptakeofNEanddopamineApomorphineApomorphineHClDopamineD1andD2dopamineAgonistforD1andD2receptorsAtenololTenorminNEBeta1Blocksbeta1receptorsAtropineAtropineSulfateAChMuscariniccholinergicBlocksmuscarinicreceptorsBaclofenLioresalGABAGABABAgonistforGABABreceptorsBenztropineCogentinAChMuscarinicholinergicBlocksmuscarinicreceptorsBethanecholUrecholineAChCholinergicmuscarinicAgonistformuscarinicreceptorBotulinumtoxinABotoxACh–BlocksreleaseofAChBretyliumBretyliumTosylateNE–BlocksreleaseofNEBromocriptineParlodelDopamineDopamine(D1,D2,etc.)Nonselectivedopaminereceptoragonist Buprenorphine Buprenex β endorphin;enkephalinOpioid(mu)Partialagonistformureceptorandakappaantagonist BupropionWellbutrin;ZybanDopamine–Blocksreuptakeofdopamine BuspironeBuspar Serotonin(5HT)5HT1aPartialagonistfor5HT1areceptor Butorphanol Stadol β endorphin;enkephalinOpioid(kappa)Kappaagonistandmuantagonist CapsaicinZostrixHP SubstanceP–DepletesCfibers(painfibers)ofSubstanceP;usedastopicalanalgesic CarbacholIsoptoCarbacholAChMuscarinicholinergic;nicotinicholinergic Muscarinicandnicotinicagonist ChlorpromazineThorazine DopamineDopamineD2Blocksdopaminereceptors

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n a f r a n i l S e r o t o n i n − B l o c k s s e r o t o
n i n r e u p t a k e C l o n a z e p a m K l o n o p i n G
A B A B e n z o d i a z e p i n e G A B A A c o m p l e x F
a c i l i t a t e s a c t i o n o f G A B A C l o n i d i n
e C a t a p r e s N E A l p h a 2 A l p h a 2 a g o n i s t
C l o z a p i n e C l o z a r i l D o p a m i n e D o p a m
i n e D 4 D 4 a n t a g o n i s t C o c a i n e C o c a i n
e H C 1 N E ; d o p a m i n e − B l o c k s r e u p t a k e
o f N E a n d d o p a m i n e C o d e i n e F o u n d i n m
a n y c o u g h s y r u p s a n d a n a l g e s i c s c o n
t a i n i n g a c e t a m i n o p h e n O p i o i d β e n d
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n d d e l t a o p i o i d r e c e p t o r s d t u b o c u r
a r i n e T u b o c u r a r i n e c h l o r i d e A C h N i
c o t i n i c c h o l i n e r g i c N i c o t i n i c r e c
e p t o r b l o c k e r D e s i p r a m i n e N o r p r a m
i n N E − B l o c k s N E r e u p t a k e D e x t r o a m p
h e t a m i n e D e x e d r i n e N E ; d o p a m i n e − I
n c r e a s e s r e l e a s e o f N E a n d d o p a m i n e
a n d b l o c k s r e u p t a k e D e x t r o m e t h o r p
h a n F o u n d i n m a n y c o u g h s y r u p s (e . g .
, R o b i t u s s i n D M) G l u t a m a t e N M D A B l o
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a m V a l i u m G A B A B e n z o d i a z e p i n e G A B A
A c o m p l e x A g o n i s t f o r b e n z o d i a z e p i
n e r e c e p t o r D i s u l f i r a m A n t a b u s e N E
− B l o c k s s y n t h e s i s o f N E D o b u t a m i n e
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A g o n i s t f o r B 1 r e c e p t o r s D o n e p e z i l
A r i c e p t A C h − B l o c k s e n z y m a t i c b r e a
k d o w n o f A C h E d r o p h o n i u m T e n s i l o n A
C h − C h o l i n e s t e r a s e i n h i b i t o r ; p r e
v e n t s d e g r a d a t i o n o f A C h E n t a c a p o n
e C o m t a n N E ; d o p a m i n e − B l o c k s e n z y m
a t i c b r e a k d o w n o f N E a n d d o p a m i n e b y
b l o c k i n g C O M T E s m o l o l B r e v i b l o c N E
B 1 B l o c k s B 1 r e c e p t o r F e n f l u r a m i n e
P o n d a m i n S e r o t o n i n − I n c r e a s e s t h e

r e l e a s e o f s e r o t o n i n F l u o x e t i n e P r
o z a c S e r o t o n i n − B l o c k s r e u p t a k e o f
s e r o t o n i n F l u r a z e p a m D a l m a n e G A B A
B e n z o d i a z e p i n e G A B A A c o m p l e x F a c i
l i t a t e s t h e a c t i o n o f G A B A F l u v o x a m
i n e L u v o x S e r o t o n i n − B l o c k s s e r o t o
n i n r e u p t a k e G a l a n t a m i n e R e m i n y l A
C h − B l o c k s e n z y m a t i c b r e a k d o w n o f A
C h G a l l a m i n e F l a x e d i l A C h N i c o t i n i
c c h o l i n e r g i c B l o c k s n i c o t i n i c r e c
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N E − B l o c k s t h e r e l e a s e o f N E G u a n f a c
i n e T e n e x N E A l p h a 2 A l p h a 2 a g o n i s t H
a l o p e r i d o l H a l d o l D o p a m i n e D o p a m i
n e D 2 B l o c k s d o p a m i n e r e c e p t o r s I p r
a t r o p i u m A t o v e n t A C h M u s c a r i n i c c h
o l i n e r g i c M u s c a r i n i c b l o c k e r I s o c
a r b o x a z i d M a r p l a n N E ; d o p a m i n e ; s e
r o t o n i n − I n h i b i t s d e g r a d a t i v e e n z
y m e (m o n o a m i n e o x i d a s e) I s o p r o t e r
e n o l I s u p r e l N E B 1 a n d B 2 A g o n i s t f o r
a l l b e t a r e c e p t o r s K e t a m i n e K e t a l a
r G l u t a m a t e N M D A N o n c o m p e t i t i v e b l
o c k e r s o f N M D A r e c e p t o r L D O P A a n d c a
r b i d o p a S i n e m e t D o p a m i n e − I n c r e a s
e s s y n t h e s i s o f d o p a m i n e L e v o d o p a L
a r o d o p a D o p a m i n e − I n c r e a s e s s y n t h
e s i s o f d o p a m i n e L o r a z e p a m A t i v a n G
A B A B e n z o d i a z e p i n e G A B A A c o m p l e x A
g o n i s t f o r b e n z o d i a z e p i n e r e c e p t o
r M a p r o t i l i n e L u d i o m i l N E − N E r e u p t
a k e i n h i b i t o r M e c a m y l a m i n e I n v e r s
i n e A C h N i c o t i n i c c h o l i n e r g i c B l o c
k s n e u r o n a l n i c o t i n i c r e c e p t o r s M e
p e r i d i n e D e m e r o l β e n d o r p h i n ; e n k e
p h a l i n O p i o i d (m u) A g o n i s t f o r m u o p
i o i d r e c e p t o r s M e t a p r o t e r e n o l M e t
a p r e l N E B e t a 2 S e l e c t i v e a g o n i s t f o
r b e t a 2 r e c e p t o r M e t a r a m i n o l A r a m i
n e N E A l p h a 1 A g o n i s t f o r a l p h a 1 r e c e
p t o r s M e t h a c h o l i n e P r o v o c h o l i n e A
C h M u s c a r i n i c c h o l i n e r g i c A g o n i s t
f o r m u s c a r i n i c r e c e p t o r s M e t h a m p h
e t a m i n e D e s o x y n N E a n d d o p a m i n e − I n
c r e a s e s r e l e a s e o f N E a n d d o p a m i n e M
e t h o x a m i n e V a s o x y l N E A l p h a 1 A g o n i
s t f o r a l p h a 1 r e c e p t o r M e t h y l p h e n i

d a t e R i t a l i n D o p a m i n e a n d N E − I n c r e a s e s r e l e a s e o f d o p a m i n e a n d N E M e t h y s e r g i d e S a n s e r t S e r o t o n i n S e r o t o n i n N o n s e l e c t i v e s e r o t o n i n r e c e p t o r b l o c k e r M e t o c l o p r a m i d e ∗ ∗ R e g l a n D o p a m i n e ; s e r o t o n i n D o p a m i n e D 2 ; 5 H T 3 B l o c k s d o p a m i n e D 2 a n d 5 H T 3 r e c e p t o r s M e t o p r o l o l L o p r e s s o r N E B e t a 1 B l o c k s b e t a 1 r e c e p t o r s M o l i n d o n e M o b a n D o p a m i n e D o p a m i n e D 2 B l o c k s d o p a m i n e r e c e p t o r s M o r p h i n e M o r p h i n e S u l f a t e β e n d o r p h i n M u o p i o i d A g o n i s t f o r m u r e c e p t o r N a l o x o n e N a r c a n β e n d o r p h i n ; e n k e p h a l i n O p i o i d N o n s e l e c t i v e o p i o i d r e c e p t o r b l o c k e r N a l t r e x o n e T r e x a n β e n d o r p h i n ; e n k e p h a l i n O p i o i d N o n s e l e c t i v e o p i o i d r e c e p t o r b l o c k e r N a r a t r i p t a n A m e r g e S e r o t o n i n 5 H T 1 D / 1 B S e r o t o n i n r e c e p t o r 1 B / 1 D a g o n i s t N e o s t i g m i n e P r o s t i g m i n A C h − B l o c k s d e g r a d a t i o n o f A C h b y c h o l i n e s t e r a s e N i c o t i n e N i c o d e r m (p a t c h) ; N i c o r e t t e (g u m) A C h N i c o t i n i c c h o l i n e r g i c A g o n i s t f o r n i c o t i n i c r e c e p t o r N i t r a z e p a m M o g a d o n G A B A B e n z o d i a z e p i n e G A B A A c o m p l e x A g o n i s t f o r b e n z o d i a z e p i n e r e c e p t o r N o r e p i n e p h r i n e L e v o p h e d N E A l p h a 1 , a l p h a 2 , b e t a 1 A g o n i s t f o r a d r e n e r g i c r e c e p t o r s N o r t r i p t y l i n e A v e n t y l N E − B l o c k s r e u p t a k e o f N E O l a n z a p i n e Z y p r e x a D o p a m i n e ; s e r o t o n i n D o p a m i n e D 3 / 4 , 5 H T 2 A B l o c k s d o p a m i n e a n d s e r o t o n i n r e c e p t o r s

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i n i c c h o l i n e r g i c (a t n e u r o m u s c u l a
r j u n c t i o n) B l o c k s n i c o t i n i c r e c e p
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u o p i o i d ; k a p p a o p i o i d M u a n t a g o n i s
t ; k a p p a a g o n i s t P e n t o b a r b i t a l N e m
b u t a l G A B A G A B A A F a c i l i t a t e s a c t i o
n o f G A B A P e r g o l i d e P e r m a x D o p a m i n e
D o p a m i n e D 1 a n d D 2 A g o n i s t f o r D 1 a n d
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; d o p a m i n e ; s e r o t o n i n − B l o c k s m o n o
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o n o f m o n o a m i n e t r a n s m i t t e r s P h e n o
b a r b i t a l L u m i n a l G A B A G A B A A F a c i l i
t a t e s a c t i o n o f G A B A A P h e n y l e p h r i n
e N e o S y n e p h r i n e N E A l p h a 1 A l p h a 1 a g
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r i n e S u l f a t e A C h − B l o c k s e n z y m a t i c
b r e a k d o w n o f A C h P i l o c a r p i n e P i l o c
a r p i n e H C 1 A C h M u s c a r i n i c c h o l i n e r
g i c M u s c a r i n i c a g o n i s t P i n d o l o l V i
s k e n N E B e t a 1 a n d b e t a 2 B l o c k s b e t a a
d r e n e r g i c r e c e p t o r s P i r e n z e p i n e G
a s t r o z e p i n e A C h M 1 m u s c a r i n i c B l o c
k s M 1 r e c e p t o r s P r a m i p e x o l e M i r a p e
x D o p a m i n e D o p a m i n e D 1 , D 2 A g o n i s t f
o r d o p a m i n e r e c e p t o r s P r a z o s i n M i n
i p r e s s N E A l p h a 1 B l o c k s a l p h a 1 r e c e
p t o r P r i m i d o n e M y s o l i n e G A B A G A B A A
F a c i l i t a t e s a c t i o n o f G A B A A P r o c h l
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a m i n e D 1 a n d D 2 B l o c k s D 1 a n d D 2 r e c e p

t o r s P r o p r a n o l o l I n d e r a l N E B e t a 1 a
n d b e t a 2 B l o c k s b e t a 1 a n d b e t a 2 r e c e
p t o r s P r o t r i p t y l i n e V i v a c t i l N E − B
l o c k s r e u p t a k e o f N E P y r i d o s t i g m i n
e M e s t i n o n A C h − B l o c k s e n z y m a t i c b r
e a k d o w n o f A C h Q u a z e p a m D o r a l G A B A B
e n z o d i a z e p i n e G A B A A c o m p l e x A g o n i
s t f o r b e n z o d i a z e p i n e r e c e p t o r Q u e
t i a p i n e S e r o q u e l D o p a m i n e ; s e r o t o
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inreuptakeinhibitorSotalolBeta
paceNEBeta1andbeta2Beta1andbet
a2blockerSuccinylcholineAnecti
neAChNicotiniccholinergic(atne
uromuscularjunction)Nicotinicr
eceptorblockerSumatriptanImitr
exSerotonin5HT1DAgonistfor5HT1
DreceptorsTacrineCognexAChNico
tinicandmuscariniccholinergicC
holinesteraseinhibitor;partial
agonistatmuscarinicreceptorsTe
mazepamRestorilGABABenzodiazep
ineGABAAcomplexAgonistforbenzo
diazepinereceptorTerazosinHytr
inNEAlpha1Alpha1blockerTerbuta
lineBrethineNEBeta2Agonistatbe
ta2receptorThioridazineMellari
lDopamineDopamineD2BlocksdopAm
inereceptorsTiagabineGabitrilG
ABA–BlocksGABAuptakeTolcaponeT
asmarNE;dopamine–Blocksenzymat
icbreakdownofNEanddopaminebybl
ockingCOMTTranylcypromineParna
teNE;serotonin;dopamine–Inhibi
tsdegradationofmonoaminesbyMAO
TriazolamHalcionGABABenzodiaze
pineGABAAcomplexAgonistforbenz
odiazepinereceptorTrimethaphan
ArfonadAChNicotiniccholinergic
(atautonomicganglia)Blocksnico
tinicreceptorValproicacidDepak
eneGABA–Increasessynthesisandb
locksdegradationofGABAVecuroni
umNorcuronAChNicotiniccholiner
gic(atneuromuscularjunction)Bl
ocksnicotinicreceptorZiprasido
neGeodonDopamine;serotoninDopa
mineD3//4,5HT2ABlocksdopaminea
ndserotoninreceptorsZolmitript
anZomigSerotonin5HT1D/1BSeroto
ninreceptor1B/1Dagonist*Includ
esonlyoneexampleofabrandname.*
*SeeTable3.4forotherdopaminere
ceptorantagonists.Abbreviation
s:ACh=acetylcholine,NE=norepin
ephrine,GABA=gammaaminobutyric

a c i d , N M D A = N m e t h y l D a s p a r t a t e , 5 H T = 5 h y d r o x y t r y p t a m i n e . 119

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4

Heterotopic Ossification in Traumatic Brain Injury

Douglas E. Garland and Arousiak Varpetian

CONTENTS

Heterotopic Ossification

The designation heterotopic ossification (HO) is preferred to such terms as ectopic ossification,

paraosteoarthropathy, or myositis ossificanse when discussing the formation of new bone

around joints as a consequence of traumatic brain injury (TBI). Heterotopic refers to the

occurrence of bone in more than one location. Microscopically, the bone is a true “ossific”

process arising de novo to new bone formation rather than calcification of soft tissue.

Heterotopic ossification associated with TBI is labeled neurogenic HO because the stimulus

to form the new bone is the cerebral insult.

The majority of HO associated with TBI is around joints, although it may also occur in

the thigh. Neurogenic HO is commonly para-articular and usually occurs in a single plane

around a joint, although it may occur in multiple sites. The bone itself lies within a well

defined tissue plane and usually does not involve the joint capsule or muscles. Patients

exhibiting marked spasticity, especially extensor rigidity, are most likely to develop this

bone. Multiple sites are common in patients with marked spasticity. The HO frequently

forms in the vicinity of the spastic musculature. The position of the extremity often permits

early prediction of the future location of the HO. It is uncommon for a patient with only

cognitive dysfunction to develop neurogenic HO.

Genetic and Patient Predisposition

Strong evidence for some type of genetic predisposition to HO formation comes from the

hereditary disorder fibrodysplasia ossificans progressiva (FOP). 1 FOP is inherited as an

autosomal dominant trait with full penetrance and variable expression. FOP was recently

mapped to human chromosome 4q 27–31. 2 It is a disorder of connective tissue with skeletal

malformations and HO. The natural history of HO from FOP has similarities to the natural

history of HO from other causes, especially neurogenic HO. Although the majority of

cases of FOP-associated HO are spontaneous, some cases also occur after trauma. A

predilection of HO for certain locations (i.e., the axial

musculature and proximal limbs)

that is similar in both traumatic and neurogenic HO is documented. Heterotopic ossifica

tion frequently recurs after surgical resection. Recurrence is also noted after resection of

neurogenic HO and, occasionally, after traumatic HO resection.

The association of human leukocyte antigens (HLAs) with neurogenic HO has been

noted. An increased prevalence of HLA-B18 and HLA-B27 antigens has been reported in

patients with HO in comparison to normal subjects. 3,4 However, follow-up studies from

other centers have not confirmed these findings, and this system does not appear capable

of predicting susceptibility to HO. 5–7

Prevalence and Onset

The reported prevalence varies for most types of HO, but much of this difference may be

the result of methodology and institutional variations. The type of center (acute care vs.

rehabilitation) and the type of impairment (hemiplegia, paraplegia, or quadriplegia) influ

ence the incidence. Methodology also affects study outcomes. Prospective vs. retrospective

studies, whole-body radiographs vs. hip only, and 6 month vs. 1 year follow-ups have the

potential to influence final data.

The prevalence of clinically significant HO — that which limits joint motion, as opposed

to HO of purely academic interest, or that which is solely a radiographic observation —

is similar when studies from similar institutions and methodologies are compared. The

most commonly reported prevalence of clinically significant HO in TBI is 10 to 20%. 8-11

Joint ankylosis occurs in less than 10% of HO lesions.

Diagnosis

Physical Examination

Limited joint motion is the most common physical finding and, frequently, the earliest

sign of HO. An increase in spasticity usually occurs. Joint erythema, or warmth, occasion

ally requires differentiation from a septic joint. Although low grade fever may be present

with HO, temperatures greater than 101˚F are uncommon. Erythrocyte sedimentation rate

(ESR) also assists in the differentiation. ESR values in septic joint are in the range of 50 to

100 mm/hour while in HO they would never be above 50 mm/hour. Lower limb swelling

may mimic thrombophlebitis which should be ruled out. The two conditions also do

coexist. HO has also been mistaken for hematoma and cellulitis. The most common

symptom of HO is pain. An increase in pain, spasticity, or muscle guarding should alert

the examiner to the impending onset of HO.

Serum Alkaline Phosphatase Determination

Serum alkaline phosphatase (SAP) is a marker of osteoblastic and osteogenic activity,

which increases with bone deposition. Early reports on HO failed to associate elevated

SAP levels. However, follow-up studies have demonstrated

that elevated levels of SAP

are present with clinically significant HO. SAP levels begin to rise, although remaining

in the normal range, within 2 weeks of injury. 12 Elevated levels may occur by 3 weeks,

and the duration of persistently high titers averages 5 months. The majority of patients

who develop clinically significant HO about the hip will have an elevated SAP level.

This may not be true at the elbow where small amounts of HO may decrease motion.

SAP titers do not correlate with inactivity, peak activity, or number of HO lesions. SAP

determination is nonspecific and not absolute, but it may constitute the earliest and,

certainly, the most convenient and inexpensive laboratory test for early detection of HO.

Many patients are in intensive care units and cannot undergo special studies. Medicinal

treatment may be initiated solely on the basis of SAP elevation if fractures are not

present.

Radionuclide Bone Imaging

Radionuclide bone imaging (RNBI) became effective as a diagnostic tool in the late 1960s

and early 1970s. Early bone scan techniques employed injection of technetium-99m poly

phosphate with follow-up scans obtained approximately 4 to 5 hours after injection.

Presently, the “three-phase” bone scan is the best method for early detection, as well as

confirmation, of HO. 13 This test involves injection of Tc-labeled methylene diphosphonate

followed by imaging in three phases:

• Phase I – A dynamic blood flow study with frequent photoscans during 1-minute frame

• Phase II – A static scan for blood pool after the completion of phase I

• Phase III – A 2- to 4-hour bone scan to determine the amount of the labeled radionuclide in bone

The first two phases are the most sensitive for early detection of HO and may show

abnormal results within 2 to 4 weeks after TBI. The period of positive uptake in Phases I

and II with a negative Phase III may range from 2 to 4 weeks. Likewise, Phase III may be

positive up to 4 weeks before HO is observed radiographically.

A large prospective, or even retrospective, study of the RNBI Phase III evaluation of

HO is not available. Correlation of RNBI with evolution of radiographic features has not

been performed. The majority of bone scans return to baseline within 7 to 12 months,

while a slowly downward activity occurs in many of the remainder of the scans. A few

scans remain fully active during the first year. The RNBI may become reactivated after a

quiescent period.

Quantitative radionuclide bone scans compare the ratio of uptake in normal ossification

vs. HO. Since HO uptake decreases with time, it is assumed that serial decreases or a

steady state in the ratio of uptake between normal and heterotopic bone indicates HO

maturity. It is proposed that the incidence of recurrence of HO is decreased after resection

if HO is removed during a radionuclide steady state. Unfortunately, this premise has not

been adequately verified in a large homogeneous series. Our large surgical resection series

demonstrated that this steady state was not a predictor of recurrence. 14 Patients with

persistently active scans predictably had recurrence, whereas in patients with negative

scans, recurrence was not always predictable. Consequently, it seems that neither the

natural history of HO nor treatment guidelines based on RNBI activity have been ade

quately established.

Radiography

Before RNBI became available, radiographs provided confirmatory evidence of HO.

Although plain films may detect HO as early as 3 weeks after injury, radiographic detection

is usually not confirmatory until 2 months after the stimulus.

Radiographs offer other benefits. They identify the site of HO at the joint and are an

easy, inexpensive, and reliable method for evaluation of treatment. Radiographs permit

evaluation of maturation of HO, especially when coupled with results of SAP determina

tions and physical examination (decrease in spasticity).

Computed Tomography

The precise role of computed tomography (CT) scanning as a clinical tool for diagnosis

and a measure of maturation of HO is not established. 15 Computed tomography may aid

in preoperative surgical planning. Multiple sites of HO at a joint may be more readily

delineated by CT. CT scan more clearly defines HO and its relation to muscle, vessel,

and nerve.

Bone Markers

Active research is ongoing in an attempt to identify newer bone markers in blood and

urine in order to detect early HO. 16–19 Bone markers are not used widely yet. When

available, their use is encouraged because early diagnosis allows earlier treatment.

Location

Our retrospective review of 496 patients revealed 57 patients (11%) with 100 joints involved

with neurogenic HO. 20 Of these patients, 30 had single joint involvement, while 27 patients

had multiple joint involvement. The ratio of the involved male to female patients was

similar to the ratio of male to female in the total population. This is significant since some

people suggest that, based on spinal cord injury (SCI) patients wherein HO in females is

uncommon, HO is a disease of males. We found that 81 of the involved joints were located

on spastic extremities. We think the other extremities may have been previously spastic

but had no spasticity at transfer to our unit.

The 11% incidence may not indicate the true incidence. A routine radiographic survey

of major joints was not undertaken. Only clinically significant HO, in a joint associated

with pain and decreased range of motion, was detected. Although the series was consec

utive, the population was selected. Patients with mild head injuries are not transferred to

our unit. The incidence of HO in these patients may be low or may occur in a mild,

clinically insignificant form. Patients with severe neurologic involvement are frequently

not candidates for rehabilitation and are not transferred to our unit. The incidence in this

group, as well as the amount of HO, may be increased.

Hip

In 33 patients, 44 hips developed HO. Three main locations were detected. The site of HO

could frequently be predicted from the abnormal posture of the extremity. Occasionally,

HO developed in more than one plane.

Heterotopic bone anterior to the hip may result in swelling of the thigh with a palpable

and visual mass (Figure 4.1). The hip often assumes a mildly flexed position with external

FIGURE 4.1

Left hip. HO (arrows) is posterior to the femoral neck.

rotation of the leg. The massive amount of HO present in SCI patients at this location is

seldom observed in TBI patients.

HO occurring posterior to the hip may be associated with hip flexion contractures. This

location of HO may not result in great limitation of motion.

The most common location of HO at the hip was the inferomedial location. HO, in this

location, is frequently associated with adductor spasticity. Ankylosis is uncommon, unless

the patient had a severe neurologic insult. Some loss of hip flexion and extension normally

occurs. If a large amount of HO is present, adduction range is compromised due to a

mechanical block.

Elbow

Two sites of HO generally occur in the elbow, although HO may form in any or all planes,

especially in the traumatized elbow. HO, anterior to the elbow, is often associated with

flexor spasticity, as noted in the hemiplegic limb (Figure 4.2 and Figure 4.3). If ankylosis

results, the bone usually bridges the distal humerus and proximal radius.

New bone occurring posteriorly at the elbow is often associated with extensor posturing

(rigidity). Since extensor rigidity resolves with neurologic improvement, the elbow may

assume a more flexed position at the time ankylosis is occurring. This explains the

paradox of posterior HO in a normal, hemiplegic, or flexed extremity. Ankylosis most

commonly occurs posteriorly at the elbow. Ankylosis is usually between the distal

humerus and olecranon.

Shoulder

The rate of occurrence is similar to the elbow. The new bone is generally located infero

medial to the joint (Figure 4.4). The shoulder position is internal rotation and adduction.

Ankylosis is uncommon, unless the patient sustains a severe neurologic insult.

Knee

HO about the knee and the quadriceps muscle is uncommon. It may appear anywhere in

the distal thigh or about the knee (Figure 4.5 and Figure 4.6).

FIGURE 4.2

Left elbow. Anterior HO (arrows) is present with complete ankylosis.

Natural History

HO in TBI probably begins shortly after injury. Serum alkaline phosphatase begins to rise

in the third week. Bone scan is positive and symptoms are present by the fourth week.

Radiographs become positive 6 to 8 weeks after injury.

FIGURE 4.3

Left elbow. The HO has been resected (arrows). Removing all the HO is not necessary (arrowheads).

FIGURE 4.4

Right shoulder. Traumatic brain injury neurogenic HO (arrows) is usually at the inferomedial location. Some

shoulder motion is usually maintained.

FIGURE 4.5

Right Knee. HO is located at the distal femur and knee medially (arrows) and laterally. The medial side is

crossing the joint (arrowheads).

FIGURE 4.6

Right Knee. The HO about the medial joint has been removed (arrowheads). The HO attached to the femur was

not removed (arrows).

The natural history of HO is defined through radiographs and not frequently empha

sized. 21–23 The natural radiographic history is similar and predictable in the majority of

patients. It also closely parallels the elevation of SAP level and the presence of spasticity.

Our retrospective review of 23 TBI patients who underwent resection of HO at an

average of 28 months after injury allowed classification of patients from I to V according

to their neurologic recovery. Class I patients had near-normal neurologic recovery, whereas

Class V patients had severe cognitive deficits and spasticity. Class I patients rarely had

recurrence after resection. In contrast, every Class V patient had recurrence regardless of

the site of HO. Radiographic progression subsided by 6 months, and SAP levels and RNBI

activity were normal, or significantly decreasing, in patients who made an early, normal

neurologic recovery (Class I). Patients with severe motor compromise had larger amounts

of HO. This HO progressed, in some instances, for more than 1 year, with elevated SAP

levels for 2 years or longer and, occasionally, persistent activity on RNBI.

Complications of HO include ankylosis in 10% of HO lesions. Joint dislocations are seen

occasionally (Figure 4.7). Pressure sores occur on bony prominences. Vascular, lymphatic,

and peripheral nerve compression and injury have been reported due to abnormal growth

of bone. 24-26 Limb fractures may result from vigorous ranging exercises.

Treatment

HO runs a gamut from being undetected, and therefore untreated, to having a poor

response to all treatment modalities. Some patients with minimal HO require no specific

treatment, whereas others may require physical therapy, medicine, manipulation, surgical

excision, or all of these (Figure 4.8). The majority of patients with HO maintain functional

FIGURE 4.7

Left Shoulder. The shoulder is dislocated (arrow). HO is circumferential (circle). This occurs because of the

combination of trauma to the shoulder plus traumatic brain injury.

FIGURE 4.8

Diagnosis and treatment of HO. Signs and Symptom of HO Bone Scan one month after injury Positive (radiographs monthly × 6 months) Early Medicinal (1 - 6 months) Negative Group I (1 - 1.5 years) Group V (1.5 - 2 years) Later Surgery (> 1 year) EHDP (primary) IV: 300mg × 3days

PO: 20mg/kg × 6months

Radiation

600 - 750 RADS EHDP 3 - 6 months NSAID 6 - 12 weeks Radiation 600 - 750 RADS EHDP 3 - 6 months NSAID 3 months NSAIDS (secondary) indomethacin 25mg tid × 6 - 12 weeks COX-2 inhibitors Treatment Plus singly or combination Plus consider all modalities

joint motion with standard physical therapies, medicines, and, occasionally, forceful manip

ulations. A small group requires surgery, with some

developing recurrence after surgery.

Medical treatment, including radiation, is used prophylactically in two general situa

tions: (1) to prevent HO formation after the primary insult and (2) to prevent recurrence

of HO after surgical resection.

Ethylhydroxybisphosphonate (Ethidronate Disodium)

In the early 1960s, research with polyphosphates and their inhibitory activity on calcium

phosphate precipitation led to evaluation of bisphosphonates, specifically ethylhydroxy

bisphosphonate (EHDP), for similar effects. Definitive studies demonstrated that bispho

sphonates inhibited the precipitation of calcium phosphate from clear solutions, delayed

aggregation of apatite crystals into layer clusters, blocked the transformation of amor

phous calcium phosphate into hydroxyapatite, and delayed dissolution of crystals. All

effects seemed related to their affinity for hydroxyapatite. The ability of EHDP to inhibit

experimental soft tissue ossification, as well as normal mineralization of bone, led to the

clinical use of EHDP to prevent HO. 27,28

For optimal effects, EHDP must be used at proper dosage and duration of treatment.

As noted above, EHDP prevents conversion of the amorphous calcium phosphate com

pounds into hydroxyapatite crystals, which is one of the final stages of bone formation.

The majority of HO evolves radiographically over a period of 6 months; therefore, the

conclusion is that EHDP should generally be given over this 6-month span. 21–23 A lower

EHDP dose is adequate to inhibit crystal resorption, but it is less effective in inhibiting

crystal growth. The 20-mg/kg dosage is necessary to prevent HO formation. Treatment

for this duration and at this dosage should prevent HO lesions in the majority of patients

and also decrease the incidence of the so-called rebound calcification. Prolonged treatment

with EHDP produces undesirable side effects such as long bone fractures in dogs. 29

Therefore, dosages of 20 mg/kg for longer than 6 months may not be warranted, and

continued treatment may be deleterious. EHDP will not be effective for the persistent

neurologically compromised patient regardless of dosages and duration of treatment.

The present method of etidronate treatment is derived from the SCI literature. 30–32 No

definitive study exists in the TBI literature. Etidronate 300 mg is diluted in 300 ml of 5%

dextrose and water and given over 4 hours for 3 consecutive days. The patient is then

given etidronate orally at a dose of 20 mg/kg for 6 months because this drug acts at the

last phase of ossification. Preferably, it is given once daily in the morning with water or

juices. If gastrointestinal disturbances occur, the dose may be lowered. The medicine is

stopped at 6 months after initiation, even if HO progresses radiographically. The drug

should not be given for more than 6 months; with prolonged treatment at this dosage,

osteoporosis and fractures may occur.

Quantitative histomorphometry demonstrates an increased number of osteoclasts, as

well as osteoblasts, in the HO lesion compared to normal bone. 33 EHDP, at a much lower

dosage than that necessary for the inhibition of ossification, interrupts osteoclastic function

but does not destroy the osteoclasts. They eventually recover full function over a prolonged

period. The impairment of osteoclast function is extremely undesirable. Resorption is the

final aspect of HO maturation and involves partial, or even complete, resolution of the

HO lesion. With cessation of treatment, the osteoid may ossify immediately, yet the

resorptive capability remains impaired until osteoclastic function returns. This may influ

ence the rebound phenomenon as well as resorption. The effect of EHDP on osteoclasts,

the recovery of rebound phase, the length of treatment, patient compliance, and the cost

of the medication may eventually contribute to the selection of another drug for treatment

of HO.

Nonsteroidal Antiinflammatory Agents (NSAIDs)

Dahl is generally credited with demonstrating the prophylactic effects of indomethacin

on HO formation after total hip replacement. 34 Other studies have verified its effective

ness. 35,36 A recent study showed that indomethacin was helpful in preventing HO in

patients with spinal cord injury. 37 The ability of

indomethacin to inhibit prostaglandin

synthetase is proposed as the primary mechanism of HO prevention, although many

effects on bone formation are known. Prostaglandins are mediators of inflammation, and

part of NSAIDs' effect is inhibition of the inflammatory response or suppression of mes

enchymal cell proliferation. It has also been observed early postoperatively that NSAIDs

may inhibit differentiation of pluripotential stem cells into osteoblasts. Because of its

potency among NSAIDs, indomethacin was used early for treatment of HO. Indomethacin

dosage is 25 mg, 3 times a day for 6 weeks, after total hip replacement. Ibuprofen and

aspirin may also be effective when used in a similar fashion. The effectiveness and the

duration of treatment of nonsteroidal, antiinflammatory drugs to prevent HO in the

neurologic patient have not been established. Since it prevents bone formation in its early

phase, its use could be for 3 months and not the entire 6 months that etidronate is used.

The newer COX-2 inhibitors are probably a better choice due to their fewer gastrointestinal

side effects and similar mechanism. Both etidronate and NSAIDs may be necessary in a

patient with aggressive HO.

Radiation

The ability of radiation to inhibit bone growth has been known by radiotherapists for

years. Irradiation prevents conversion of precursor cells to bone-forming cells. Early

reports of irradiation in the treatment of myositis ossificans were often anecdotal. Now it

appears that 1000 rads or less, immediately after total hip replacement, is effective in

preventing HO. 38,39 However, one study, comparing radiation to indomethacin, showed

both methods used as prophylaxis were equally effective in this population. 40 The location

of HO formation in the neurologic patient cannot be predicted. Because radiation is

relatively ineffective once HO is detected, its use in prevention and early treatment of

initial neurogenic HO may be limited. It may have some use after HO resection but its

effectiveness in the follow-up of patients with neurogenic HO has not been demonstrated.

Forceful Manipulation

The role of ranging joints involved with HO for maintenance or increasing joint motion

is controversial. Some authors have suggested that ranging increases the amount of HO,

whereas others have reported beneficial gains or maintenance of joint motion. A review

of patients who underwent forceful manipulation under anesthesia demonstrated its

usefulness in maintaining motion in most patients and actually increasing motion in

others. 41 Traumatic brain injury patients frequently have spasticity, intolerance to pain,

and voluntary muscle guarding. Consequently, anesthesia is usually required for manip

ulation. Examination under anesthesia allows differentiation of spasticity and true anky

losis. If spasticity is determined to be a major factor, treatment may also be directed

toward it.

Large increases in motion are sometimes achieved under anesthesia, but motion may

be gradually lost thereafter. If neurologic improvement continues, joint manipulation may

be repeated as necessary. If the patient remains at a low level of neurologic recovery,

repeated manipulations are not beneficial. We have not manipulated a joint more than

three times. Final arc of motion is closely related to the amount of neurologic recovery.

Of 28 joints, 23 (82%) gained motion with anesthesia. Further motion was maintained or

gained by 18 joints (64%) with rehabilitation. Review of the radiographs did not reveal

an exacerbation of the ossific process.

Surgery

Surgery is indicated for joint mobility, limb positioning, or sitting. Various operative

procedures have been described. 14,22,23,42 Precise timing for surgery is mentioned infre

quently but is determined in respect to the quiescent state, indicated by normal SAP levels,

mature radiographic appearance, and baseline RNBI. Postoperative complications are

common when compared to standard orthopedic procedures.

The natural history of neurologic recovery is the best indicator for time of surgical

excision, recurrence, and functional outcome. The majority of motor recovery occurs by

1 1 / 2 years and resection should be considered at that time. Excision in the patient with a

rapid neurologic recovery may be undertaken earlier when alkaline phosphatase is normal

and no spasticity is present. Surgery should be delayed longer than 1 1 / 2 years if the motor

recovery is prolonged. Recurrence is common in the presence of normal or abnormal

laboratory values in the neurologically-compromised patient. Investigators have shown

that continuous passive motion, postoperatively, decreases recurrence and achieves greater

range of flexion. 43,44 Delaying excision because of abnormal laboratory values is not war

ranted: surgery is indicated for limb positioning in neurologically-compromised patients.

No currently available studies have defined the role of medical prophylaxis after resec

tion. The stimulus to form HO has subsided in the normal recovery group and medical

prophylaxis may not be necessary for these patients. Since the neurologically-compro

mised patient continues to form HO after resection, present prophylaxis methods may be

inadequate. A mildly to moderately neurologically-compromised patient should respond

to prophylaxis after resection. This would include any of the three treatment methods

described singly or in combination.

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Rehabilitation for Posttraumatic Vestibular Dysfunction

Peter S. Roland, Debbie Eaton, and Erik Otto

CONTENTS

Acknowledgment

Introduction

Vestibular injury is frequently overlooked in the diagnostic evaluation of the traumatically

brain-injured individual. Many of the patients we see in our postacute setting have never

been formally evaluated for vestibular dysfunction. Yet, an important percentage of these

patients suffer from vestibular dysfunction.

The complaint of vertigo is not the only symptom of vestibular injury. Other symptoms

may include decreased ability to balance, visual complaints (double vision, blurriness),

or nausea. Complaints that may or may not be symptoms of vestibular injury per se, but

often accompany a vestibular lesion after a head injury, are: headache, irritability, over

sensitivity to sounds and/or lights, and decreased attention and concentration span. These

symptoms are often seen as a psychological response following a head injury and not

related to organic damage. In addition to the vestibular and associated complaints, there

is the issue of litigation that can cloud the mind of the patient and caregiver alike. Only

following a complete evaluation can the process of treatment begin. Treatment may include

exercise, medication, and/or a surgical procedure. Finally, when complete rehabilitation

is not expected, the role of a counselor can be crucial in dealing with adjustment to

disability. This process should also include patient education about the extent of the lesion

and its consequences. Patient education is critical to help bring under control a process

that otherwise might lead to a degree of disability not warranted by the lesion itself.

Recovery from head injury is now recognized to be a complex process which progresses

over many months. The patient recovering from a head injury is frequently afflicted with

more than a single area of difficulty or dysfunction. Many of these areas are the focus of

specific chapters in this book. Such problem areas frequently cross disciplinary boundaries

and, in practical clinical situations, symptoms outside the specialty area of the primary

caregiver may receive less than adequate attention. Comprehensive care is, therefore,

improved when the post–head-injury patient is served by a multidisciplinary team whose

efforts are orchestrated by a designated coordinator.

Review of the literature suggests that dizziness or disequilibrium following a head injury

represents an area which requires considerably more attention and postinjury rehabilita

tion than it has received to date.

Demographics

Although previous investigations are few in number, the evidence presented by available

studies argues powerfully that postconcussive balance disturbance is the primary cause

of very substantial morbidity and long-term disability. Indeed, Healy asserted in the

Journal of the American Medical Association that “cochlear

and vestibular dysfunction rep

resent the largest group of delayed complications of head injury.” 1,2

Berman and Fredrickson 3 evaluated 321 head injury patients within the Canadian Work

man’s Compensation System. In this group, 40% complained of postinjury vertigo and, of

those complaining of vertigo, 50% had objective electronystagmographic (ENG) findings

of organic dysfunction. When the 140 patients with complaints of vertigo were evaluated

5 years after injury, only 14% had returned to their preaccident or equivalent work. In this

group, 46% had not returned to any work at all. Vertigo, together with headache, was of

prime importance in determining long-term work status. Although no long-term studies

exist for U.S. populations, since social, cultural, and compensation variables are quite

similar, it seems reasonable to extrapolate these results to the United States.

Rantanen et al. 4 evaluated 41 patients within several days of head injury. In this group,

60% complained of vertigo. When eye movement was evaluated by physical examination

alone (even with Frenzel lenses), only 20% had observable nystagmus. However, when

electronystagmography (ENG) was performed with eyes closed, nystagmus was detect

able in over 60%. Elimination of “visual fixation” by eye closure releases pathological

nystagmoid eye movement in a significant percentage of injured people, and Rantanen et

al. emphasize that formal ENG evaluation is important in the objective evaluation of

postinjury patients complaining of dizziness.

Saito et al. 5 evaluated 22 patients who complained of dizziness after head injury. All

had positional nystagmus on ENG, and 11 had ENG findings suggestive of central nervous

system injury. Of the 11 patients with ENG findings suggestive of CNS injury, only four

recovered in 2 months or less, and four were still unrecovered after 3 months. Patients

with ENG indicators of peripheral vestibular dysfunction recovered much more quickly.

By differentiating between central and peripheral pathology, ENG was helpful in estab

lishing a prognosis.

Tuohimaa 6 carefully studied 82 patients who had sustained only “mild” head injuries

(duration of unconsciousness less than 2 hours or not at all) and compared them to a

matched control group. Of the postinjury patients, 78% complained of vertigo. Central

ENG disturbances were observed immediately after injury in 60% of the patients, but the

incidence fell to 12% at 6 months postinjury. The incidence of persistent central ENG

changes increased with increasing age of the post-head-injury patient. Tuohimaa’s group

of patients demonstrated a dramatic impairment of the ability to suppress nystagmus by

deliberate visual fixation. He argues that diminished fixation suppression indicates that

reduced central inhibition is a frequent consequence of

mild head injury. The incidence

of both spontaneous and positional nystagmus was significantly higher in mild-head

injury patients immediately after injury than in normal controls.

Grimm and his colleagues 7 studied 102 patients with mild craniocervical trauma who

experienced positional vertigo. This group displayed a set of symptoms often referred to

as postconcussion syndrome. Over 95% of these patients suffered from disequilibrium and

70% from vertigo. Headache, memory loss, tinnitus, nausea, confusion, clumsiness, alter

ation of subjective visual perception, and stiff neck were all present in over 50% of this

group of patients. Their conclusion that all of these patients had a perilymphatic fistula

is highly controversial, but their work does highlight the importance of balance distur

bance in patients with even mild head injury. Moreover, they have documented well the

pattern of characteristic symptomatology found so frequently after head injury.

Vartiainen et al. 8 examined 199 children after blunt head trauma. In this group, 50% had

positional or spontaneous nystagmus and 50% had central ENG disturbances. The inci

dence of abnormalities dropped rapidly after 2 to 8 years but was somewhat higher in

the peripheral group (18%) than in the central group (12%). Clinically, when compared to

adults, a much lower percentage of these children (1.5%) remained symptomatic at 2 to

8 years.

Evator, Bergtraum, and Randel 9 evaluated 22 children, ages 6 to 18 years, for posttrau

matic vertigo. Children with hearing loss were excluded. Five pathologically distinct

etiologies were identified, including posttraumatic migraine (five), seizure disorders

(four), postconcussion syndrome (four), whiplash injury (four), and posttraumatic neuro

sis (five). Their work emphasizes the variety of processes which can produce posttraumatic

disequilibrium and emphasizes the value of objective ENG testing in distinguishing

among various etiologies.

Anatomy and Physiology of the Vestibular System

The anatomy of the vestibular system is complex and, especially in its ramifications within

the central nervous system, poorly understood. Anatomically speaking, one may divide

the vestibular system into four parts: (1) the peripheral vestibular end-organ enclosed

within the bony labyrinthine capsule, (2) the vestibular nerve, (3) the brainstem vestibular

nuclei together with their vestibulo-ocular, vestibulo-cerebellar, vestibulo-spinal radiations

and feedback loops, and (4) vestibular cortex (Figure 5.1).

FIGURE 5.1

Conceptual schema of the vestibular system. This subdivides the various components of the vestibular system

into a vertically oriented hierarchy with receptor organs at the bottom and perception at the top. Lateral

organization distinguishes between various different

receptors at the lowest level and brainstem nuclei at

higher levels. A fully functional vestibular system requires coordination and integration of sensory receptor

information. Plasticity of the vestibular system arises from the fact that deficiencies in information provided

by receptors can be compensated for at the integrative or perceptive level by reorganizing input from residual

receptors. (From Brown, J. J., A systematic approach to the dizzy patient, Neurol. Clin., 1991; 8(2), 210. With

permission.) Perception Integration Reception Cortex Thalamus Vestibular Nuclei Cerebellum Oculomotor Nuclei Anterior Horn Cell Inf. Olive Labyrinth Retina Cervical and Pedal Joint Receptors

Vestibular End Organ

The labyrinth (inner ear) consists of a folded, fluid filled tube (membranous labyrinth or

endolymphatic space) which lies within the bony labyrinthine capsule. The membranous

labyrinthine is suspended in and cushioned by a second fluid compartment (perilymphatic

space). Anteriorly within the bony labyrinth is the spirally shaped cochlea, the organ of

hearing. Posteriorly are the three semicircular canals. Between the cochlea and semicircular

canals is a central chamber, the vestibule, which contains the utricle and saccule (Figure

5.1 and Figure 5.2).

FIGURE 5.2

The labyrinth is seen from the lateral position (top) and from below (bottom picture). The bony labyrinth has

been opened to show the position of the membranous endolymphatic duct. Asterisks indicate the cupular

dilatations of the semicircular canals. S = saccule, U =

utricle. (From Lindermann, H. H., Studies on the Morphology

of Sensory Regions of the Vestibular Apparatus, Springer-Verlag, New York, 1969. With permission.) Space for Superior Semicircular Duct Site of Ampulla of Duct Fissula Ante Fenestram Vestibule U S P Basal Middle Apical Turns of Cochlea: Fissula Ante Fenestram Vestibular Fenestra Fossula Post Fenestram Vestibular Fenestra (Impression of Strapedial Base) Fossula Post Fenestram Space for Posterior Semicircular Duct Semicircular Canals: Superior Lateral Posterior Semicircular Canals: Superior Lateral Posterior Orifices for Nerves Space for Semicirc. Duct Vestibule Cochlear Fenestra (At Cul De Sac of Scala Tympani) Cochlear Vein Cochlear Canaliculus (for Periotic Duct) Space for Cochlear Duct Cul De Sac of Scala Tympani (Site of Secondary Tympanic Membrane) Vestibular Tympanic Scalae Helicotrema {

The two inner fluids are chemically distinct. Endolymph (like intracellular fluid) contains

a relatively high concentration of potassium and a relatively low concentration of sodium.

Perilymph (like extracellular fluid) contains much sodium but relatively little potassium.

The difference in electrolyte composition between these two fluids is essential in mainte

nance of the resting electrical potential, which is critical to normal functioning of the

receptor cells.

The composition of endolymph is thought to be regulated by a vascular structure within

the lateral wall of the endolymphatic duct called the stria vascularis. The production and

composition of endolymph may, therefore, be altered by conditions and substances that

alter blood flow, vascular permeability, or systemic fluid balance. Perilymph is, at least

partially, an ultrafiltrate of spinal fluid. The perilymphatic space is connected with the

subarachnoid cerebrospinal fluid space via the cochlear aqueduct. Changes within the

subarachnoid space may alter the perilymphatic compartment. Increased intracranial pres

sure produced by disease or by straining may be transmitted to the perilymphatic space

and produce chronic or acute perilymphatic hypertension. Chemicals, toxins, and viral

and bacterial infectious agents may all pass from the cerebrospinal fluid to the perilymph

via the cochlear aqueduct.

Alterations in the chemical composition, relative volumes, or mixing of the inner ear

fluids may incapacitate both the vestibular and hearing end organ. Depending upon the

anatomic extent and severity of the alteration, various combinations of balance distur

bance, hearing loss, aural fullness, and tinnitus may result.

The common sensory receptor within the inner ear is the hair cell. Its function is to

translate fluid motion into a pattern of neuronal electrical discharge. The labyrinthine

fluids first translate both head acceleration and sound waves into fluid movement. Move

ment of fluid across the stereocilia of receptor hair cells deflects the stereocilia and changes

the resting rate of discharge in the nerve attached to the hair cell (Figure 5.3). Movement

in one direction may increase the rate of discharge and movement in the opposite direction

may decrease the rate of discharge. It is this change in rate of neuronal activity which is

processed by the central nervous system into conscious and subconscious information

about spatial orientation and sound.

The vestibular end organ consists of five separate structures, each with its own special

ized sensory epithelium. The three semicircular canals are at right angles to each other:

one in the horizontal, one in the sagittal, and one in the coronal plane. The receptor organ

of the semicircular canals is the crista ampullaris (Figure 5.1 and Figure 5.2). Each crista

consists of a group of hair cells, the stereocilia of which protrude into a dilated portion

of the membranous labyrinth called the ampulla. The stereocilia of the hair cells are

embedded in a gelatinous matrix that fills the ampulla (Figure 5.4). Head acceleration in

the plane of the semicircular canals results in the bending of stereocilia due to inertial lag

in the movement of endolymph. The same “bending” event occurs when head movement

is stopped because the endolymph will “keep going” for a few milliseconds after the head

comes to a complete rest. The semicircular canals, therefore, respond exclusively to angular

acceleration. They do not respond to constant velocity — only to changes in velocity. This

distinction is important. Once constant velocity is achieved, the sense of motion is elimi

nated. A pilot in a rolling airplane may, absent visual clues, lose all sense of rotation if

the rotation continues at constant velocity for more than a few seconds.

The saccule and utricle are the two otolithic end organs. They sense linear acceleration

and static tilt. They are gravity sensitive and maintain the ability to distinguish “up” from

“down.” Each otolithic end organ consists of an outpouching of the endolymphatic duct

on one wall of which rests a collection of hair cells called the macula. The hair cells are

covered with a gelatinous matrix in which are embedded crystals of calcium carbonate

called otoconia (Figure 5.5). The otoconia (Figure 5.6) are acted upon by gravitational forces

FIGURE 5.3

This is an actual microdissection. The bone has been completely removed leaving only the membranous en

dolymphatic duct system. The microdissection is oriented in approximately the same position as the top drawing

in Figure 5.2. AA = cupula of the superior canal, AL = cupula of the lateral semicircular canal, AP = cupula of

the posterior semicircular canal. CC = crus communis, U = utricle, S = saccule, and C = cochlea. (From Linder

mann, H. H., Studies on the Morphology of Sensory Regions of the Vestibular Apparatus, Springer-Verlag, New York,

1969. With permission.)

FIGURE 5.4

This is a scanning electron micrograph of the stereocilia from the cochlear hair cells. (Photomicrograph courtesy

of C. Gary Wright.)

FIGURE 5.5

The open cupula of a semicircular canal reveals the underlying otogenous matrix into which hair cells protrude.

(Photomicrograph courtesy of C. Gary Wright.)

FIGURE 5.6

Scanning electron micrograph of calcium carbonate otoconia. (Photomicrograph courtesy of C. Gary Wright.)

as well as linear acceleration. A change in head position alters the direction in which the

otoconia are pulled by gravity and bends the stereocilia of the macular hair cells in that

direction. Thus, any change in head position produces a sense of head movement. Since

resting head position produces constant otoconial displacement and stereociliar “bend

ing,” the otolithic organs are also sensitive to static “tilt”and help maintain orientation

to “up and down.”

Vestibular Nerve

Information from the vestibular labyrinth is carried to the brainstem by the vestibular

nerve. The superior vestibular nerve carries fibers originating from the superior and

horizontal semicircular canals, utricle, and a small portion of the saccule. The inferior

vestibular nerve carries fibers originating from the posterior semicircular canal and from

most of the saccule. Within the internal auditory canal, the superior and inferior vestibular

nerves join together, first with each other and then with the auditory nerve, and form a

single cochleovestibular nerve. The facial nerve also travels through the temporal bone

within the internal auditory canal in close proximity to the vestibular and auditory nerves.

The vestibulocochlear nerve crosses the subarachnoid spinal fluid space to the brainstem

where the vestibular fibers synapse within the vestibular nuclei. The anterior inferior

cerebellar artery, or one of its branches, is often closely associated with the vestibuloco

chlear nerve either within the internal auditory canal or within the subarachnoid space

between the temporal bone and the brainstem.

The Central Vestibular System

The first-order vestibular neurons constitute the vestibular nerves synapse with one or

more of the four brainstem vestibular nuclei. The neurons from one labyrinth will often

synapse within the vestibular nuclei on both sides of the head, thus providing bilateral

representation of the vestibular system even at the brainstem level. The wide-ranging

ramifications of the vestibular system within the central nervous system are very complex

and poorly understood. Four principal areas can be conceptually distinguished even if

they cannot always be precisely anatomically delineated: vestibulo-ocular, vestibulo-spi

nal, vestibulo-cerebellar, and vestibulo-cortical.

Vestibulo-ocular connections form the basis of the vestibulo-ocular reflex (VOR). 10–12

Each semicircular canal has an elaborate pattern of both direct and indirect synaptic

connections to the oculomotor nuclei that control eye movements. The vestibular nuclei

on each side are connected to the oculomotor nuclei of both eyes in such a way that

stimulation of each semicircular canal can produce eye movements in the plane of that

canal, i.e., stimulation of the horizontal semicircular canal can produce horizontal eye

movement. These complicated connections are responsible for the production of nystag

mus. Stimulation of one labyrinth produces slow movement of the eyes in the opposite

direction from the direction of head movement and of roughly equal magnitude. Eye

movement continues until a predetermined amount of lateral deviation is reached. Ocular

centers within the brain are able to recognize that no further eye movement is appropriate.

In order to prevent “pinning” of the eyes in extreme lateral gaze, the eyes are returned to

the neutral “straight ahead” position from which lateral deviation can begin again. The

eye movement perceived by an observer, therefore, is of slow lateral deviation followed

by a very “quick” return movement which, in turn, is followed by another slow movement

phase. The rapid return phase is a saccade. Saccades are the mechanism of eye movement

utilized during volitional change of focus when we “look around.” Saccades may occur

with speeds of up to 800°/seconds. During each saccade, reflex brainstem activity sup

presses vision so that the visual field is prevented from constant “jumping.” During the

fast phase of nystagmus (a saccade), vision is suppressed as it occurs. Since this is not

true of the “slow” phase, which is controlled by the

labyrinth, some patients will complain

that their visual field “jumps” in the direction opposite to slow phase when they have

nystagmus. The slow phase of nystagmus is about equal to, but in the opposite direction

of, head movement, so it appears to be a mechanism which reflexively permits retention

of visual fixation during head movement or when falling.

Vestibulo-Cerebellar

There are extensive direct and indirect descending (efferent) and ascending (afferent)

pathways between the midline cerebellar nuclei (principally the vermis and fastigial

nucleus) and the brainstem vestibular nuclei and associated integrative centers. These

extensive connections permit precise modulation of equilibrium both at rest and during

complex body movements. Since most of the pathways discussed have a pattern of inhib

itory connections as complex as the excitatory ones, brainstem centers subserving the

vestibular system are capable of making very fine discriminations and executing highly

precise adjustments of movement and balance.

Cortical Projections

The vestibular system (via the thalamus) projects onto the superior temporal gyrus near

the auditory cortex. Stimulation of this cortical area can produce a sense of movement

often described as “spinning.” Input from proprioceptive and visual centers is integrated

to produce the final conscious “sensation.” Occasionally,

epileptiform discharges or neo

plasms produce “vertigo” by direct stimulation of these areas of cerebral cortex.

Pathophysiology: Specific Disease Processes

While the pathophysiologic mechanisms of posttraumatic vertigo are frequently obscure,

several specific injuries with reasonably well-described mechanisms are recognized.

Temporal Bone Fracture

Because the largest portion of the skull base is made up of the temporal bone, most basilar

skull fractures involve some portion of the temporal bone. Such fractures are loosely

categorized into two types: longitudinal and transverse. Longitudinal fractures are more

common and, fortunately, are accompanied by a low incidence of fracture into the laby

rinthine capsule and facial nerve paralysis. Transverse temporal bone fractures are less

common (5 to 10% of temporal bone fractures) but are much more likely to fracture into

the labyrinthine capsule despite the labyrinthine bone being the hardest bone found

anywhere within the human body. 13 When fracture lines extend into the labyrinthine

capsule, complete ipsilateral hearing loss and total ablation of ipsilateral vestibular func

tion is the rule. If normal vestibular function is retained in the contralateral ear, then,

following several days of overwhelming rotational vertigo with nausea and vomiting,

normal functioning will likely return. The rate of improvement depends on the presence

or absence of associated injuries and on the age of the injured subject. Younger patients

recover at a much faster rate than older patients. An individual in his twenties may be

expected to be able to ambulate unassisted in 3 to 4 days. He may be able to resume fairly

demanding activities like bicycle riding and ladder climbing in 3 to 4 weeks. (Ultimately,

clinical recovery in this age group is usually complete, although subtle testing will con

tinue to uncover abnormalities of the vestibular system.) The pattern of recovery will be

quite different in more elderly persons; it will be slower. A person who is in his 60s or

70s may not be able to ambulate unassisted for several weeks and may be able to perform

demanding tasks only after several months. Recovery of fine balance skills may never be

complete in the older person. Although vestibular rehabilitation therapy will hasten recov

ery in the younger individual, many younger patients will do well without a formal

rehabilitation program. The outcome in persons over 40, even if the vestibular loss is an

isolated disability, may depend critically on the early implementation of a comprehensive,

individualized rehabilitation program. This may also be so in younger patients if the

vestibular injury is accompanied by other motor, sensory, or neurologic deficits.

Perilymphatic Fistulas

Head injury may produce rupture of the membranes which seal the inner ear and prevent

escape of perilymphatic fluid into the middle ear space (Figure 5.7). When perilymph is

removed from the labyrinth, inner ear function is degraded. A combination of otologic

symptoms may result and symptoms may fluctuate in complex ways that are difficult for

the patient to explain. In obvious cases, trauma is accompanied (or followed within a few

minutes) by rapid, severe hearing loss, loud roaring tinnitus, and severe rotational vertigo.

Vertigo is often incapacitating and accompanied by visceral autonomic symptoms (sweat

ing, pallor, nausea, vomiting). Even cursory examination will demonstrate marked insta

bility and nystagmus. Audiometric evaluation reveals sensorineural hearing loss. Platform

posturography will confirm disequilibrium with a vestibular pattern and the platform

fistula test will be positive. Vertigo and, to a lesser degree, tinnitus and hearing loss are

sometimes exacerbated by straining or Valsalva maneuver. Repair of the fistula by grafting

the round and oval windows often produces immediate and complete elimination of

vertigo. Infrequently, hearing will be improved as well.

FIGURE 5.7

Diagrammatic representation of a perilymph fistula. Perilymph can escape from either the oval window (upper

arrow) or round window (lower arrow). Since the amount of fluid is extraordinarily small, the patient has no

subjective sense of fluid within his middle ear space. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular

dysfunction after traumatic brain injury: evaluation and management, Traumatic Brain Injury Rehabilitation, 1st

ed., ch. 6, 1995, 131–169. With permission.)

Unfortunately, many perilymph fistulas do not manifest themselves in this straightfor

ward manner. 7,14 Onset of symptoms may be delayed for several days or the acute phase

may be masked by more serious injuries in other areas. Rotational vertigo may be entirely

absent and disequilibrium may be mild, vague, and episodic. Hearing loss, tinnitus, and

aural fullness may come and go unpredictably. Such protean and elusive symptomatology

has lead to controversy. Opinions differ widely among credible otologists about how

frequently perilymph fistulas occur, what types of injuries and forces produce them, and

what sorts of ancillary symptoms (headache, concentration defects, phobias, and impaired

mentation) accompany them. Although one might hope that middle ear exploration could

resolve this controversy by establishing the actual frequency with which perilymph fistulas

occur, it has not. The average human inner ear contains only 0.07 cc (70 µl) of perilymph

and, therefore, even relatively rapid leaks will, in absolute terms, be quite small. Even

with magnification, leaks involving only 5 to 10% of the perilymph will be difficult to see

in an operative field where local anesthetics have been injected, irrigating fluids have been

used, and where there is even minimal bleeding.

Because no reliable method of proving the absence or

presence of perilymph fistula is

yet available, reliable incidence and prevalence figures do not exist. At the present time,

considerable effort at the national level is being expended to clarify the perilymph fistula

controversy, but at this time, it remains unresolved.

Posttraumatic Ménière's Syndrome

In 1861, Prosper Ménière described a syndrome of episodic rotational vertigo accompanied

by tinnitus and fluctuating neurosensory hearing loss. A sense of aural fullness or pressure

is now also considered an important part of this syndrome. Attacks generally last 15 to

100 minutes and are followed by several hours of asthenia, nausea, and disequilibrium.

When no cause (i.e., syphilis, acoustic tumor, or viral labyrinthitis) can be established, the

syndrome is idiopathic and may be termed Ménière's Disease. Histopathologic evidence

demonstrates that this syndrome arises as a consequence of excess amounts of endolymph

which produce distension of the endolymphatic space. Both Ménière's syndrome and

perilymph fistula share a common factor — the ratio of endolymph to perilymph is altered

in the same direction (relative excess of endolymph compared to perilymph). In Ménière's,

it results from excess endolymph, whereas in perilymph fistula, it results from loss of

perilymph. While these conditions are clinically separable in their typical or classical

presentations, they are indistinguishable in their atypical manifestations. Ménière's disease

may, like perilymph fistula, manifest as a highly variable and changing combination of

aural fullness, disequilibrium, hearing loss, and tinnitus. No physical finding, laboratory

test, or radiographic or audiometric study can definitively separate these two conditions.

Although uncommon, the development of Ménière's syndrome after traumatic brain

injury (posttraumatic Ménière's syndrome) is well established and not rare. 15 It usually

appears weeks or months (perhaps even years) after the original injury. Diagnosis depends

on history, documentation of fluctuating neurosensory hearing loss, positive electrococh

leography, and/or positive dehydration audiometry and electrocochleography.

Treatment for Ménière's syndrome, whether idiopathic or posttraumatic, should begin

with attempted medical management. Surgical intervention should be limited to patients

who fail aggressive medical therapy. Rigorous adherence to a salt restricted diet (2000 mg

daily) and diuretic therapy are the mainstays of medical treatment. A vestibular suppres

sant should be added during symptomatic periods. If aggressive medical management is

inadequate or poorly tolerated, then consideration should be given to one of the many

surgical options available.

Benign Paroxysmal Positional Vertigo

Traumatic injury may dislodge an otoconia from the macula of the saccule or utricle. Two

hypotheses have been developed to explain how dislodged otoconia can produce the

clinical phenomenon of benign paroxysmal positional vertigo (BPPV). The cupulolithiasis

theory proposes that these loose otoconia migrate and become attached to the ampulla of

the semicircular canal. The additional mass added to the ampulla makes it gravity sensi

tive. Consequently, cupular deflection occurs with a variety of head movements and not

only as a result of angular acceleration.

The canalithiasis theory proposes that otoconia are floating freely in the endolymphatic

fluid of the vestibule. Provocative positioning results in displacement of these mobile

otoconia into the fluid of the semicircular canal, producing unilateral movement of laby

rinthine fluid, cupular deflection, and a sensation of movement. 16 BPPV may arise from

a combination of these two mechanisms.

BPPV is a common cause of vertigo. Many cases are idiopathic, but this entity is often

seen after upper respiratory infection, trauma, Ménière's disease, surgery, otologic infec

tion, and in combination with other inner ear disorders.

BPPV classically presents with intense, brief, rotary vertigo, which occurs when rolling

from side to side while in the supine position (such as in bed). The rotary sensation itself

typically lasts for about 30 seconds, but patients frequently describe a second component

consisting of persistent dysequilibrium. BPPV will cause vertigo and nystagmus with five

characteristic features: (1) latency of onset, usually 2 to 6 seconds, (2) short duration,

usually less than 30 seconds, (3) reversibility, (4) fatigability, and (5) direction. The nys

tagmus is typically rotational in nature with the fast phase directed toward the undermost

side. Many patients experience mild vertigo and nystagmus to the opposite side when

brought back to the upright position; this is referred to as reversibility.

BPPV constitutes a specific pathophysiologic entity with characteristic ENG findings

and should not be confused with benign positional vertigo from other causes.

BPPV can be diagnosed during physical examination if the “Dix-Hallpike” maneuver is

performed. For Dix-Hallpike testing, the patient starts in the sitting position. He is then

rapidly moved into a supine position with head turned to the side. 12 When this maneuver

is performed to the affected side, vertigo and nystagmus will be induced after a latency of

a few seconds and will continue for 15 to 40 seconds, after which it will disappear. The

nystagmus is away from the undermost ear. If the patient is returned rapidly to the sitting

position, the nystagmus may reappear (again, with a brief latency), beating this time in the

opposite direction. The response fatigues quickly and repeated Dix-Hallpike maneuvers

will eliminate the phenomenon within a few repetitions at most. ENG evaluation is always

helpful and frequently essential in clarifying and

documenting these classic characteristics.

Most cases of BPPV are self-limited, resolving over a 2- to 6-month period. Published

reports of treatment outcomes focus on patients with symptoms persisting beyond 6

months. There are three different bedside treatments for BPPV: the canalith repositioning

procedure (CRP), the liberatory maneuver, and Brandt-Daroff habituation exercises. 17–19

Each has specific indications, but CRP is the most widely used because it is well tolerated

by patients and is easy to perform.

CRP is based on the theory of canalithiasis and is effective for either superior or posterior

semicircular canal involvement. This treatment involves a five-position cycle in which the

patient is taken through a series of head positions to move the head around the debris

(Figure 5.8). This is repeated until no nystagmus is observed during the last cycle. The

patient is first moved into the Dix-Hallpike position with the head rotated 45 degrees

toward the side of the affected ear. The head is then slowly rotated (while extended) toward

the unaffected side, kept in that position briefly, and then the head and body are rotated

together into a side-lying position with the head turned 45 degrees down. While the head

is kept turned, the patient is brought to a sitting position. Lastly, the head is turned forward,

with chin down 20 degrees. At each position, the operator should pause until induced

nystagmus approaches termination. Reversal of nystagmus

during the second portion of

the maneuver suggests that debris is moving back toward the cupula and has been iden

tified as a factor predicting poor response by Parnes et al. 20 Most authors recommend a

soft cervical collar and neutral head position for at least 48 hours postmaneuver.

The liberatory maneuver is a more aggressive repositioning sequence where the patient

begins by lying on the involved side with the head turned 45 degrees up. The patient is

rapidly rotated through the sitting position to lie on the contralateral side with the head

turned 45 degrees down. This is an awkward manipulation, especially in the elderly

population, and has fallen out of favor.

Brandt-Daroff exercises require the patient to move repeatedly into the provoking side

lying position several times per day. Recovery is reported in approximately 95% of patients

but often requires several weeks. 16 Patient compliance issues make CRP preferable to the

Brandt-Daroff exercises.

In general, approximately 80 to 85% of patients with BPPV will experience remission of

vertigo with just one episode of repositioning. 16,18 Many patients with BPPV, however,

have persistent balance problems lasting several weeks after resolution of the episodic

FIGURE 5.8

Positions for canal repositioning, targeting left posterior semicircular canal (PSC). S (Start) — Patient is seated,

operator behind. (1) Head is placed over the end of the table, 45 degrees to the left (canaliths gravitate to center

of PSC). (2) While head is kept tilted downward, it is rotated to 45 degrees right (canaliths reach common crus).

(3) Head and body are rotated until facing downward 135 degrees from supine position (canaliths traverse

common crus). (4) While head is kept turned right, patient is brought to sitting position (canaliths enter utricle).

(5) Head is turned forward, chin down 20 degrees. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular

dysfunction after traumatic brain injury: evaluation and management, Traumatic Brain Injury Rehabilitation, 1st

ed., ch. 6, 1995, 131–169. With permission.) S 1 2 543 Ant Ant Ant Ant Ant Ant Post Post Post Lat Lat Lat Post Post Post Lat Lat Lat Endolymphatic Duct

vertigo. An exercise program directed by a physical therapist is recommended for those

patients.

The role of medications in the treatment of BPPV is limited to vestibular suppressants

and antiemetics. Benzodiazepines (such as diazepam and alprazolam) are effective vesti

bular suppressants but have sedative side effects and must, therefore, be used with caution.

Promethazine is a commonly used antiemetic which is available in oral and intravenous

formulations but may also cause sedation. Cases refractory to repositioning maneuvers

have been successfully treated surgically with posterior semicircular canal occlusion. 20 The

first published reports of posterior semicircular canal occlusion were in 1990 by Drs. Parnes

and McClure. 21 This procedure is based on the theory of

cupular deflection and endolymph

displacement. The goal of the technique is to occlude the semicircular canal, thereby

creating a closed, fluid-filled space and causing the cupula to become fixed. In this pro

cedure, a mastoidectomy is performed and the posterior semicircular canal is punctured.

Various materials, including bone dust, bone wax, fibrin glue, and fascia, may then be

used to occlude the semicircular canal.

Labyrinthectomy, vestibular neurectomy, and singular neurectomy are further surgical

options that have largely been replaced by posterior semicircular canal occlusion.

Labyrinthine Concussion

Labyrinthine concussion is an imprecise term which subsumes a variety of symptoms,

complaints, and, possibly, etiologies. Generally, it is assumed that the injury arises from

bleeding within the labyrinthine capsule, but mechanical membrane disruption caused by

acceleration and deceleration effects may also occur. 13,14 Diagnosis depends on detecting

objective vestibular abnormalities in the vestibular laboratory. ENG testing is the most

frequently helpful diagnostic test and pathologic positional nystagmus is the most common

abnormality. Unilateral weakness on ENG testing occurs less commonly but is compelling

when identified. Platform posturography showing reduced function with a vestibular pat

tern is confirmatory. Sinusoidal harmonic acceleration (SHA) may show asymmetry with

or without phase lag depending on the extent of the injury and the degree of compensation.

Symptoms may include vertigo and disequilibrium, with or without hearing loss, tin

nitus, or aural fullness. Recovery depends upon the extent of the injury and the presence

or absence of associated abnormalities. Often, recovery is complete within a few weeks.

When recovery is slow, vestibular rehabilitation can hasten its arrival and often improve

the final outcome. If unilateral weakness can be demonstrated on ENG, consideration

should be given to surgical ablation of the injured labyrinthine end organ.

Posttraumatic Vascular Loop

From time to time, head injury may displace one of the posterior fossa intracranial vessels

and cause it to come to rest against the eighth cranial nerve in the cerebello-pontine angle.

Generally, the anterior inferior cerebellar artery or one of its branches is involved. Vascular

compression of the cochleovestibular nerve produces a characteristic syndrome. The

afflicted individual is overwhelmed by an almost constant, severe positional vertigo often

associated with visceral symptoms. While actual severity may vary over a fairly wide

range, the patient is frequently not able to function. Motion usually results in marked

exacerbation of symptoms. Unilateral tinnitus and hearing loss may accompany the ves

tibular symptoms but are frequently absent. Diagnosis depends on the presence of typical

abnormalities seen during auditory brainstem response audiometry (ABR). Specifically,

changes in interpeak latency suggestive of cochlear-vestibular nerve pathology will be

noted. Radiographic demonstration of the juxtaposition of the nerve to the vessel is helpful

but not essential. When present, surgical decompression is curative.

Cervical Vertigo

Since cervical position sense receptors and muscle stretch receptors provide information

to the central nervous system about the orientation of the head in space, musculoskeletal

abnormalities of the neck and cervical spine may result in “dizzy” sensations. 22–25 Most

commonly, myofascial pain dysfunction syndromes involving either the lateral or posterior

cervical muscles are responsible. Since cervical proprioception is not the most important

sensory modality subserving equilibrium, disorders of the cervical musculoskeletal system

usually produce symptomatology that is relatively mild. Patients typically complain of a

vague disquiet and uneasiness about their balance. They resist free movement and fre

quently use support structures (wall, handrails, etc.). “Spinning” is not experienced and

falls do not, in fact, occur, although the patient is ever fearful that he will fall. Frequent

headaches occur commonly. Physical examination will generally detect muscle spasms

and tenderness. Tenderness is frequently focal and of the “trigger point” variety. 26 Com

mon focal points are the spinous process of the seventh cervical vertebrae and along the

posterior nuchal line where the posterior cervical muscles insert into the periosteum of

the skull or at the insertion of the sternocleidomastoid and splenius capitis muscles into

the mastoid tip. Aggressive physical therapy, exercises, and antiinflammatory medications

must be combined regularly for several weeks in order to achieve relief.

Central Vertigo

Dizziness and disequilibrium originating within the nervous system and not from the

labyrinth or eighth nerve is a relatively common component of posttraumatic head injury.

Vertigo which arises within the CNS itself is accompanied more often by other cranial

neuropathies and neurologic deficits than is peripheral vertigo. Dysarthria, dysphagia,

oculomotor deficits, numbness and tingling in the extremities, and focal motor weakness

are common. 13,22,27-31 A significant number of these individuals have been severely injured

so that they have been in prolonged coma. Many have significant long tract signs.

Involvement of the cerebellum produces “dizziness” and disequilibrium only in the

standing position and when attempting to walk. Subjective rotational vertigo is notably

absent. Ambulation, however, may be severely impaired and is no better with eyes open

than with eyes closed. Nystagmus will also be as vigorous with eyes open as with eyes

closed. Indeed, nystagmus may be so pronounced as to be apparent from several feet

away but, when queried, the patient will often deny subjective vertigo.

Frequently, disorders of balance are recognized relatively late in the rehabilitation of

these individuals. Early in treatment, other injuries are more apparent and need to be

addressed more urgently. As consciousness returns, mentation improves, motor weakness

resolves, and efforts can be directed toward beginning ambulation and resuming normal

activities. It may be when such retraining is begun and proceeds poorly that balance

disturbance is first recognized.

The pathophysiology of central balance disturbance remains unclear. Windle et al. have

demonstrated punctate hemorrhage and degeneration within the vestibular nuclei of head

injured guinea pigs. 13 Much evidence of central involvement comes from ENG evaluation.

Many investigators have shown a high incidence of central ENG findings in the head

injured population. Tuohimaa has argued cogently that ENG findings imply that vestibular

dysfunction may be the result of impaired cortical inhibition and not solely the result of

disruption of brainstem nuclei or pathways. 6 Subjective vertigo from stimulation or injury

to the temporal cortical projections of the vestibular system is uncommon but may occur

as a component of a seizure disorder.

There are no medical or surgical methods for managing central vestibular injury. Indeed,

the presence of a central component is frequently cited as a cause for the reduced effec

tiveness of eighth nerve section in head-injury patients even when a clear-cut peripheral

component is present. Vestibular rehabilitation will continue to be the mainstay of treat

ment for patients who have a significant central component, but medical and surgical

treatment may be of significant ancillary assistance when there is a concomitant peripheral

vestibular injury.

Clinical Evaluation

History

An adequate history is frequently the key to both diagnosis and management of vestibular

disorders. This can be a difficult undertaking in the individual recovering from brain

injury. However, every effort should be made to elicit as much information as possible

even though this may be taxing to the evaluator.

Patient’s History

Questions about premorbid leisure activities can give important information regarding

physical impairment, including vestibular injury. Did the patient return to sports and

leisure after his injury and, if not, why? Are there any close relatives or friends able to

substantiate this information?

Does the patient’s direct family report any changes regarding the patient’s participation

in the family circle? Specifically, are there complaints of balance (i.e., in darkness or with

leisure activities)? Has the patient become less physically active at all? Are there any com

plaints of visual or auditory overstimulation that can be associated with a vestibular lesion?

When balance dysfunction is present, it should first be established whether or not the

patient suffers from a subjective sense of vertigo or disequilibrium. Individuals with

central dysfunction and cerebellar disorders, although clearly impaired by balance dys

function, may have no associated sense of disequilibrium or vertigo. When present, such

sensations are frequently referred to as feeling “dizzy.” It is astonishing how frequently

this term may remain unclarified and ill-defined even though treatment persists for

months. It is critical to clarify, in as much detail as possible, what the individual means

by the term dizzy. Often, the patient will protest that he is unable to further elucidate the

experience, but, if pressed, this is almost never the case and important information can

almost always be obtained with perseverance. Vertigo is a technical term which refers to

the illusion of movement when no movement is in fact present. The most obvious example

of such a sensation is the sense of rotation when one is still. However, a sense that one is

falling when one is not falling, or the sense that one is “veering” when one is not, also

constitute an illusion of movement when none is present.

These sensations are appropri

ately subsumed under the term vertigo. It will turn out that a goodly number of patients

do not have an illusion of movement even when they use the term dizzy. Such patients

may be referring to a sense of lightheadedness, giddiness, a vague feeling of nausea, a

sense that they are walking on air, a feeling of being "closed in," of weakness, disorien

tation, or a general sense of "confusion."

After clarifying the character of the dizzy sensation, it is crucial to determine if the

sensation is invariably present or present only episodically. If present episodically, how

frequently and how long it persists will be important data to gather. Whether or not the

symptoms are always of the same severity needs to be ascertained and, if the severity is

variable, a search for exacerbating or remitting factors needs to be made. The relationship

of the symptoms to movement is crucial. Many patients either have their symptoms only

in certain head or body positions or the act of moving into certain positions precipitates

symptomatic episodes. The patient should be questioned as to whether there is any

relationship between his symptoms and diet, exercise, or situational stress. One should

determine if the symptoms are reliably reproduced in a given place. Individuals suffering

from anxiety disorders, for example, will frequently have their symptoms very reliably

"place associated." They may experience symptoms in open

places, or closed places, or

in church, or in the car. When symptoms are closely linked to a specific place or situation,

organic vestibular dysfunction is improbable. On the other hand, certain types of visual

stimuli will reliably produce symptoms in patients with vestibular disease. Complex

geometric patterns and rapid movement in the peripheral visual field are two such com

mon stimuli. A surprising number of patients will complain of disequilibrium when

shopping in the grocery store because of the rapid movement of the high, grocery laden

shelves in their peripheral visual field as they move down the aisle.

A search for associated symptoms should be made. The patient must be carefully queried

as to the presence or absence of dysarthria, dysphagia, visual change, numbness or tingling

in the extremities or around the mouth, and focal motor weakness. He should be ques

tioned about the presence or absence of headache and syncopal episodes.

Physical Examination

A complete neurotologic examination must be performed. It should start with close

examination of the external auditory canals and tympanic membranes. Such an exami

nation will not only determine the stigmata of temporal bone fracture or serious head

injury but also the more mundane findings of middle ear effusion, cholesteatoma, or

tympanic membrane perforation. It must always be remembered

that the traumatically

brain-injured individual is not immune to the commonplace afflictions of everyday life.

The pneumatic otoscope should be utilized in order to assure adequate tympanic mem

brane mobility. A complete cranial nerve examination is mandatory. Eye movement abnor

malities should be noted prominently because they will affect interpretation of the

electronystagmogram. Similarly, evaluation of the facial nerve must be compulsive

because it travels so closely with the vestibular nerve that it is an invaluable localizing

sign. Evaluation of hearing is compelling for the same reasons and should include Rinne

and Weber tests as well as a complete audiometric battery. Abnormalities of the lower

cranial nerves, including swallowing dysfunction and disorders of voice, may indicate

significant brainstem injury.

Coordination is evaluated using standard tests of cerebellar function such as the finger

tip-to-nose test, test for dysdiadochokinesia and rebound phenomenon which are per

formed for the upper extremities, and the heel-shin maneuver for the lower extremities.

Cerebellar ataxia in gait comprises a widened base of support, an irregular step length,

and weaving from side to side. Vestibular dysfunction can also result in an ataxic gait

quite similar to the one described above but does not result in positive cerebellar tests.

Gait and station should be evaluated using the Romberg test

and tandem gait, as well as

heel and toe walking. A severely disabled individual might not be able to perform some

of these tests and they will have to be omitted in such cases.

Clinical Testing

Clinical evaluation of head-injury patients suspected of vestibular dysfunction will have

to go beyond the administration of a few clinical tests as, in addition to the suspected

vestibular dysfunction, other symptoms of CNS injury might compromise overall physical

functioning. Also, clinical vestibular tests are not pathognomonic for specific lesions but

only indicators. Additionally, the vestibular patient will not always be able to clearly

discuss/communicate the changes that are a result of the vestibular injury.

The evaluation of a brain-injured individual comprises, next to taking the patient’s

history, a number of standard tests of range of motion, muscle strength, and cardio

respiratory conditioning. In addition, we evaluate coordination, weightbearing, weight

shift with rolling, quadruped crawling, and crawling on the knees, balance in standing,

during ambulation, and more complex balance activities, reflexes, and sensation.

Preambulatory Activities

Rolling on a 10-foot long, floor-placed exercise mat for a number of repetitions (usually

five times left and right) regularly provokes dizziness to the extent that clients spontane

ously stop the activity with complaints of dizziness and/or nausea (Figure 5.9).

This response can be seen as vestibular sensitivity toward angular repetitious movement

without lower extremity weightbearing. Such sensitivity can be a result of general decon

ditioning or be the first clinical sign of vestibular pathology.

Balance

A total of 14 balance tests are used to evaluate the spectrum from simple static balance

to complex dynamic balance (Table 5.1A and Table 5.1B). Balance can be affected by a

FIGURE 5.9

Mat rolling is an effective general technique for desensitization. The patient is asked to roll back and forth along

a mat. The duration of dizziness after exercise is then measured. This patient’s graph shows progressive

improvement over a period of 2 weeks. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction

after traumatic brain injury: evaluation and management, Traumatic Brain Injury Rehabilitation, 1st ed., ch. 6, 1995,

131–169. With permission.) (Seconds) D u r a t i o n o f D i z z i n e s s A f t e r E x e r c i s e 250 200 100 50 0 150 Rolling Left and Right ×5 Lengths on Mat M a y 1 1 M a y 1 2 M a y 1 3 M a y 1 5 M a y 1 8 M a y 1 9 M a y 2 0 M a y 2 1 M a y 2 2 M a y 2 6 M a y 2 7 J u n 1 J u n 2 J u n 9 J u n 1 0 J u n 1 1 J u n 1 7 J u n 1 8 Date

vestibular deficit, but also by generalized weakness, dyscoordination, spasticity, rigidity,

decreased vision, or lack of sensation.

A vestibular deficit can be expected when any of the

following indicators of vestibular

involvement are present:

• Difficulty with any balance task that either limits or excludes vision. Example of the first is walking backwards on a balance beam; of the latter, the classic Romberg test with eyes closed. Vestibular patients rely heavily on visual input to compensate for the loss of (reliable) vestibular information. When this is denied in a testing situation, they score poorly.

• Difficulty with postural adjustment with static balance tests such as one foot balance or the sharpened Romberg test. The tests require a period of 30 seconds for a normal score. Normal subjects can adjust smoothly to balance disturbance. Vestibular patients can perceive gravitational effects sometimes, but not accurately, and therefore overcorrect, ultimately leading to a loss of balance or excessive weaving.

• Difficulty with complex, repetitious dynamic balance tasks. An example is hopping 10 times on both feet. Vestibular patients have difficulty with this test because of poor gaze stabilization or because they are unable to make the quick postural adjustment necessary to maintain balance.

Clinical Vestibular Testing

The vestibular system is generally tested in two steps. The vestibulospinal and cerebellar

systems are examined by testing balance, posture, coordination, and fine motor skills as

TABLE 5.1A

Clinical Balance Testing — Test and Score Sheet Attempts Score

Static and Dynamic Balance Test List

Static Balance 1. Romberg, eyes open 1 2 3 4 5 _____ sec 2. Romberg, eyes closed 1 2 3 4 5 _____ sec 3. One foot balance left, eyes open 1 2 3 4 5 _____ sec 4. One foot balance right, eyes open 1 2 3 4 5 _____ sec 5. Sharpened Romberg, eyes open, left foot posterior 1 2 3 4 5 _____ sec 6. Sharpened Romberg, eyes open, right foot posterior 1 2 3 4 5 _____ sec

Dynamic Balance 7. Heel-toe ambulation, 50 ft, eyes open, straight line (errors) _____ ft 8. Balance beam forward, 50 ft, eyes open (errors) _____ ft 9. Balance beam backward, 50 ft, eyes open (errors) _____ ft 10. Hop both feet, times 10, maintain one rhythm 1 2 3 4 5 _____ reps 11. Hop left foot only, times 10, maintain one rhythm 1 2 3 4 5 _____ reps 12. Hop right foot only, times 10, maintain one rhythm 1 2 3 4 5 _____ reps 13. Jump rope, times 10, maintain one rhythm, jump both feet 1 2 3 4 5 _____ reps 14. Jump alternately on 10 inch elevation, maintain one rhythm, times 20 1 2 3 4 5 _____ sec

Notes:

Source: From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury:

evaluation and management, Traumatic Brain Injury Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With

permission.

discussed previously. The vestibulo-ocular system is examined by observing ocular motil

ity and assessing the vestibulo-ocular reflex (VOR). The vestibulo-ocular system is eval

uated separately from other parts of the vestibular system.

The oculomotor examination includes an assessment of ocular alignment and range of

motion. Misalignment may result in complaints of diplopia, vertigo, or oscillopsia. Subtle

misalignments may be detected by alternately covering each eye while having the patient

fixate on a distant object. If movement is noted in one eye after covering the other, an

ocular misalignment is present. Misalignment, which is variable in different fields of gaze,

may be due to an abnormality of an extraocular muscle. Obvious misalignment in a patient

with no complaints likely represents long-standing

strabismus. Vertical misalignment is

associated with brainstem or cerebellar lesions. Three different types of eye movement

should be assessed: vergence, saccades, and smooth pursuit. Vergence movements can be

elicited by asking the patient to follow a finger toward and away from the nose; these

movements are normally slow and smooth. Abnormal oscillation is suggestive of a func

tional disorder. Saccades are evaluated by having the patient fixate alternately on two

stationary targets. Velocity, accuracy, and initiation time of the saccades should be assessed,

and any abnormality points to a central etiology. Smooth pursuit movements are assessed

by having the patient track a target, such as a pen, without head movement. Asymmetry

in horizontal smooth pursuit movement is suggestive of central nervous system pathology.

Mild impairment, however, may be seen in the elderly or as a side effect of medications.

Only very gross abnormalities can be detected on physical examination. Subtle dysfunc

tion, which is much more common, can only be detected by electro-oculography.

TABLE 5.1B

Clinical Balance Testing — Explanation of Test Procedure

How the Balance Test is Performed

Static Balance

Tests 1–6: Client is tested barefoot on a wooden, circular (25 in. diameter) surface and needs to stay in one place.

Five attempts are given; only the best effort is entered. A

normal score is 30 sec.

Tests 1–2: A comfortable base of support, chosen by client, on the support surface.

Dynamic Balance

Tests 7–9: Client is instructed to perform each of the tasks at leisurely pace, barefoot.

Test 7: Mistakes are counted and entered. A mistake is stepping out of the straight line or not placing the feet

heel to toe.

Tests 8–9: Client is instructed to walk forward (8)/backward (9) the 4 in. wide beam. Heel-to-toe placement is

not necessary. A mistake is when client steps off the beam. Total number of mistakes is entered. We use a 10

ft long, 4 in. wide beam. Client travels the beam × 5 forward/backward.

Tests 10–14: These are the most complex of this test. Tests 10–13 are performed on the floor. Client is allowed

to hop “around,” as long as a sequence of 10 repetitions is maintained. Five attempts are given, with the best

result entered.

Test 14: One foot is placed on the floor, the other on a 10 in. high support surface (e.g., first step of exercise stairs

of physical therapy department). Client is instructed to alternate this foot placement while jumping straight

up, again for a sequence of 10 smooth repetitions.

This test moves from simple to complex balance tasks. The more complex balance tasks are sometimes too

strenuous for deconditioned clients. The therapist needs to be attentive to this and can stop the test when

necessary. An explanation can be entered at the bottom of the score card in the “Notes” section.

Testing is repeated after 1 month, following therapy. Therapy excludes any of the tests used for evaluation to

avoid “teaching the test.”

Testing is performed in a quiet corner of the gym. Movement of others should be excluded from the visual field

of the client, as it might interfere with performance.

Source: From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evalu

ation and management, Traumatic Brain Injury Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With permission.

Clinical vestibular testing can be divided into two categories, namely functional testing

and provocation of specific deficits. Provocation of specific deficits can be done if the

patient’s history indicates a specific lesion. A good example is the Dix–Hallpike maneuver

done when a patient’s complaints are suspect for benign paroxysmal positional vertigo.

Routinely, we perform several functional vestibular tests. If any is positive, a vestibular

lesion should be suspected. 32,33

Several bedside tests may be used to evaluate the VOR. These are based on a unilateral

reduction of the VOR causing motion of the visual surround during head movement

(oscillopsia), primarily with movements toward the affected ear. A bilateral reduction

results in oscillopsia with all head movements.

The head thrust test assesses the Doll’s eye reflex and is performed by rapidly rotating

the patient’s head to midline from an initial position 30

degrees off midline. This is

performed with the patient maintaining fixation on a target and is considered positive if

the eyes have to make a saccade to refixate.

Testing visual acuity during head movement is another method of assessing the VOR.

This can be done by rotating the patient’s head through a 60-degree arc at a frequency of

one to two cycles per second while testing visual acuity with a Snellen chart. Normal

individuals lose one line of acuity. Patients with a unilateral loss of vestibular function

may lose two to four lines and those with bilateral loss may lose five to six lines.

Post-head shake nystagmus may be elicited by passively or actively rotating the

patient’s head at a high frequency for 10 to 20 seconds and then stopping abruptly. Patients

with severe unilateral vestibular loss will have nystagmus with the initial slow phase

directed toward the affected side and a subsequent reversal phase toward the unaffected

side. Bilateral vestibular hypofunction and acute unilateral hypofunction do not produce

nystagmus after head shaking.

Tests for positional and positioning nystagmus help to separate peripheral from central

pathology and often localize peripheral pathology. Positional nystagmus is assessed by

placing the patient in each of the upright, supine, right-ear-down, and left-ear-down

positions for at least 30 seconds and observing for nystagmus. Nystagmus that lasts longer

than 1 minute and changes direction typically indicates central pathology. Positional

nystagmus that lasts longer than 1 minute but does not change direction can be seen in

peripheral or central disorders. Transitory nystagmus that lasts less than 1 minute is

usually described as positioning nystagmus and indicates peripheral pathology (usually

benign paroxysmal positional vertigo).

The Dix-Hallpike maneuver is the most commonly performed positioning test and is

designed to elicit nystagmus during dynamic head movement. The test is performed by

starting with the patient in the seated upright position, head turned 30 degrees toward

the examiner. The patient’s head is held between the examiner’s hands and the patient is

rapidly moved into the supine position, with head extended 30 degrees over the edge of

the table. The patient’s eyes are observed for nystagmus as this position is held for at least

30 seconds before returning to the upright position. This maneuver is then repeated for

the opposite ear, with the head turned in the opposite direction. Observed nystagmus is

generally horizontal-rotary, beating toward the side of the lesion.

A vestibular lesion may be classified as peripheral or central based on the nystagmus

elicited during positioning (Table 5.2). In general, peripheral nystagmus has a latency

period, short duration, and fatigability. Central nystagmus is often vertical or direction

changing and lacks fixation suppression.

None of these tests is pathognomonic for a particular type of vestibular lesion, but the

entire evaluation can give strong indicators of vestibular dysfunction that can be clarified

by an in-depth laboratory evaluation. A vestibular evaluation by an otolaryngologist

specializing in vestibular dysfunction is often requested.

Unterberger test: The patient is asked to make 50 steps in place with the eyes closed. A

positive test is turning to either side of more than 45 degrees. The patient will turn to the

side of the lesion. 34

Babinski-Weil test: The patient is asked to walk five steps forward and backward five

times with the eyes closed, maintaining an imaginary straight line. A positive outcome is

seen when the patient constantly drifts to the affected side walking forward and away

from that side walking backward.

Unterberger and Babinski-Weil tests are done while the patient listens to music through

headphones to prevent spatial orientation through environmental sounds.

None of these tests are pathognomonic for a type of vestibular lesion or localization of

a lesion, but the entire evaluation can give strong indicators necessitating further labora

tory evaluation. A vestibular evaluation performed by a neurotologist or otolaryngologist

specializing in vestibular dysfunction should be added to these clinical evaluation tools.

Laboratory Evaluation

Auditory Testing

Because the vestibular system and auditory system are so closely interrelated at the level

of the labyrinth, the eighth cranial nerve, and within the brainstem, complete audiometric

testing is essential in the evaluation of any patient with balance disturbance. This should

include a formal audiogram which tests pure tone reception at octave intervals from 125

Hz (cycles per second) to 8000 Hz. Both air conduction and bone conduction should be

tested. Speech discrimination scores should be obtained and the speech reception thresh

old measured. If inconsistent or ambiguous information is developed within the pure tone

audiogram or speech testing, then this information should be confirmed or expanded

using auditory brainstem response audiometry (ABR). 35 The initial pure tone evaluation

should be accompanied by immittance testing which measures not only tympanic mem

brane compliance but also assists in identification of ossicular disarticulation and assesses

the stapedius reflex at several frequencies. Stapedius reflex testing is sensitive to a variety

of different sorts of retrocochlear pathology. Abnormalities of stapedius reflex testing, if

not explained by known difficulties, should be considered indications for further evalua

tion with auditory brainstem response audiometry or radiographic imaging. Based on the

history and the pure tone audiogram, further evaluation with electrocochleography, ves

tibular testing, middle latency response evaluation, or central auditory testing can be

considered. 29,36,37 The results of auditory testing should be consistent with the results of

tuning fork tests as determined in the physical examination. If there are inconsistencies

between these test results, these inconsistencies need to be resolved. This subject is further

discussed in Chapter 8. TABLE 5.2 Charasteristics of Central and Peripheral Positioning Nystagmus Central Peripheral Latency None 2–15 sec Duration 30–120 sec 5–30 sec Fatigability +/- + Vertigo Absent Present Fixation No suppression Suppression Direction Vertical, horizontal Horizontal, rotary Characteristic Direction changing Direction fixed

The Electronystagmogram

Nystagmus is the only sign on physical examination uniquely linked to the vestibular system.

Therefore, the electronystagmogram plays a crucial and pivotal role in evaluating the vestib

ular system and offers a number of advantages. First and foremost, it is capable of detecting

nystagmus with eyes closed. The vast majority of peripheral nystagmus is effectively sup

pressed by visual fixation and will not be apparent to the examiner with the patient’s eyes

open. Frenzel lenses are thick 20-diopter lenses used to assist in the detection of nystagmus

on physical examination. These lenses make the detection of pathologically significant nys

tagmus easier in two ways. First, they prevent visual fixation by the patient since they make

it virtually impossible to see anything but light. Second,

they magnify the cornea and iris when

the examiner views the patient’s globe through the Frenzel glasses. Frenzel lenses will permit

the detection of clinically significant nystagmus which would be otherwise inapparent. But

even with Frenzel lenses, about half of pathologically significant nystagmus will be missed. 38,39

The electronystagmogram is capable of detecting subtle abnormalities of both volitional

and reflex eye movement controlled at the brainstem and even higher levels. These abnor

malities cannot be detected by any other method. Their detection can be the most signif

icant and easily documented evidence for brainstem dysfunction.

An additional advantage to electronystagmography is the ability of this testing method

to test each labyrinthine end-organ separately. No other clinical test of vestibular function

permits unequivocal isolation of one labyrinth from its contralateral partner.

Electronystagmography produces a permanent objective record of labyrinthine function.

Such a record can be reviewed months or years after it was made and compared with new

tracings to determine the evolution of a pathological process or to document improvement.

There are some disadvantages to ENG. The stimulus is not physiologic, and stimulus

intensity is subject to a variety of variables only partially under the examiner’s control.

These include the shape and nature of the external auditory canal, the size of the tympanic

cavity, and the thickness and position of the tympanic membrane. The test requires a

compulsive and meticulous examiner who is willing to recalibrate his equipment before

every examination, remove any cerumen impeding the flow of air/water into the canal,

and assure good contact between the electrodes and the skin. A first-rate ENG technician

will also interact with the patient in a tactful, compassionate, and sympathetic fashion.

Not only is this an intrinsically desirable end in itself, but it will also encourage maximum

effort from the patient and procure the most consistent and reliable tracings.

Electronystagmography requires relatively intact extraocular muscle function. Thus,

individuals with certain intrinsic abnormalities of the extraocular muscles or paresis of

Cranial Nerves III, IV, or VI may generate tracings that are uninterpretable.

Electronystagmography is perhaps more properly termed electro-oculography (EOG).

Although generally used to measure and detect nystagmus in the evaluation of individuals

with vertigo, the test actually measures the movement of the globe within the orbit. The

positively charged cornea and the negatively charged retina together create a dipole whose

movement can be detected when electrodes are placed around the orbits. The testing

apparatus is calibrated so that eye deviations to the right produce an upward deflection

and eye deviations to the left produce a downward deviation of the pen. In the vertical

channel, upward eye movements create an upward deviation of the pen and downward

movements generate a downward movement of the pen. The system is calibrated so that

each degree of eye movement produces a 1 mm deflection of the pen. The system needs

to be recalibrated before each test.

The complete electronystagmogram consists of a set of seven different subtests: (1)

Saccade Test, (2) Gaze Test, (3) Tracking Test, (4) Optokinetic Test, (5) Positional Test, (6)

Hallpike Maneuver, and (7) Bithermal Caloric Test.

The saccade test is usually done first because the system can be calibrated at the same

time the test is performed. With lights on, the patient is instructed to look back and forth

between two spots located on the wall directly in front of him/her without moving his

head. An arbitrary distance of about 6 feet is selected so that the patient’s eyes move about

20 degrees in the horizontal and vertical plane as he looks back and forth, as directed,

between spots. The spots on the wall are then selected to produce a 20 mm pen deflection.

The speed and accuracy with which these movements are produced is inspected and

measured. Normal individuals can perform this test with great rapidity and with very

high degrees of accuracy. Brainstem dysfunction produces well-recognized abnormalities

including systematic “overshoot” and “undershoot.” These abnormalities may occur in

one or in both directions of gaze.

Gaze testing is performed by having the patient look straight ahead and then 30 degrees

to the right, left, up, and down. Gaze in these positions is maintained for at least 20 seconds

with eyes open, and then an additional 20 seconds with eyes closed. Any nystagmus

present during these sustained eye deviations is recorded. Gaze nystagmus can arise from

both central and peripheral vestibular pathology as well as a consequence of normal

variations such as endpoint nystagmus or congenital nystagmus (Figure 5.10). Frequently,

one can distinguish between various etiologies by carefully examining the eye position in

which the nystagmus occurs and the morphology of typical nystagmoid beats. Nystagmus

which occurs with eyes open and disappears with eyes closed is reliably attributed to

central nervous system pathology.

Sinusoidal tracking or pursuit testing is also performed in a lighted room. The patient

is asked simply to visually track an object moving back and forth in front of his visual

field. This may be a ball suspended on a string from the ceiling or a sophisticated

computer-driven light bar. Normal individuals can track such sinusoidal motions with

amazing accuracy. A variety of possible abnormalities can be detected (Figure 5.11).

Certain of these are characteristic of central nervous system (particularly, brainstem)

pathology and others may simply represent the

superimposition of peripherally-induced

nystagmus on the tracing.

FIGURE 5.10

Gaze nystagmus is present in all gaze positions. It is most obvious in the 30 degree left and right deviations

(lower tracings) than in the upper 20 degree eye deviation tracings. (From Ashley, M. J. and Krych, D. K., Eds.,

in Vestibular dysfunction after traumatic brain injury: evaluation and management, Traumatic Brain Injury

Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With permission.) R20 R10 0 L10 L20 D E G R E E S GAZE 1 SEC 0.10 R20 R10 0 L10 L20 D E G R E E S GAZE 1 SEC 0.10 GAZE 20° Right/Horizontal Eye Position 30° Left/Horizontal Eye Position R20 R10 0 L10 L20 D E G R E E S GAZE 1 SEC 0.11 R20 R10 0 L10 L20 D E G R E E S GAZE 1 SEC 0.11 20° Left/Horizontal Eye Position 30° Right/Horizontal Eye Position 30-Sep-91 Id:70909360

Optokinetic testing is performed by moving a series of alternating black and white

stripes in front of the patient’s visual field. This reliably induces nystagmus in normal

individuals. Typically, the stripes are moved first to the right and then to the left in front

of the patient’s visual fields at 20 and then 40 degrees per second. Comparisons are then

made between the resulting tracings. Several possible abnormalities can occur. Optokinetic

nystagmus can be effectively and normally induced in one direction but not in the other.

Occasionally, the system breaks down under stress and individuals whose optokinetic

nystagmus is normal at lower speeds produce abnormal optokinetic nystagmus when the

speed is increased. Virtually all abnormalities of optokinetic testing arise from central

pathology, most commonly within the brainstem.

Positional testing is important not only to document pathological eye movements in

patients whose chief complaint is positional nystagmus but also because abnormal test

results occur in individuals who complain of nonpositionally related disequilibrium and

vertigo. The test is performed by examining electronystagmographic tracings produced

in four positions: with the patient sitting up, looking straight ahead; with the patient lying

supine, looking straight ahead; with the right ear down; and with the left ear down. Not

only does the tracing need to be examined for the presence of nystagmus produced in

one position or another, but in patients with preexisting spontaneous nystagmus, the

record needs to be carefully examined to see if positional changes produce any alteration

in the underlying nystagmus pattern. A large variety of different patterns of positional

nystagmus have been detected. These include direction-fixed and direction-changing vari

eties. Among direction-changing varieties are those which beat consistently away from

the ground (ageotropic) and those which beat consistently toward the ground (geotropic).

Although direction-fixed nystagmus is more characteristic of peripheral disorders and

FIGURE 5.11

Horizontal tracking is illustrated in this computerized electronystagmographic tracing. Most subjects can follow

a sinusoidal pattern very accurately. This patient follows it in a step-like “saccadic” fashion which is usually

pathognomonic for central nervous system pathology. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular

dysfunction after traumatic brain injury: evaluation and management, Traumatic Brain Injury Rehabilitation, 1st

ed., ch. 6, 1995, 131–169. With permission.) R20 R10 D E G R E E S 0 L10 L20 1.25 1.00 V E L O C I T Y G A I N 0.50 0.75 0.09 0.08 0.25 30-Sep-91 Id: 70909360 Frequency = 0.20 Hz R Gain = **** L Gain = **** Phase Shift = **** 500 MS0.04 0.21 ABNORMAL 0.17 0.16 0.05 Rightward Leftward 0.7 0.6 0.5 0.4 0.3 0.2 0.2 0.3 0.4 0.5 0.6 0.7 Cyolest 20 TARGET FREQUENCY (HZ) TRACKING: Horz Bino Horizontal Eye Position Tracking Gain

direction-changing more characteristic of central disorders, so many exceptions to these

rules have been identified that it is not possible to make definitive statements about the

etiologic significance of particular positional patterns. 40–42 An exception is the individual

in whom the direction of the nystagmus changes while in a single head position. Such a

pattern is invariably associated with central nervous system pathology.

An objective record of fistula testing can be made using the electronystagmogram and

the impedance bridge. In order to accomplish this, the immittance probe is placed into

first one ear and then the other. The pressure in the external auditory canal is varied

between +200 and −200 mm of mercury. The electronystagmogram is then examined for

induced nystagmus. Each ear is tested separately. A positive test result is identified by

the production of nystagmus associated with a change in pressure on the tympanic mem

brane. In some cases, the nystagmus can seem to change direction as the pressure changes

from positive to negative. One would expect that the patient’s subjective symptoms of

vertigo, with or without nausea, would be induced during the presence of nystagmoid

eye movements in positive tests. The results of the ENG fistula test can then be compared

(when available) to platform fistula test results. 11,29,43

Dix-Hallpike testing is a test of positioning nystagmus. In this test, the patient is rapidly

moved from a sitting position to the supine position with first the right ear and then the

left ear down. The test is specifically designed to identify benign paroxysmal positional

nystagmus. The test is positive when, after latency of 10 to 15 seconds, bursts of hori

zonto-rotary nystagmus lasting 20 to 30 seconds are observed. The response fatigues

rapidly so that, when the maneuver is repeated, the response will be much less vigorous.

Usually, several repetitions in rapid succession are sufficient to eliminate any detectable

response whatsoever. Positive Dix-Hallpike testing is classically associated with cupu

lolithiasis. Cupulolithiasis is not an uncommon consequence of blunt head injury. Since

the response fatigues rapidly, Dix-Hallpike testing should precede other forms of posi

tional testing. If it follows conventional positional testing, the expected response may

actually have been inadvertently “fatigued out” by the previous positioning maneuvers.

Bithermal caloric examination permits quantification of the “strength” of the response

obtained from each labyrinth separately. Although the strength of the bithermal caloric

response is generally assumed to represent the activity of the individual labyrinth as a

whole, it is important to remember that, in actuality, only the horizontal semicircular canal

is stimulated. Careful evaluation of patients and comparison of electronystagmographic

and SHA responses clearly demonstrate that it is possible to have residual function in the

superior and posterior semicircular canals even when no response can be generated using

bithermal caloric testing in the horizontal canal.

The test depends on the production of convection currents within the horizontal semi

circular canal. Warmed and cooled air or water is systematically irrigated through the

external auditory canal. This produces a raising or lowering of the temperature of the

tympanic membrane and produces a temperature change within the middle ear space. As

air is cooled or heated in the middle ear space, that portion of the horizontal semicircular

canal which protrudes effectively into the middle ear space is also cooled or warmed.

Since the nonexposed portions of this canal do not suffer the same temperature change,

convection currents are produced within the endolymphatic space of the horizontal semi

circular canal. This fluid movement will produce cupular deflection, discharges within

the vestibular nerve, and nystagmus which can be measured. Thermal stimuli reliably

produce nystagmus in a specific direction. Cold water will produce nystagmus with its

fast component away from the irrigated ear. Warm stimuli, on the other hand, will produce

nystagmus with the fast component toward the stimulated ear. A useful pneumonic for

these relationships is COWS (cold opposite, warm same). The simplest clinical application

of this principle is seen in the utilization of ice water caloric examination which can be

performed at the bedside or in the emergency department. Ice water calorics are performed

by putting 10 to 20 cc of ice water into the external auditory canal. This will produce an

extremely vigorous response in normal individuals with easily detected gross nystagmus

away from the irrigated ear. Unfortunately, nausea and vomiting often accompany such

intense stimulation. The vigorous response produced by ice water caloric examination is

poorly accepted by patients, and therefore, current testing protocols use stimuli which

produce a less violent response. When water is used, the temperature is usually adjusted

to 30ºC for the cool irrigation and 44ºC for the warm irrigation. If air is chosen as the

stimulating medium, then temperatures of 24ºC and 50ºC are generally utilized. Under

standing the mechanics of the test makes it obvious that certain types of ear pathology

invalidate or change test results. An individual with a

unilateral tympanic perforation can

be expected to have a much more vigorous response on the perforated side than on the

intact side because the irrigant will pass through the perforation and stimulate the hori

zontal semicircular canal directly. Individuals with stenoses, mass lesions, or other types

of obstruction of the external auditory canal can be expected to produce little or no

response on the affected side. This, however, does not mean that the examination should

not be performed. It means that the interpreter must be aware of the condition and make

his interpretation in light of the existing pathologic process. Should, for example, an

individual have no response in an ear with a perforated tympanic membrane, the perfo

ration does not invalidate the pathological finding. Indeed, the presence of the perforation

makes one even more secure that this labyrinth lacks appropriate physiologic function.

Normal individuals produce a fairly typical nystagmus response to caloric irrigation.

There is generally a latency of 20 to 30 seconds followed by the onset of nystagmus which

rapidly peaks in intensity at 60 to 90 seconds. The response then gradually diminishes

over the next 3 to 4 minutes. In order to compare one labyrinth to the other, it is crucial

that comparisons of nystagmoid response be made between peak responses for each

irrigation. This is done by examining the tracing and picking out the strongest beats on

each irrigation. Three or four of these beats should be measured and then averaged in

order to obtain a typical “peak” response. The magnitude of the response is quantified

in terms of eye speed in degrees per second. One should note that this is a different

measurement than the assessment of total amplitude of the response. Very large deviations

can be obtained at slow speeds. A variety of calculations can then be made to assess

labyrinthine integrity. The most useful measurement is that which detects unilateral

weakness (UW). This measurement compares the total response from the right ear to the

total response from the left ear using the formula below when all of the responses are

measured in degrees per second:

Using this formula, negative values indicate weakness on the right and positive values

indicate weakness on the left. Convention dictates that the weakness is expressed accord

ing to the weaker side in absolute magnitude (i.e., one would say that there is a left

unilateral weakness of 28%).

Most practitioners utilize a 20% difference between ears as the threshold for abnormality.

Some examiners, however, use a more stringent 25 or 30% difference.

In addition to evaluating the strength of an individual labyrinth, one can also compare

the total strength of all beats in one direction to all the beats in another (i.e., one can

compare the strengths of right-beating nystagmus to that of

left-beating nystagmus). In

order to make such a calculation, one uses the following formula: ( ) ( ) ( ) RW RC LC LW RW RC LC LW + − + + + + × =100 Percent Unilateral Weakness (UW)

When there is an apparent preference for the eyes to beat in the right or left direction, this

is referred to as a direction preponderance. As a general rule, directional preponderances are

a reflection of spontaneous nystagmus. Although directional preponderances can occur

in the absence of spontaneous nystagmus, one should be suspicious that there has been

some technical error in the irrigations whenever directional preponderance occurs in the

absence of spontaneous nystagmus.

The significance of directional preponderance when not associated with spontaneous

nystagmus remains unclear and, for that reason, some evaluators do not make this

calculation.

An important part of the caloric examination is the test for visual fixation suppression.

At some point, when the induced nystagmoid response is still brisk, the patient should

be asked to open his eyes. Eye opening should produce a marked reduction in the intensity

of nystagmus (Figure 5.12). Indeed, the strength of the response should be reduced by at

least 60%. When this is not the case, central nervous system pathology is implied.

Computed Sinusoidal Harmonic Acceleration

An alternative method of assessing the vestibular ocular reflex utilizes a motorized chair

to produce a back and forth (sinusoidal) movement (Figure 5.13). In response to such

movement, the vestibular ocular reflex will induce compensatory eye movements in the

opposite direction to body movement. These eye movements can be measured and com

pared to the rotational stimulus. Since the stimulus which initiates the vestibular ocular

FIGURE 5.12

Electronystagmographic tracing taken from a patient with a central nervous system tumor. The right warm

caloric is shown. At the vertical bar in the middle of the tracing, the patient was asked to open his eyes and

fixate on a mark on the wall. Visual fixation produced only very slight decrease in the velocity of his nystagmus.

Failure of visual fixation is a reliable sign of central nervous system pathology. (From Ashley, M. J. and

Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, Traumatic

Brain Injury Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With permission.) ( ) ( ) ( ) RW LC RC LW RW LC RC LW + − + + + + × =100 Percent Directional Preponderance (DP) R20 R10 D E G R E E S 0 L10 L20 U20 U10 D E G R E E S 0 D10 D20 CALORICS: Right Warm Horizontal Eye Position Vertical Eye Position 25-Oct-91 Id:587-24-1836 2:00 1 SEC

reflex is, in this case, mechanically generated by a chair in which the patient sits, it can

be very precisely and accurately controlled. One advantage of sinusoidal harmonic accel

eration is that the stimulus can be determined with much greater precision than can the

thermal effects utilized to generate a caloric response in conventional electronystagmo

graphy. An additional advantage of slow harmonic acceleration is that the stimulus is

physiologic. That is, the sort of rotational movement used to generate a response in the

vestibular ocular reflex (VOR) arc is qualitatively and quantitatively like many of the

stimuli encountered in everyday movement. Generally speaking, most movements per

formed during ambulation are a bit quicker, but certainly the stimuli used to generate a

response utilizing the motorized chair are basically normal. This same characteristic (of

providing a physiologic stimulus) which constitutes a principle advantage of SHA is also

responsible for one of its principle disadvantages compared to conventional ENG. By

necessity, both labyrinths are stimulated simultaneously and it is not possible to collect

data from one side alone.

The patient is tested at five separate rotational speeds measured in cycles per second

(Hertz). Typical speeds are one hundredth (0.01 Hz), two hundredths (0.02 Hz), four

hundredths (0.04 Hz), eight hundredths (0.08 Hz), and sixteen one hundredths (0.16 Hz)

of a rotation per second. Three separate characteristics of the VOR response are determined

for each frequency of rotation. 39,44–46

FIGURE 5.13

A rotational chair. The subject is seated in the chair and is seen through the open door. With the door closed,

the patient will be in complete darkness. The subject can be monitored from outside the booth by infrared

photography. Electrodes are placed in the appropriate positions for monitoring of the induced vestibulo-ocular

reflex. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evalu

ation and management, Traumatic Brain Injury Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With permission.)

Phase

It is reasonably appropriate and much easier to understand phase relationships as synon

ymous with latency. Because the SHA uses a rotational stimulus, it happens that relation

ships usually characterized as latency can be appropriately described as phase

relationships. Suffice it to say that abnormalities of phase (latency) represent changes in

how long after the start of the stimulus the compensatory eye movement occurs. It so

happens in SHA (as in many other neurodiagnostic tests) that changes in latency are

relatively reliable and sensitive indicators of pathological disturbance of function and most

peripheral vestibular disorders (i.e., severe viral labyrinthitis, Ménière's disease, traumatic

ablation, etc.) have been associated with abnormalities of phase. It is quite typical in these

cases for the phase abnormality to be more pronounced at lower frequencies and to return

toward normal at the higher frequencies. In fact, if phase abnormalities are the same or

worse at higher frequencies, then central dysfunction should be suspected. The data is

presented by comparing the patient's response to

established norms. As a rule, any

response more than two standard deviations from normal is considered pathologic. Once

injury has occurred, phase generally remains abnormal indefinitely. Adaptation and com

pensation do not eliminate phase abnormalities.

Gain

Another parameter of the vestibular ocular reflex evaluated at each frequency during SHA

is the magnitude of the induced eye movement compared to the magnitude of the rota

tional stimulus. This comparison is referred to as gain. If the eye movements induced by

a given rotation (in degrees per second) were exactly the same as the magnitude of the

chair rotation (in degrees per second), the gain would be said to be 1.0. If the induced eye

movements were twice as large as the initial movement of the chair, the gain would be

2.0 and, if they were half as large, the gain would be 0.5. Not surprisingly, the amount of

gain depends on the velocity of rotation. Very slow rotational movements induce relatively

small eye movements and typical gains for 0.01 Hz stimuli are 0.5. As the speed of rotation

increases, the amount of eye movement similarly increases. It increases faster than the

rotational speed so that, at 0.16 Hz, normal gains are in the 0.7 range.

Patients with bilateral vestibular weakness have abnormal gains and, generally speak

ing, the abnormality is more pronounced at the lower frequencies. As the frequency of

rotation is increased, the amount of gain tends to return toward normal even in patients

with bilateral vestibular hypofunction. When gain is very low, there is insufficient vesti

bular input to provide meaningful data and, with very low gains, one should not interpret

abnormalities of phase or symmetry. Low gains will occasionally occur in response to

acute labyrinthine lesions when the cerebellum deliberately suppresses output from the

vestibular nuclei. However, very low gains are more usually a consequence of chronic

bilateral vestibular weakness. Patients with central vertigo will occasionally show

increased gain due to the absence of descending inhibition.

Symmetry

Asymmetric responses are a manifestation of directional preponderance or bias. That is to

say, if there is asymmetry to the right, right-beating nystagmus is always greater than left

beating, regardless of the stimulus. The most obvious examples are situations in which

there is spontaneous nystagmus to one side. If the patient, at rest, has 10 degrees of right

beating nystagmus, his right-beating responses to rotational stimuli will be enhanced by

10 degrees per second but his left-beating responses will be reduced by 10 degrees per

second. Thus, when examining the response to rotational stimuli, it appears that the

individual’s eyes “prefer” to beat toward the right. Acute peripheral lesions frequently

have significant asymmetries associated with them. If the lesion is peripheral, one would

expect a phase abnormality to be apparent as well. With classic unilateral vestibular injury,

marked phase and symmetry abnormalities are present during the first several weeks or

months. With the passage of time and the development of compensation, the asymmetry

tends to disappear, but the phase lag will remain. Some types of central disorders will

have associated with them variable low level asymmetries (Figure 5.14).

Rotatory chair testing has a number of advantages that make it a useful addition to the

armamentarium of vestibular testing:

- The stimulus is precisely controlled and physiologic.

- The test is quite sensitive and very repeatable. Test variability is minimized.

- It produces an objective, quantified assessment of vestibular function.

- In many cases, elimination of asymmetry can document compensation and adaptation.

- Generally speaking, it is well accepted by patients and produces less subjective discomfort than electronystagmography.

There are some disadvantages associated with SHA:

- Both labyrinths are stimulated simultaneously.

- The test is relatively expensive and requires fixed equipment installation.

- It was initially thought that asymmetry data could not be utilized to identify the side of lesion.

FIGURE 5.14

Summary of diagnostic information obtained from sinusoidal harmonic acceleration. In this patient, there is a

significant phase lag. The circles are shown above the lines showing that they are significantly outside the usual

standard deviation. In the bottom graph, one can see a mild asymmetry to the right. However, the small squares

indicating gain on the upper tracing are below two standard deviations from the norm, indicating a bilateral

weakness. In the face of such reduced gain, it is not possible to accurately interpret phase or symmetry changes.

This is from a patient after head injury with significant reduced bilateral vestibular function. ENG evaluation

showed no response to warm or cold water irrigations bilaterally. (From Ashley, M. J. and Krych, D. K., Eds., in

Vestibular dysfunction after traumatic brain injury: evaluation and management, Traumatic Brain Injury Rehabil

itation, 1st ed., ch. 6, 1995, 131–169. With permission.) 80 40 0 –40 Phase (Deg) 40 0 –40 Asymmetry (%) University of Texas (Dallas) MePatient: File: NORM0014.%01 Date:05-29-92 Test :CHR SINE R L .01 .02 .04 .08 .16 .32 .64 1.28 0.0 0.4 0.8 Gain (Ratio) 1.2 Frequency (Hz)

Recently, Mohammed Hamid has documented convincingly that asymmetry is reliably

toward the side of the lesion when phase abnormalities are present. 47 In the absence of

phase abnormalities, asymmetry has no localizing value whatsoever. If additional centers

are able to confirm this observation, the role for SHA testing will be considerably enhanced.

Vestibular Autorotation Testing

The vestibulo-ocular reflex (VOR) is the dominant mechanism for gaze stabilization during

locomotion. Because other ocular control systems are relatively insensitive above 2 Hz,

high-frequency vestibular autorotation testing (VAT) was developed to isolate the VOR

for testing. VAT uses high frequency (2 to 6 Hz) active head movements to stimulate the

horizontal and vertical VOR to produce measurable eye movements that can be used to

calculate gain and phase. 48

Patients are fitted with a rotational sensor (on a head strap) and conventional electro

oculographic electrodes during testing. They are instructed to move their heads in syn

chrony with computer-generated auditory tones, with an interval ranging from 0.5 to 6

Hz. Gain and phase data are collected from the last 12 seconds of the test at higher

frequencies (2 to 6 Hz).

Advantages of VAT over SHA include the ability to test both horizontal and vertical

VOR gains and phases in the most clinically relevant frequency range. Saadat et al. 49

compared the results of VAT to alternate bilateral bithermal calorics and found that many

patients with normal caloric test results had abnormal VAT results. This emphasizes the

fact that cognitive processes or competing oculomotor systems can influence the VOR at

low frequencies but are ineffective at higher frequencies. They recommend VAT as an

adjunct to traditional vestibular testing.

In 1994, Murphy evaluated 120 patients with vestibular dysfunction using both ENG

and VAT. 50 He noted that ENG continued to demonstrate abnormal vestibular responses

in patients with permanent labyrinthine injury even after central compensation. VOR

results often normalized after compensation. In this series, ENG was determined to be

the most useful initial study in the evaluation of patients with probable peripheral vesti

bular dysfunction. Certain diagnoses (such as trauma and nondescript dizziness which

are not easily determined to be peripheral) were best evaluated initially with VAT.

In short, ENG and VAT provide valuable complimentary information in the evaluation

of vertigo. ENG allows localization of peripheral vestibular dysfunction without informa

tion about central compensation. VAT examines the VOR in the clinically relevant fre

quency range and provides information about central compensation, though it does not

allow localization of the injury.

Dynamic Platform Posturography

The development of dynamic platform posturography has been an important addition to

the armamentarium in evaluating individuals with disorders of balance (Figure 5.15). The

use of dynamic platform posturography directly assesses the individual’s ability to main

tain his balance in a variety of circumstances. It is capable of assessing not only vestibular

function but also contributions to balance from the visual and proprioreceptive systems.

Dynamic platform posturography assesses changes in the subject’s center of gravity (COG)

in response to a variety of stimuli in different test conditions. Movement of the center of

gravity around a fixed point is termed sway. Sway can be measured in both the ante

rior-posterior and in the lateral planes. Excessive sway can occur at rest in a variety of

circumstances, but occurs most frequently in response to deliberate perturbations. 51-53

Sensory Organization Testing

The amount of sway produced in response to six different situations is recorded. The

different test conditions are designed either to eliminate information normally utilized in

maintaining equilibrium or to subvert the system by providing inaccurate information.

Movement of the patient's center of gravity is assessed in the following situations:

• Sensory Test Condition 1 — the patient stands on the platform with eyes open.

• Sensory Test Condition 2 — the patient stands on the platform, but his eyes are closed. This test condition eliminates vision as a source of information in maintaining balance.

• Sensory Test Condition 3 — the patient stands on the platform with eyes open; however, when the patient sways, the amount of movement he makes is exactly compensated for and mimicked by the movement of the visual surround. He will stay exactly the same distance from the visual surround regardless of what movement his body makes. Thus, vision will provide inaccurate information as to where he is in space relative to his visual surround. In short, in this test condition, the patient's visual system will "lie" to him. This is a more stressful situation than the mere absence of visual information produced in Sensory Test Condition 2. This condition is termed sway referenced vision (i.e., the visual surround is "referenced" to the amount of sway the patient has).

FIGURE 5.15

Neurocom ® (registered trademark for NeuroCom International, Inc., Clackamas, OR.) dynamic platform posturography. The patient is standing on a moveable platform within the visual surround. Safety straps prevent injury from falling. Sway is monitored in response to a variety of different sensory test conditions. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, Traumatic Brain Injury Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With permission.)

- Sensory Test Condition 4 — the patient stands on the platform with eyes open. Each swaying motion the patient produces is now exactly compensated for by a similar movement in the platform on which he is standing. This is a condition analogous to Sensory Test Condition 3 except that, in this condition, it is the patient's lower extremity proprioreceptive system that is "lying" to him. This is referred to as sway referenced support.

- Sensory Test Condition 5 — this condition is exactly the same as Sensory Test Condition 4. There is sway referenced support, but the patient is asked to keep his eyes closed. This functionally produces a situation where the patient's lower extremities are "lying" to him and his visual system is providing no helpful information. Theoretically, his balance is now dependent on vestibular function.

- Sensory Test Condition 6 — the patient stands on the platform with eyes open, but both vision and support are sway referenced. That is to say, each sway excursion is matched both by compensatory movement in the platform and in the visual surround. Thus, both the patient's visual and proprio systems are "lying" to him. In this condition, balance is determined solely by the intact vestibular system which must overcome false information from the visual and proprioreceptive systems.

If the patient does not perform well during the first trial, he is allowed two additional chances in which to improve his performance. "Learning" is frequent and many patients will be able to develop a normal response given two or

three tries. If, when compared to

statistical norms, the patient’s center of gravity shows abnormal excursions (i.e., sway),

he is considered to have “failed” that test condition.

As it turns out, different types of pathology produce different patterns of dysfunction

on dynamic platform posturography. Not surprisingly, vestibular disorders are reliably

associated with very poor performance in Conditions 5 and 6 when compensatory mech

anisms are crippled by the test conditions. Patients who are overly dependent on vision

tend to perform very poorly in Test Conditions 3 and 6. Patients who are visually depen

dent and also have vestibular abnormalities tend to do poorly on Conditions 3, 5, and 6.

If Conditions 4, 5, and 6 are abnormal, it suggests that the patient is quite dependent on

somatosensory input to maintain balance. Additional combinations and patterns can be

correlated with different sorts of abnormalities. Patients with functional disorders or

patients who are malingering frequently produce as bad or worse results on the easier

conditions than on the harder ones.

An important contribution of dynamic platform posturography is the ability of this test

to determine what sort of “strategy” the patient is utilizing to recover his balance. While

standing still, the platform is suddenly “jerked” and the patient response is assessed.

Several forward and several backward perturbations (jerks) are evaluated. Well-function

ing, normal individuals tend to move their center of gravity around their ankles in

response to impending disequilibrium. The use of movement about the hips or “hip

strategy” is maladaptive and counterproductive. Fortunately, vestibular rehabilitation may

be able to redirect the patient’s efforts and reorient his strategy from hip to a more effective

ankle strategy.

In addition to assessing the sensory modalities utilized to maintain and correct balance,

dynamic platform posturography is able to partially characterize the motor response

generated after perturbations. The length of time it takes for the muscle response to occur

is measured and called latency. In actual clinical situations, it turns out that abnormalities

of latency are almost always associated with extravestibular CNS pathology. The strength

“symmetry” is measured. This simply assesses the amount of strength utilized in each leg

to retain balance. In normal persons, equal amounts of strength will be utilized in each

leg in the process of balance recovery. Once again, in the absence of obvious peripheral

or orthopedic problems (i.e., peripheral muscle atrophy, unilateral hip disease, etc.),

abnormalities of symmetry also reflect central nervous system disorders. The size of the

response is also measured. If minor induced external perturbations produce very large

compensatory excursions, large sway oscillations are induced.

Dynamic platform posturography is useful not only in diagnosis but also in the assess

ment of risk and in rehabilitation. Not surprisingly, patients who perform poorly on

platform posturography are at greater risk for falling than patients who perform normally.

Specific pattern abnormalities in sensory organization and movement coordination testing

correlate even more closely with risk for falling.

An understanding of what sort of compensatory mechanisms the patient is using in

response to balance perturbations can be helpful in guiding vestibular rehabilitation

therapy. Patients who are overly dependent on vision can be given tasks to enhance their

ability to utilize vestibular and proprioreceptive information. Persons utilizing a maladap

tive hip strategy, for example, can be redirected to a more appropriate ankle strategy

(Figure 5.16).

FIGURE 5.16

Six different sensory organization test conditions are monitored and the patient’s performance compared with

statistically valid norms. A typical summary form is illustrated here. This patient had an acute unilateral

vestibular lesion resulting in a very poor performance in sensory organization Test Conditions 5 and 6. (From

Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and

management, Traumatic Brain Injury Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With permission.) 100 75 50 25 1 2 3 4 Equilibrium Score Sensory Conditions 5 6 F A L L Composite 61 Fall Sensory Conditions Ankle 75 50 25 3 4 5

Strategy 6 Hip CONDITION 1 CONDITION 2 CONDITION 3 CONDITION 4 CONDITION 5 CONDITION 6 +--------Within Normal Limits---------------+ +---Reduced Responses---+ Movement Coordination Test Symmetry: Within normal limits Latency: Within normal limits Amplitude Scaling: Grossly within normal limits Adaptation: Patient is able to adapt INTERPRETATION/RECOMMENDATION: Reduced responses on conditions 5 and 6 are consistent with a deficiency in the vestibular system.

Platform Fistula Testing

Dynamic platform posturography can be used to generate a sensitive test for perilymphatic

fistula. In this test, pressure is applied to the external auditory canal. This increase or

decrease (i.e., “negative” pressure) is transmitted to the tympanic membrane, middle ear

space, and, if a fistula is present, the inner ear. When perilymph fistula is present, abnormal

sway will be generated by these pressure changes. Using the acoustics impedance bridge

to quantify changes in external auditory canal pressure and the dynamic platform to

quantify anterior–posterior and lateral sway in response to such pressure changes, a

sensitive assessment for perilymph fistula can be developed. Several studies have dem

onstrated that patients with positive platform pressure testing have a high likelihood of

suffering from a perilymphatic fistula.

Vestibular Rehabilitation

The clinical rehabilitation process of the brain-injured individual can be much more com

plicated than the rehabilitation of an individual suffering from vestibular dysfunction only.

Cognitive impairment with decreased attention span,

inability to concentrate, and poor

frustration tolerance can discourage the patient as well as the therapist.

In addition, patients present with a wide spectrum of central neurological impairments

affecting different subsystems of the central nervous system. These impairments demon

strate themselves with symptoms of upper motor neuron lesion (spasticity, weakness),

rigidity, and dyscoordination.

Given these complicated circumstances added to the vestibular dysfunction, the task at

hand is, to say the least, very difficult. It is necessary to develop a treatment philosophy

and to explain this philosophy to the patient each time circumstance dictates the need for

more comprehension or motivation.

Vestibular rehabilitation depends on two important characteristics of the vestibular

system: redundancy and plasticity. 28 Redundancy occurs principally at the receptor level.

That is to say, there are several sensory systems which process information about the

body’s position in space and relay that information to the central nervous system. These

include the vestibular system, the visual system, muscle stretch and position sense recep

tors in the lower extremity, and muscle stretch and position sense receptors in the cervical

area. The last two are generally subsumed under the single heading of the somatosensory

or proprioreceptive system, but in fact, they often function quite independently of each

other. The visual and vestibular systems are themselves redundant in the sense that the

system has two separate sides. When information from one side is eliminated, the system

can function using the intact contralateral side alone. Data received from all of the available

sensory receptors is initially processed in the brainstem where decisions are made on a

reflex basis. Details of this process remain obscure, but it appears that most of the pro

cessing is done in or close to the vestibular nuclei with significant input from both the

cerebellar nuclei and descending cortical projections. The ability of sensory receptor infor

mation to be evaluated, emphasized, de-emphasized, or changed at this level is the prin

cipal feature of the vestibular system allowing for progressive modification or plasticity. 54

One way plasticity can be achieved is by the systematic “substitution” of sensory input

from one receptor cell system for another. For example, individuals with bilateral vestib

ular weakness come to utilize visual information more intensively for maintenance of

balance and equilibrium. Habituation is an additional mechanism for compensation

although its exact physiologic basis remains unclear. Despite its elusive electroneurophys

iologic basis, it is clear that constant exposure to situations which produce unpleasant and

counterproductive stimulation will reduce or eliminate the unpleasant response.

An instructive example of neuroplasticity is the central

nervous system’s response to

acute unilateral labyrinthine ablation. In the circumstance of abrupt and devastating injury

to one inner ear (i.e., temporal bone fracture), the afflicted individual will immediately

experience rapid, violent rotation with massive visceral autonomic outflow producing

intense diaphoresis, weakness, nausea, and vomiting. This effect is a consequence of

asymmetry at the level of the vestibular nuclei. Vestibular nuclei connected to the intact

labyrinth are continuing to receive normal sensory input and continue to respond in an

appropriate way. Cells in the vestibular nuclei connected to the affected side now no longer

receive stimulation from the ablated labyrinth and are “silent.” Initial adaptation to this

injury occurs within several hours to a couple of days and consists of marked inhibition

of those cells still connected to the intact labyrinth. Control of this process occurs in the

cerebellum and is accomplished via afferent cerebello bulbar fibers. This response has

been termed the cerebellar clamp by McCabe because it diminishes activity in normally

functioning vestibular cells. 55,56 By reducing function in the normal intact cells, the level

of imbalance between the nonfunctioning cells and intact cells is reduced and the symp

toms of disequilibrium, nausea, vomiting, and rotational vertigo are reduced. This

response has been documented in acute vestibular lesions using sinusoidal harmonic

acceleration where occasionally, within a day or two after ablative vestibular procedures,

a marked decrease in gain can be documented on SHA testing. Over time, those vestibular

nuclei originally connected to the now nonfunctioning labyrinth will develop a sponta

neous rate of discharge. As spontaneous activity develops in these neurons, inhibition of

the “clamped” normal vestibular nerve cells by the cerebellum is reduced. As the indi

vidual regains normal activity and as he is exposed to situations challenging the vestibular

system, he will slowly regain normal function. This series of events is an excellent example

of neuroplasticity in the vestibular system. 57,58

Data from patients and animals with acute unilateral vestibular ablation as well as from

other types of studies suggest that “relearning” is an important characteristic of vestibular

compensation. Stressing the system by having the individual engage in activities which

produce disorienting or discomforting symptoms is an important stimulus for compen

sation and rehabilitation.

Vestibular rehabilitation capitalizes on the natural plasticity of the vestibular system. 59

A good vestibular rehabilitation program should both extend and accelerate the normal

process of physiologic adaptation to injury.

Because of the wide variety of possible separate injuries and the almost infinite possible

combinations of different sorts of injuries, we believe that each vestibular rehabilitation

program needs to be specifically tailored to a particular individual’s needs. This is partic

ularly true when dealing with post-head-injury patients because they will almost always

have significant concomitant deficits outside the vestibular system. This is best accom

plished by a physical or occupational therapist who has made a special study and gained

experience in managing vestibular injuries. Such an individual will be best qualified to

create programs which take into consideration all of the patient’s deficits and all of his

potential assets.

Propaedeutic to developing a program for rehabilitation, the vestibular rehabilitation

therapist needs to make his own assessment. 54,60 At first glance, this would appear to be

redundant, but in fact, it is not. The assessment made by the rehabilitation expert will not

only review the history and physical and laboratory findings already obtained by physi

cians and other healthcare professionals, but will make a detailed assessment of specific

situations which induce vertigo (i.e., elevators, crowded stores, driving), assess the severity

on a quantitative scale, and do a detailed assessment of the affect of both position and

positioning. As many as 20 separate positions and movements can be separately assessed,

and each position or movement can be rated for intensity, duration, and presence of

nystagmus and/or dizziness. The patient’s history and type of complaint dictate how

much positional testing is required. A separate evaluation of eye, head coordination, and

gaze stabilization is made as well as a separate and detailed assessment of postural control,

both in the sitting and standing positions. Gait is evaluated separately.

Whenever making an assessment for vestibular rehabilitation, it is important to determine

whether or not there are other areas of difficulty outside the vestibular system which may

affect rehabilitative strategies. This is especially important in the post-head-injury area.

A complete evaluation of the musculoskeletal system needs to be made in order to

determine whether there are any coexisting difficulties or deficits. Reduction in strength

is common in the post-head-injury patient. Such reduced muscle strength may be second

ary to muscle atrophy from coma or inactivity, or may be secondary to direct neural injury.

It may, therefore, be generalized or affect only a specific body part. Reduced range of

motion should be determined. Range of motion is frequently reduced in the extremities,

secondary to orthopedic extremity injuries and may then be limited to a specific body

part. Many patients will have associated back injuries. The effects of cervical spine injuries

especially need to be taken into consideration. Patients with significant cervical spine

injuries will either have had surgery or prolonged periods of neck immobilization. Many,

if not all, of these patients will have disordered

somatosensory feedback from cervical

muscle stretch and joint position sense receptors.

The presence of pain will frequently limit movement. The nature of the pain, its severity,

what movements provoke it, and which positions relieve it all need to be detailed as part

of the initial assessment.

Some musculoskeletal abnormalities, especially those involving the cervical spine and

neck musculature, may actually be secondary to the vestibular disorder itself. Individuals

prone to vertigo and disequilibrium will limit head and trunk movements in order to

avoid symptoms. Over time, these limitations of movement may cease to be volitional

and require specific consideration.

The presence or absence of associated neurological injuries also needs to be addressed.

Such injuries may limit or prohibit motor control. These abnormalities may be subtle and

manifested only on sophisticated testing as increased response latencies or may be quite

blatant in the form of spasticity or paralysis. Such disorders may arise out of injury to

either the peripheral or central nervous system. Special note should be made of injuries

to the extraocular muscle system. Inability to appropriately move and position the eyes

may have a significant effect on balance and equilibrium and certainly can be expected

to complicate a proposed program of vestibular rehabilitation.

Additionally, and perhaps particularly, important in post head injuries is injury to the

cortical, subcortical, and brainstem areas. Such injuries may produce abnormalities of

sensory selection, gaze control, and perceived stability. It is probable that some of the

abnormal oculovestibular reflex (production of vertigo secondary to repetitive rapid move

ment in the visual field) seen in post-head-injury patients also occurs at this level. Often

times, sophisticated neuropsychiatric testing will have documented abnormalities of

memory, perception, and cognitive processing which are frequently associated with post

head-injury cortical dysfunction.

Any or all of the above associated difficulties may contribute to the patient’s symptom

atology and require specific and special consideration when a vestibular rehabilitation

program is being designed. 61,62 Clearly, individuals with significant associated visual def

icits will need management different from those who have associated spastic hemiparesis.

Many patients requiring vestibular therapy, and especially the post-head-injury patient,

will have suffered significant deconditioning and require directed programs to improve

both muscle strength and general aerobic conditioning.

Vestibular Rehabilitation Process

The process of rehabilitation consists of several parts:

- Vestibular adaptation
- Substitution of other strategies

- Desensitization (habituation)
- Balance retraining
- Cardiorespiratory training or conditioning

Vestibular Adaptation

Adaptation describes the ability of the vestibular system to make long-term changes in the

neuronal response to input. The signal that induces adaptation is the movement of a visual

image across the retina, referred to as retinal slip. The brain adapts by increasing the gain

of the vestibular responses. This can be accomplished using two simple exercises that are

designed to progressively increase the gain of the vestibular system by inducing retinal

slip. In one exercise, the patient is instructed to maintain visual fixation on a stationary

object while moving his head back and forth. A second exercise uses a moving target, with

the target and the head moving in opposite directions while maintaining fixation.

Substitution

Substitution exercises aim to enhance other strategies for balance (such as postural stability

and gaze) in patients with severe bilateral loss of vestibular function. Unfortunately, no other

mechanism can completely compensate for the loss of vestibular function, and most patients

will continue to have some instability and oscillopsia while pursuing daily activities.

Desensitization (Habituation)

Peripheral lesions produce hypersensitivity to movement

with dizziness and nausea as

common complaints. Patients are particularly sensitive to specific angular or linear accel

eration and deceleration. 63 Desensitization is accomplished by giving the patient a variety

of positional exercises designed to reproduce his vertiginous symptoms. These are

repeated twice daily for 10 to 15 minutes until the symptoms are ameliorated. The simplest

(though often effective) habituation exercises are those first used by Cawthorne (Table

5.3). 64 A variety of more sophisticated techniques are also used. 17,55,65,66 It is important to

explain to the patient that, in order to get less sensitive to these complaints, it is necessary

to provoke them. With repetition of the prescribed exercise, sensitivity to these movements

will subside (Figure 5.9).

Graphs are used to illustrate progress over a period of time. They are good tools for

motivation for the patient and give the clinician information regarding the effectiveness

of the program.

Balance Retraining

Balance retraining with any vestibular lesion will always start at a level that the patient

is independently able to perform. It is very important to stress the issue of independence

with rehabilitative exercise, as this will build confidence.

Repetition of the balance exercise, during the session as well as for an agreed period of

time after the session, helps build confidence because the

exercise will become easier to

perform and can be performed quicker. Simplicity of design will enhance both repetition

and independence. Obstacle courses are good exercise, but in the beginning of the reha

bilitation process, they may increase the patient’s sense of frustration rather than his feeling

of accomplishment. Functionality of the exercise is important — nothing will frustrate the

balance-impaired subject more than exercise that has no bearing in daily life. Realistically,

do we improve a person’s ability to balance if we teach him to stand on one leg?

The treatment approach with balance retraining is not identical for peripheral or central

lesions; however, the philosophy remains the same. The difference is that centrally affected

patients are exposed to the same exercise longer during a treatment session and for a longer

period of time. (The time necessary until they can move to more complex balance activities.)

Central Vestibular Lesions

Central vestibular lesions are hard to deal with as they do not respond to desensitization

exercises as described in the above group. Central vestibular pathology gives rise to TABLE 5.3 Cawthorne Head Exercises Begin in a sitting position — Lie flat on your back Roll to the left side Roll to the right side Back flat Sit up Now stand — Turn to the right Turn to the left Sit again — Put your nose on your left knee Place your right ear on your right shoulder Nose to right knee Left ear on left shoulder While sitting — Turn your head counter-clockwise Now turn it clockwise Repeat while bending forward Repeat while going from a sitting to erect standing position Repeat as you move your head forward Repeat as you move your head backward In a sitting position — Hang your head between your legs, turning to the left Sit

Hang your head, turning to the right Sit Hang your head in the middle, between your legs Sit Note: These exercises have been used since the 1940s as effective treatment for vertigo and disequilibrium. The patient is asked to select the six exercises from the above list which provoke the most severe symptoms. He is asked to perform these six selected exercises for 10 minutes twice a day. Source: From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury: evaluation and management, Traumatic Brain Injury Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With permission.

complaints that cannot be specifically provoked by certain movements or positions but

form a more steady ingredient in the activities of daily life of a patient. 61,66,67

A diagnosed central lesion does, therefore, require a somewhat different approach. The

diagnosis “central lesion” does not exclude the possibility of adaptation of the central

nervous system. The expectation, however, is that rehabilitation will be less complete and

usually take a longer period of time.

A program based on angular and linear acceleration and deceleration can be imple

mented, but with more repetitions per session, usually at a lower speed and maintaining

the program for a period of 6 to 12 weeks. Cardiorespiratory endurance training (discussed

later in this chapter) is even more crucial to these patients than to the above-described

group as physical reconditioning will enhance self-confidence and esteem, which will

impart overall motivation.

The effects of such an approach are:

- A decrease in vestibular symptoms

- An increase in self-confidence
- An increase in physical activity

Cervical Vertigo

This is a condition where the complaint of dizziness is related to posterior or lateral cervical

myofascial pain dysfunction syndrome, i.e., decreased range of motion of the cervical

spine with pain. The proper approach here is to deal with the orthopedic dysfunction first

— that is, first treat the pain and impaired motion.

Several recent studies support the benefit of customized vestibular rehabilitation in

patients with vestibular deficits. In a 1998 report, Cowand et al. 68 used the Dizziness

Handicap Inventory (DHI) to retrospectively study a group of 37 patients undergoing

vestibular rehabilitation and found a significant improvement in test scores of 78% of

patients posttreatment. This is in agreement with previously published reports of Cohen, 69

Keim, 70 and Telian et al. 71

Horak et al. studied the relative effectiveness of vestibular rehabilitation, general con

ditioning exercises, and vestibular suppressant medication on dizziness and imbalance in

patients with chronic vestibular symptoms. 72 They found that all methods reduced dizzi

ness but that only vestibular rehabilitation improved postural stability. A 1995 report from

Shepard et al. analyzed the benefits of customized vs. generic vestibular rehabilitation

therapy programs and found that a superior level of

vestibular compensation was

achieved in the patients undergoing customized rehabilitation. 73 After 3 months of therapy,

only the group performing customized vestibular rehabilitation exercises had a significant

reduction in dizziness during daily activities, improvement in postural stability, reduction

in motion sensitivity, and a decrease in asymmetry of vestibular function. Patients receiv

ing generic vestibular rehabilitation improved only in static postural stability.

An unsupervised program of Cawthorne-Cooksey 64 exercises is not as effective as a

customized, supervised program of vestibular adaptation exercises. Each patient with

vestibular dysfunction after traumatic brain injury should, therefore, be independently

evaluated in the context of his unique cognitive and vestibular symptoms.

Cardiorespiratory Endurance Training or Conditioning

The vestibularly-impaired patient experiences difficulty with balance, or nausea and diz

ziness, when moving about and, therefore, becomes less active, no matter what the pre

morbid lifestyle. As a consequence, patients experience deconditioning and, sometimes,

undesirable weight gain as a result.

Ideally, patients can be started on the Schwinn Air Dyne bicycle with a modified Cooper

test to get baseline information on the level of conditioning. This stationary bike provides

a gentle form of exercise which rarely triggers vestibular complaints. Patients are encour

aged to maintain a pace that will elevate their heart rate to a level appropriate for their

sex and age group (target heart rate). Resting heart rate, postexercise heart rates (imme

diately after stopping and 5 minutes thereafter), and resting blood pressure are monitored

(Figure 5.17).

Not all patients can be motivated to participate in such a rigorous exercise routine and

they are asked to participate in another form of endurance exercise. Most patients can be

motivated to participate in some form of cardiorespiratory training, and it is best to engage

the patient in a form of training that has his or her full motivation because it will increase

the possibility of overall success of the rehabilitation process. Therefore, in addition to

the use of the Schwinn Air Dyne bicycle, treadmills, swimming pools, walking groups,

stair climbers, or anything else that will increase the activity level of vestibular patients

can be used.

A number of variables will influence the outcome. First and foremost is compliance.

The program of vestibular rehabilitation requires the patient to spend 15 minutes twice a

day in specifically directed exercises which are advanced on a weekly or biweekly basis.

A typical program will require 8 to 12 weeks. Poor compliance is common in individuals

with multiple deficits and they generally do less well. Poor compliance may result because

the patient has had serious central nervous injury which impairs motivation and cognition,

or because associated musculoskeletal or sensory injuries make it impossible to perform

the most helpful sorts of exercises. In many of these patients, two to three rehabilitation

programs will be in progress simultaneously, which may overwhelm the patient's ability.

Individuals with central dysfunction improve at a much slower rate and may never

FIGURE 5.17

The above cardiorespiratory endurance table is used on a weekly basis to evaluate cardiovascular fitness

improvements. (From Ashley, M. J. and Krych, D. K., Eds., in Vestibular dysfunction after traumatic brain injury:

evaluation and management, Traumatic Brain Injury Rehabilitation, 1st ed., ch. 6, 1995, 131–169. With permission.) Cardiorespiratory Endurance Clearance for Fitness Program Obtained: From Formula 12 Minute Cooper Air-Dyne Bicycle: Distance Post Exercise Heart Rate 5 Minute Recuperating Heart Rate Fitness Category: Men 205 – 1/2 age × .8 Women 220 – age × .8 (M.D.) Date Resting Blood Pressure: Resting Heart Rate: Target Heart Rate for M/F Age

achieve the same improvement as those who have peripheral receptor-level disorders.

Age is another variable which works against rapid recovery.

There is objective evidence to support the usefulness of vestibular rehabilitation. Telian

et al. have evaluated the outcome in 98 patients with a variety of different vestibular

problems. 66,74 Some patients were excluded because of disease process but all had to meet

one of the following criteria: (1) positional or motion provoked vertigo, (2) abnormalities

of SOT or abnormal recovery strategies, and (3) abnormal

chair/ENG findings. After a

10- to 15-week program performed at home, 87% of patients reported significant subjective

improvement and 83% had objective improvement in disability ratings. Of the patients,

31% were completely asymptomatic at the time a follow-up evaluation was performed,

and 10% were worse. Half of the latter had unequivocal progressive unilateral vestibular

injuries and underwent deafferentation surgical procedures.

Summary

In summary, vestibular rehabilitation is an effective way of utilizing the central nervous

system’s natural plasticity to compensate for vestibular dysfunction. Specifically, it is

useful to improve postural and balance control, eliminate vertigo and disequilibrium, and

reduce the effects of visually provoked stimuli. While most patients achieve improvement,

only about one third achieve complete elimination of symptomatology. It is useful to

present these techniques to the patient as methods for managing and controlling symptoms

rather than eliminating them. Vestibular rehabilitation needs to be integrated into an

overall plan which takes into consideration all of the patient’s deficits as well as his assets

and abilities. Those therapists whose priority is improvement in balance and elimination

of vertigo need to constantly coordinate with the patient’s multidisciplinary team leader

to achieve a maximally effective overall rehabilitation strategy for the posttraumatically

brain-injured individual.

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6

Visual Dysfunction Following Traumatic Brain Injury

Ronald L. Morton

CONTENTS

Introduction

Individuals sustaining traumatic brain injury (TBI) often sustain other injuries in tandem

with injury to the brain. Injuries involving the face, neck, back, torso, and extremities are

commonly associated with TBI. Frequently, these injuries are readily diagnosed and treated

as they are easily evidenced when the person presents at the emergency room.

Less obvious injuries, however, can be overlooked during lifesaving endeavors, in par

ticular, those involving systems which are more difficult to thoroughly evaluate, such as

the vestibular or visual systems. This chapter focuses on deficits commonly observed in

the visual systems of people with TBI. The purpose of the chapter is to provide a review

of the neuroanatomy of vision and illustrate the relationship of commonly observed

visual-perceptual and visual-motor deficits following TBI to neuroanatomical structures.

Visual system dysfunction following TBI is fairly common and can be quite subtle or

relatively frank. Bontke et al. found the overall incidence of cranial nerve injury, for

example, in persons hospitalized following traumatic brain injury to be 19%. Cranial Nerve

VII was most frequently injured (9%), while Cranial Nerves III (6%) and VI (6%) followed. 1

The visual system has not been long regarded as one which can respond to treatments

that are other than compensatory (i.e., lenses) or surgical in nature. That the visual system

can respond to treatments which impact visual-perceptual and/or visual-motor skills is

a relatively recent concept as applied to acquired neurological damage. The visual system

functions as a primary sensory receptor for motor, social, cognitive, communicative, and

emotive functions. As such, the visual system is highly integrated with many neural

functions other than simply sight. Visual system disorders, then, require a fair amount of

attention in the person with TBI and should be considered an integral part of the rehabil

itation program. Remediation of visual-perceptual and visual-motor disorders can

enhance function in all of the aforementioned areas as well as reduce the likelihood of

reinjury and enhance maximal functional improvement.

Anatomical Considerations

Retina

In order to fully appreciate the complexities of the visual system, one must recognize that

visual integration is not just a cortical process. Rather, visual integration begins periph

erally in the visual receptor fields of the retinas. 2

The fact that visual processing starts in the retina may seem strange until it is recalled

that the eye is actually an outpouching of the brain from early in embryological develop

ment. 3,4 Figure 6.1 depicts the organization of the photoreceptors, bipolar cells, and gan

glion cells. Photoreceptors, when stimulated, pass information to adjacent bipolar cells,

which, in turn, differentially affect firing of the ganglion cells. Linear and cross connections

FIGURE 6.1

Eye anatomy. (From The Eye (chart), Jacobson, W., Jr., Ed., Anatomical Chart Co., Skokie, IL,1986. With permission.)
Internal

Limiting Membrane External

Limiting Membrane Pigmented Epithelium Layer of

A) Rods and B) Cones Inner

Plexiform Layer Outer

Plexiform Layer Inner

Nuclear Layer Outer

Nuclear Layer

Nerve Fiber Layer

Ganglionic Layer Cell Body of Müller Cell Ganglionic Cells
Amacrine Cells Bipolar Cells Horizontal Cells Rods Cones
Pigment Cells

Choriocapillaris Retina C C B B B A A D Müller Cell:
A-Horizontal Fibers B-Honeycomb Meshwork C-Radial Processes
D-Fiber Baskets

of ganglion and adjacent bipolar cells is demonstrated by the fact that the adjacent bipolar

cells increase the firing rate of ganglion cells when certain conditions are met.

For example, if a spot of light lands on one photoreceptor while adjacent photoreceptors

remain unilluminated, the stimulated photoreceptor will fire at a higher rate compared

to the rate at which it will fire when all surrounding photoreceptors are simultaneously

illuminated. These patterns of illuminated and nonilluminated photoreceptors were

referred to by Werblin and Dowling 5 as on-center and off-surround groups.

On-center and off-surround groups may be joined in such combinations as to form units

sensitive to stimuli in the environment of particular spatial orientations. These include, for

example, vertical, horizontal, and diagonal lines or edges. Stimuli which are thus organized

are relayed to the cortex via the optic tract. The processing of visual stimuli continues, via

the optic tract, to be further processed in the lateral geniculate bodies, the occipital cortex,

and associated cortices receiving radiations from the primary occipital areas.

As a normal individual gazes upon an object, the image is

registered simultaneously in

both the right and left retina. Each retina, however, is situated slightly differently in

orientation to the object, thus producing a slightly different image to the brain from each

retina. 6 This can be demonstrated by gazing at an object and alternately closing one eye,

then the other. The object appears to move due to the fact that the image registered is

different because of the distance separating the eyes and the slight difference in angular

orientation of each eye to the object. Stereopsis, which is the ability to visualize the

dimension of depth, arises from the fusing of these two separate images by the sensory

system 6 and, consequently, plays a major role in several visual perceptual skills.

Optic Tract Organization and Lesion Characteristics

Knowledge of organization of the optic tract is of great importance in determination of

site of lesion from visual deficits presented. Lesions at different points in the optic tract

will be demonstrated by pathognomonic visual deficits. 4 In the days prior to CT scanning

and magnetic resonance imaging (MRI), the localization of injury was dependent upon

knowledge of anatomical relationships. Knowing the proximity of motor and sensory

pathways adjacent to the visual pathways allowed determination of site of lesion based

upon the constellation of signs and symptoms. Localization of the site of lesion or injury

can assist in further diagnosis, determination of etiology,

and likely systemic sequelae.

Each retina must direct its information toward the cortex and does so via the optic nerve.

The information passes from the ganglion cells, located in each retina, posteriorly via the

optic nerve to the optic chiasm. Figure 6.2 illustrates how, at the optic chiasm, right and

left visual space are segregated with the contribution of each hemi-retina passed to a single

corresponding lateral geniculate body, the specific thalamic relay nucleus for the visual

pathway. 7 Right visual space images upon the nasal retina of the right eye and the temporal

retina of the left eye. At the chiasm, the optic fibers of the nasal retina of the right eye

cross to the left to join the optic fibers of the temporal retina of the left eye. The temporal

fibers of the left eye continue uncrossed in the optic tract beyond the chiasm and find

their way to the lateral geniculate body on the left. Thus, the left lateral geniculate body

receives information from the right visual space from both eyes.

Information from the upper retinal fibers (nasal crossed, temporal uncrossed) passes

through the corresponding lateral geniculate body and continues in a portion of the optic

tract known as the geniculocalcarine tract until it projects to the primary visual cortex

(cuneate gyrus, Area 17) of the occipital lobe. 8 The geniculocalcarine tract courses through

the parietal lobe; a lesion involving the geniculocalcarine tract on the right would result

in an inferior contralateral quadranopsia (Figure 6.2, Item 9).

Information from the nasal lower retina, however, after crossing over at the optic chiasm

to join the temporal lower retinal fibers, leaves the lateral geniculate body and courses

into the temporal lobe (Figure 6.3) in a band of fibers known as Meyer’s loop. 8 These fibers

terminate in the lingual gyrus of the occipital lobe. A lesion involving Meyer’s loop on

the right would cause a contralateral left superior quadranopsia (Figure 6.2, Item 10).

Bitemporal hemianopsia (Figure 6.2, Item 4), for example, results from a lesion which

involves the optic chiasm, in particular, the fibers which cross from the nasal field of each

retina, serving temporal visual space, to the lateral geniculate body of the contralateral

side of the brain. Pituitary hormone dysfunction may be associated with this visual system

deficit due to the proximity of the optic chiasm to the pituitary gland. Binasal hemianopsia

(Figure 6.2, Item 5), on the other hand, would implicate a lesion of the lateral aspects of

the optic chiasm involving the uncrossed temporal fibers from the nasal fields of each

retina. In this instance, carotid disease may be involved.

The primary visual cortex is made up of the region of the cortex immediately surround

ing the calcarine fissure, extending anteriorly toward the splenium of the corpus callosum. 9

This area is known as the calcarine cortex. Lesions involving selective portions of the

FIGURE 6.2

Visual pathway and resultant field defects. (From Jones, L. T., Reeh, M. J., and Wirtschafter, J. D., Ophthalmic

Anatomy: A Manual With Some Clinical Application, American Academy of Ophthalmology, San Francisco, 1970,

Figure 9, p. 176. With permission.) VISUAL Left Right 1. 3. 4. 6. 7. 8. 8. 11. 7. 9. 10. 10. 9. 4. 3. 6. 1. 2. 5. Left VISUAL Right Eye Left Eye Retinal Ganglion Cells Optic Nerves Optic Chiasm Optic Track Lat. Geniculate Body Parietal Lobe Left Hemisphere Lateral View Temporal Lobe Lateral Ventricle Optic Radiation Calcarine Fissure Left Hemisphere Medial View FIELDS Right 11. 12. 13. 14. 12. 13. 14. FIELDS

calcarine fissure and occipital pole can likewise present with specific visual field defects.

Figure 6.2, Item 12, depicts an occipital pole lesion induced central scotoma. A lesion at

the mid-portion of the calcarine fissure or of fibers to this area would result in a contralat

eral homonymous hemianopsia with macular sparing (Figure 6.2, Item 13). Lastly, a lesion

involving the anterior portion of the calcarine fissure results in a contralateral temporal

crescentic field deficit (Figure 6.2, Item 14).

Oculomotor and Brainstem Organization

Discussion of the visual system must include a review of the oculomotor system and its

innervation. Oculomotor deficits following brain injury can result in misalignment of the

eyes which, in turn, may be reported by the person as double vision, blurred vision,

impaired eye/hand coordination, impaired tracking during reading, and so on. Misalign

ment of the eyes can also lead to cortical image suppression with resultant perceptual

deficits which will impact therapeutic performance, balance, coordination, and safety.

Perhaps the most common oculomotor dysfunction seen is that of esophoria. In this

condition, the lateral rectus of one eye is weakened, presumably due to injury to the

corresponding Cranial Nerve VI nucleus or pathway. These people may report blurred or

double vision, though they may also accommodate to misaligned images via cortical

suppression of the image from one eye. Careful evaluation may turn up additional subtle

impairments of other extrinsic muscle innervations. Suffice it to say that innervational

deficits resulting in complete or partial motor paralysis of the corresponding extrinsic

muscles are prevalent following TBI and require careful delineation and treatment.

The six extrinsic muscles of the eye 10 are innervated by three cranial nerves as listed in

Table 6.1. Cranial Nerve III is responsible for innervation of the superior rectus, medial

rectus, inferior rectus, and inferior oblique. The superior rectus rotates the eye upward

when the eye is abducted; however, when the eye is adducted, this muscle moves the

superior part of the eye toward the medial wall of the orbit (intorsion). The medial rectus

rotates the eye nasally. The inferior rectus rotates the eye downward when the eye is in

abduction and extorts the eye when in adduction. The inferior oblique elevates the eye

when the eye is adducted and extorts the eye during

abduction.

Cranial Nerve IV innervates the superior oblique which is responsible for eye depression

during eye adduction and intorts the eye during abduction (Figure 6.4). Cranial Nerve VI

innervates the lateral rectus which produces temporally directed rotation of the eye.

FIGURE 6.3

Meyer’s loop. (From Willis, W. D. and Grossman, R. G., Medical Neurobiology: Neuroanatomical and Neurophysio

logical Principles Basic to Clinical Neuroscience, 2nd ed., C.V. Mosby, St. Louis, MO, 1977, p. 287. With permission.)

The nuclei of Cranial Nerves III, IV, and VI are found in the brainstem, ranging from

the midbrain to the pons. 11 Figure 6.5 shows the nuclei of Cranial Nerve III located inferior

to the superior colliculus and lateral to midline on either side. The axons innervating the

four extrinsic muscles of the eye innervate ipsilateral muscles, except for the superior

rectus which may project contralaterally. 2

The nucleus of Cranial Nerve IV is located below the inferior colliculus. Innervation of

the superior oblique muscles is contralateral in nature. Finally, the Cranial Nerve VI nucleus

is located in the pons. Its axons remain ipsilateral as they innervate the lateral rectus muscles.

These three cranial nerves are interrelational in function. The medial longitudinal fas

ciculus (MLF) comprises the major projection system allowing such interrelation (Figure

6.5). 2 Vestibular projections influencing eye movement connect to these cranial nerves via

the MLF and account for a good portion of the MLF. The vestibular projections arise

mainly from the superior and medial vestibular nuclei. These interconnections between

vestibular and ocular nuclei are responsible for coordination of head/eye movements and

the production of nystagmus following vestibular over-stimulation.

Cranial Nerves III, IV, and VI receive afferents from the retina, the frontal and occipital

lobes, the vestibular nuclei, and the superior colliculus. There may be reticular projections

as well. 2

The nucleus of the oculomotor nerve, Cranial Nerve III, is located dorsally within the

midbrain beneath the Aqueduct of Sylvius connecting the third and fourth ventricles. The

nuclear complex represents a collection of subnuclei that have specific identifiable TABLE 6.1 Cranial Nerve Innervation Cranial Nerve Muscle Innervated Brainstem Nucleus III Pupiloconstrictor and Ciliary Muscles Superior, Inferior, and Medial Rectus Inferior Oblique Levator Palpebra Edinger-Westphal Oculomotor IV Superior Oblique Trochlear VI Lateral Rectus Abducens

FIGURE 6.4

Musculature of the eye and cranial nerve innervation.

functions. Most dorsally, the levator complex is a midline structure that supplies both

third cranial nerves. Rostrally, the Edinger-Westphal nucleus is a paired structure that

sends parasympathetic signals to the sphincter muscles of the pupil via the ciliary ganglion

and the muscles of accommodation of the ciliary body (Figure 6.6). The medial complex,

which lies most ventrally, has been shown to contain three subnuclei that play variable

roles in medial rectus functions. One of these subsets may receive input from the mesen

cephalic reticular formation, firing in response to retinal temporal disparity that indicates

a near target. The inferior rectus subnucleus lies dorsally and rostrally. The inferior oblique

subnucleus lies laterally between the inferior rectus subnucleus and the more ventral

medial rectus subnucleus. Fibers exit ventrally along with the fibers destined to innervate

the medial rectus, inferior rectus, and the pupil and ciliary body. The superior subnucleus

which lies along the midline is unique in that the fibers cross within it before exiting

ventrally with the fibers destined for the levator and superior rectus. Cranial nerve III

runs slightly oblique to the tentorial edge parallel to the posterior communicating artery.

Pupillary fibers are usually found to run on the medial surface of the nerve where they

are particularly sensitive to compression and potential inflammation. The most medial

aspect of the temporal lobe, the uncus, which is located just above the tentorium and the

subarachnoid third cranial nerve, may be forced through the tentorial notch with a supra

tentorial mass lesion or hemorrhage and stretch the third cranial nerve against the superior

cerebellar artery resulting in abnormality. As can be seen from the relationships in Figure

6.5, with the sixth cranial nerve tethered as it exits the

brainstem and prior to entering

Dorello’s canal, an axial movement of the brainstem can result in stretching or damage to

Cranial Nerve VI. The fourth cranial nerve is not pivoted as tightly but is exposed to the

tentorium which sweeps around it and so an anterior-posterior movement or swelling of

the brain can push on cranial nerve IV and damage that as well during its exposed, long

course outside the brainstem.

The fourth cranial nerve lies within the gray matter in the dorsal aspect of the caudal

midbrain, just below the Aqueduct of Sylvius, contiguous with the rostral third cranial

FIGURE 6.5

Brainstem and nuclei and oculomotor complex in mesencephalon cutaneous. Oculomotor Complex in Mesencephalon Cerebral Aqueduct Edinger-Westphal Nucleus III Caudal Central Nucleus III Lateral Nucleus III Edinger-Westphal Lateral Nucleus III Anterior Median Velum Oculomotor Nerve III MLF Red Nucleus Periaquenductal Gray Trochlear Nerve IV Superior Oblique Muscle Cliliary Ganglion Inferior Rectus Muscle Inferior Oblique Muscle Medial Rectus Muscle Levator Palpebra Muscle Superior Rectus Muscle IV Nucleus Brainstem at Level of Pons Medial Longitudinal Fasciculus Red Nucleus

Midbrain Pineal Body Superior Colliculus Inferior Colliculus IV Nerve Trochlear Vestibular Nuclear Complex Facial Nucleus Medulla VI Nerve

VII Nerve

Pons

III Nerve

Oculomotor Nucleus

Pontine Paramedial

Oculomotor Nucleus

FIGURE 6.6

Edinger-Westphal nucleus and ciliary ganglion. Lateral Geniculate Nucleus of the Thalamus Medial Longitudianal Fasiculus Nucleus of the Posterior Commissure Posterior Commissure Edinger-Westphal Nucleus (CNIII) Mammillary Bodies Optic Chiasm Nasal Field Pupilloconstrictor Muscle in the Iris Temporal Fields Cilary Ganglia Retinal Ganglion Cell Nasal Field Cranial Nerve III

nerve nucleus (Figure 6.7). The intra-axial portion of cranial nerve IV runs dorsally around

the periaqueductal gray to cross within the anterior medullary vellum below the pineal

gland. The fourth cranial nerve is the only cranial nerve exiting on the dorsal surface of

the brain and brainstem. It has the longest unprotected intracranial course and lies just

under the tentorial edge where it is easily damaged by closed head trauma. Just below

the anterior tentorial insertion, cranial nerve IV enters the posterior lateral aspect of the

cavernous sinus just underneath Cranial Nerve III, runs forward within the lateral wall

of the cavernous sinus, then enters the superior orbital fissure just outside the Annulus

of Zinn, and crosses over the optic nerve down to the superior oblique muscle.

The sixth cranial nerve originates in the dorsal caudal pons just beneath the fourth

ventricle, surrounded by looping fibers of the seventh cranial nerve. The nucleus contains

the primary motor neurons and interneurons across from the contralateral medial longi

tudinal fasciculus to reach the third cranial nerve nucleus for coordination. Pathology

affecting the sixth cranial nerve nucleus produces an ipsilateral gaze palsy. The axons exit

the nucleus, travel ventrally and slightly laterally, medial to the superior olivary nucleus,

to exit on the ventral surface of the caudal pons. After exiting the brainstem, the sixth

cranial nerve runs rostrally within the subarachnoid space and over the surface of the

clivus from the area of the cerebellopontine angle to the posterior superior portion of the

posterior fossa. The nerve pierces the dura and travels forward to lie free within the

cavernous sinus but runs parallel to the horizontal segment of the carotid artery within

the cavernous sinus (Figure 6.7). It enters the supraorbital fissure through the Annulus of

Zinn to enter and innervates the lateral rectus muscle.

Frontal Eye Fields

The frontal lobe contains two regions which are also of importance in oculomotor control.

Much of what we know about these fields arises from studies with monkeys. The frontal

eye field (FEF), the supplementary eye field (SEF), and the dorsolateral prefrontal cortex

are primarily implicated in saccadic control mechanisms (Figurer 6.8). Two specific types

FIGURE 6.7

Course of cranial nerves through the cranial vault. Trigeminal Nerve (V) Trigeminal Ganglion I II III Oculomotor Nerve (III) Abducens Nerve (VI) Trochlear Nerve (IV) Superior Orbital Fissure Pituitary Gland Cavernous Sinus Midbrain Optic Nerve (II)

of neurons are found in the FEF — movement-related neurons

and visuomovement neu

rons. Movement-related neurons fire during all saccades regardless of whether the saccade

is directed for the purpose of target location. These neurons fire only when the saccades

are relevant to the organism’s behavior and project to the superior colliculus. Electrical

stimulation of a unilateral FEF will cause a saccade to the movement field of the neuron

which has been stimulated. Bilateral stimulation to the FEFs causes vertical nystagmus.

Visuomovement neurons are implicated in visually-guided saccades. They are active in

both visual- and movement-related activity. 12

Saccadic movements which are involved in cognitive processing appear to be located

in the supplemental eye field and the dorsolateral lateral prefrontal cortex. Saccades to a

part of a target involve the SEF while saccades to a remembered target involve the

dorsolateral lateral prefrontal cortex. 12

Persons with damage to the FEF may have difficulty suppressing a saccade to a visual

target to which they are attending. Parietal neurons implicated in attentional processing

send a signal to the superior colliculus, while the signal arising from the FEF which should

suppress the saccade by inhibiting the stimulus sent to the superior colliculus fails to do so. 12

Eye movements in mammals occur largely in coordination with cognitive function.

Direction of eye movement involves cortical centers which communicate with the superior

colliculus in order to effectuate eye movement. 12

Pupillary Responses

Pupil size is modulated by both the sympathetic nervous system with its dilator fibers

and the parasympathetic system with its constrictor fibers. Pupils are normally of equal

size, but differences of less than 1 mm may be present in as much as 20% of the normal

population. Pathologic anisocoria is caused by lesions either of the sympathetic or para

sympathetic pathways or by local iris disease, such as tumors or scar adhesions.

Sympathetic impulses to the eye originate in the hypothalamus. They are transmitted

along the spinal cord, synapsing in the lateral grey columns. They exit the cord via

FIGURE 6.8

Frontal and supplementary eye fields of the frontal lobe. Supplementary Eye Fields Posterior Parietal Cortex Frontal Eye Fields Caudate Nucleus Substantia Nigra Pars Reticulata Mesencephalic and Pontine Reticular Formations Superior Colliculus

preganglionic fibers at C8 to T2 and travel upward in the sympathetic chain to synapse

in the superior cervical ganglia, lying at the level of C1 and C2. Nonmyelinated, postgan

glionic fibers form a plexus around the common carotid artery with vaso-motor fibers to

the face and the external carotid artery. The internal carotid artery carries sympathetic

nerves through the cavernous sinus where the fibers join the nasociliary branch of cranial

nerve V. From the nasociliary nerve, they travel into the

eye to the radial dilator muscle

fibers in the pupils, resulting in dilation.

Parasympathetic pre-ganglionic axons originate in the Edinger-Westphal nucleus of the

third cranial nerve (medulla) where they produce a simultaneous and bilateral response

in each third nerve through intraneuronal connections. The parasympathetic pre-gangli

onic axons run forward in the third nerve and pass through the inferior division of the

anterior aspect of the cavernous sinus to the ciliary ganglion for synapse on their way via

the short ciliary nerves into the annular constrictor pupillary fibers. The output of the

Edinger-Westphal nucleus represents the summation of the input from both the right and

left eyes via a certain set of the ganglion cells, some of which cross in the chiasm, along

with the other visual fibers through the optic tract and lateral geniculate body on their

way to synapse at the Edinger-Westphal nucleus.

This summation, at the Edinger-Westphal nucleus, allows one to elicit a relative afferent

pupillary defect — a different pupil size in response to a monocle light stimulus. This

reaction is caused by an asymmetry of conduction in the afferent visual system, either at

the retina or optic nerve, specifically in the area anterior to the lateral geniculate body. To

illustrate, when a traumatic optic atrophy causes the loss of a significant number of

ganglion cell axons, the conduction of a light stimulus to the Edinger-Westphal nucleus

is diminished and a larger pupil will result (i.e., 5 mm) rather than the small pupil resultant

from full stimulation (i.e., 3 mm). Therefore, as a light is swung 13 from the normal side,

with 3-mm pupils in both eyes, to the affected side, the pupils will dilate to 5 mm.

Visual Fields

An understanding of visual field integrity is of key importance in accurate diagnosis of

visual deficits and their neurological correlates in the person with TBI. 14 Visual field is

measured in degrees and the center of fixation is used as a zero referent. Visual field

extends to approximately 90 degrees in all directions. Decreasing sensitivity is found the

farther out the stimulus is from center. Targets in the less sensitive periphery must be

larger and brighter to be seen.

Two types of measurement devices are available for delineation of visual fields. Devices

can be categorized as kinetic or static, depending upon whether the stimulus moves or is

stationary. The Goldmann Perimeter is a kinetic device in which the stimulus presented

is a spot of light of specific size and intensity which is moved toward the center of fixation

until the person reports seeing it. The Humphrey Perimeter is a static device which

measures visual field by increasing the brightness of a spot at a fixed location until the

person sees it. These two devices have been demonstrated to be fairly accurate and reliable

in tests of both a neurologically- and nonneurologically-impaired population. Goldmann

fields have been shown to be 97% reliable while Humphrey fields were 91% reliable. 15

Diplopia fields are evaluated using the Goldmann Perimeter. The person is not patched,

as they would be for peripheral field testing. The person is positioned at the machine so

that the fixation light is aligned between the person's eyes. A light is introduced. The

person follows this light from the center outward and informs the examiner when it

breaks into a double image. Thus, a specific map of the person's diplopia is made and

can be tracked as treatment progresses. It should be noted that the vast majority of

diplopia can be accounted for as a result of acquired paresis or palsy of one or more of

the extraocular muscles. 16

Visual fields can also be evaluated by "confrontation" which requires no elaborate

devices. Confrontation testing is performed by movement of the examiner's finger or a

red bottle cap slowly into the person's visual field, with central visual fixation, until the

stimulus is viewed. While not a precise system of measurement, confrontation testing can

reliably demonstrate certain visual field deficits in the absence of more elaborate testing. 16

Fading of the color red in the field periphery can be an early sign of visual field depression.

Examination

Examination of the person with TBI should first establish

best corrected visual acuity, if

at all possible. This can be difficult to establish due to problems the person may have in

cooperating with the evaluation. Communication problems may be lessened by using the

services of a speech pathologist or family member familiar with the communication deficits

of a given person.

The face should be examined for lacerations, scars, or foreign bodies. Check the lids for

position, remembering that cranial nerve III is responsible for palpebral elevation and

cranial nerve VII for closure via the orbicularis muscles. 17 These motor systems should be

evaluated for weakness. Skin sensation should be checked in distributions of cranial nerve

V (Figure 6.9), possibly manifesting as anesthesia or abnormal sensation, as well as asso

ciated motor functions which can manifest as paresis of mastication. 18 Head and neck

positioning should be carefully evaluated as compensatory head tilts are quite common

due to diplopia and the person’s attempt to compensate for same. 6

Following any facial neuropathy, including a traumatic crush injury, regenerating axons

may reinnervate muscles different from those originally served. Such aberrant regener

ation can cause synkinetic movements. In this situation, the involved facial muscle may

remain weak. Axons originally destined for the orbiculans muscle may reinnervate lower

facial muscles and each blink may cause a twitch in the

corner of the mouth or dimpling

of the chin. Conversely, movement in the lower face, such as pursing the lips or chewing,

may invoke involuntary lid closure. Other disorders of aberrant facial innervation include

lacrimation invoked by chewing, as in crocodile tears, in which fibers originally supplying

the mandibular and sublingual glands reinnervate the lacrimal gland by way of the

greater superficial petrosal nerve. This is commonly seen following severe proximal

seventh cranial nerve injury and may be accompanied by decreased reflex tearing and

decreased taste from the anterior two thirds of the tongue. Another example is a Marcus

Gunn jaw-winking syndrome characterized by eyelid elevation with jaw movement

caused by an anomalous communication between the trigeminal (pterygoid) and oculo

motor (levator) nerves.

The testing of different subsets of the seventh cranial nerve such as salivation, lacrima

tion, and sensation may help to localize a lesion (e.g., sugar/vinegar on the anterior two

thirds of the tongue to test taste). Cutaneous sensation can be evaluated along the posterior

aspect of the external auditory canal and tympanic membrane. All functions of cranial

nerve VII may be involved if the lesion is relatively proximal from the cerebellar pontine

angle to the geniculate ganglia, whereas more distal lesions may affect only certain func

tions, depending on their location. Testing should include

functions of cranial nerves V,

VI, and VIII as this may help further localize the cause of seventh cranial nerve palsy.

Ocular Examination

Examination of the anterior structures of the eye is facilitated by magnification and illu

mination ranging from penlight and bifocals to slit-lamp examination. Slit-lamp exami

nation allows greater detail to be viewed, as well as better assessment of the depth of any

foreign body lodging or scar tissue. The anterior chamber, thus examined, may show blood

or inflammatory debris.

Examination of the pupil can provide clues as to the integrity of cranial and optic nerve

functions. The responsiveness of a pupil to light and accommodative stimuli can provide

information regarding the integrity of the pupillary nerve fibers between the lateral gen

iculate body, the Edinger-Westphal nucleus (part of the nucleus of cranial nerve III in the

medulla of the brainstem), and the sympathetic and parasympathetic nerves which inner

vate the dilators and constrictors of the pupil. Thus, a relative afferent pupillary defect

(APD) may imply optic nerve lesion, traumatic vascular insult, an inflammatory process,

or multiple sclerosis.

As shown in Figure 6.10, behind the pupil is the lens. 2 The lens may be affected by

trauma in a number of ways. These include penetration by a foreign body, laceration of

the globe, blunt trauma to the globe, electrical injury, chemical injury, or concussion. Any

of these injuries can result in a loss of lens clarity and result in cataract formation.

Cataracts may become dense enough to significantly limit visual acuity and may interfere

with the rehabilitative process. In this circumstance, surgical intervention may be

required. It is important to note that cataract formation can be accelerated by some

tranquilizers or steroids.

FIGURE 6.9

Distribution of Cranial Nerve V. (From Warwick, R. and Williams, P. L., Gray's Anatomy, 35th ed., Churchill

Livingstone, London, 1973. With permission.)

Opacities of the ocular media, such as a dense cataract, are usually not sufficient to

produce an APD. However, very dense vitreous hemorrhage or dense amblyopia may be

sufficient, although it is usually indicative of pathologic lesion in the afferent visual system.

This can be correlated with an asymmetric loss of visual field, central acuity, color satu

ration, or subjective brightness. It should be noted, also, that monocular diplopia can arise

from media opacities which cause splitting of the image. 6

The diagram in Figure 6.11 shows that the intact right eye causes more firings of the

central nucleus with light stimulating that side. As the light stimulus is moved to the left

side, relatively less stimulus is received at the nucleus, resulting in less tone at the con

strictor fibers. The result is a larger pupillary aperture. Thus, as the light stimulus is moved

from the intact right eye to the affected left eye, the pupils will dilate as the swinging

flashlight crosses to the affected side. This is called a positive swinging flashlight test or

a left Marcus Gunn pupil. This is an apparent paradox, with a pupil dilating as it is struck

by light, as the light moves from the position determined by the intact right side (i.e., a

3-mm pupil) to the affected left side (i.e., a 5-mm pupil).

FIGURE 6.10

Major components of the human eye. (From Willis, W. D. and Grossman, R. G., Medical Neurobiology: Neuroan

atomical and Neurophysiological Principles Basic to Clinical Neuroscience, 2nd ed., C.V. Mosby, St. Louis, MO, 1977,

p. 282. With permission.)

FIGURE 6.11

Anatomy of pupillary defect. Edinger-Westphal Nucleus Lateral Geniculate Body III Nerve with Afferents to Pupil Motor Fibers Light Stimulus Optic Nerve Lesion L R L R

Trauma may extend to the posterior segment of the eye. As such, injuries can include

retinal breaks, tears, or detachment in which the retina separates from its underlying

supportive tissues, losing function, and ultimately causing wrinkling and scarring. Hem

orrhage may occur and it is possible for there to be contusion to the optic nerve itself.

Extraocular Motility: Peripheral and Central Dysfunction

The extraocular muscles of the eye are responsible for aligning the eyes, enabling them

to be pointed at the same object, and moving the eyes to different positions of gaze in a

manner which allows the continuous perception of a single image. The movement of each

eye is managed by six muscles and controlled by three cranial nerves. Therefore, between

the two eyes, there are twelve muscles and six cranial nerves involved. Any of these

muscles or nerves can be adversely affected following injury, resulting in interference

with the alignment and tracking of the eyes. Injuries such as direct contusion to the orbit

or fracture of the orbit can cause injury to the muscle or nerve complex. Mechanical

entrapment of a muscle can occur or bony fragments from an orbital fracture can impinge

cranial nerves.

The course of the cranial nerves from the brainstem to the orbit makes them subject to

contusion injuries. In particular, cranial nerve VI exits from the ventral side of the brain

stem and ascends the bone along the base of the skull. It enters the superior orbital fissure

of the orbit on its way to the lateral rectus muscle. Cranial nerve IV exits from the dorsal

side of the brainstem and sweeps around to the sides. It also passes through the superior

orbital fissure to innervate the superior oblique. Blunt head trauma, with the associated

violent shaking of the brain, can cause the dura along the dorsal aspect of the brain to

impinge on the nerve as it exits and crosses the dorsum of the brain. The result is a fourth

nerve palsy which manifests in the person as the inability to rotate the eye downward

during adduction and a loss of intorsion during abduction.

In addition to lesions which can affect individual cranial nerves and muscles, resulting

in misalignment, there is also coordination which occurs between various cranial nerve

motor nuclei in a tract in the brainstem known as the medial longitudinal fasciculus (MLF).

The MLF serves as a coordination and integration center between the third, fourth, and

sixth cranial nerve motor nuclei. As an example, when an individual who is looking

straight ahead wishes to turn his/her gaze to the right, several things must happen in a

coordinated fashion. First, the firing rate of the right lateral rectus muscle via the sixth

motor nucleus must increase as must the firing rate for the left medial rectus muscle,

mediated by the third motor nucleus on the left side. At the same time, a relative inhibition

or decrease in the firing rate of the right medial rectus muscle and the left lateral rectus

muscle must occur leading to a deviation of the eyes to the right. A lesion in the brainstem

involving the MLF would interfere with the coordination of these four motor nuclei and

coordination of eye and/or head movements might subsequently be impaired.

Eye movements must be coordinated with changes in head position or acceleration of

the body in any plane which might stimulate the vestibular apparatus. The vestibular

apparatus is mediated through the eighth cranial nerve which has projections into the

lateral gaze center located adjacent to the sixth motor nucleus on the ipsilateral side. The

right horizontal gaze center fires directly into the adjacent right sixth motor nerve nucleus

for its contribution to conjugate deviation of the eyes.

This can be contrasted to a request for a volitional turning of the eyes to the right.

Compliance with such a request would require involvement of the left frontal premotor

area which feeds posteriorly in the white tracts and projects to the right horizontal gaze

center. Consequently, an injury to the frontal lobe or its conduction path to the horizontal

gaze center could adversely affect the ability of a person to voluntarily turn the eyes from

one side to the other. At the same time, vestibular input to the lateral gaze center may

remain intact. The Doll’s Head maneuver, wherein the head is rotated by the examiner

to one side and the normal response is such that the eyes deviate to the opposite side,

can be utilized to test the integrity of pathways from the vestibular nuclei to the lateral

gaze center.

Horizontal and vertical gaze systems are located in different anatomical locations and

tend to function independently of each other (Figure 6.12). Therefore, each should be

examined separately to check for impairment. Also, it is important to note if a person can

hold steady gaze in the primary or eccentric positions in the presence of any type of

nystagmus.

Horizontal gaze palsy with an inability to make a conjugate ocular movement to one

side may result from either pontine or supranuclear lesions. Evaluation by the Doll's Head

maneuver or caloric stimulation 16 to the external auditory meatus allows differentiation

of a lower pontine lesion from one of the supranuclear pathway, which would cause a

loss of saccadic gaze in the direction opposite the site of Lesion A (Figure 6.13). Input

from the intact hemisphere causes ocular deviation toward the site of the lesion. If the

person is unable to look toward that gaze direction by either a voluntary or tracking

movement but can deviate the eyes to the involved side during a Doll's Head rotation,

this demonstrates that the lower pontine reflexes are intact and that the lesion is in the

supranuclear pathway.

The vertical gaze centers are divided above and below the Aqueduct of Sylvius anterior

to the motor nuclei of cranial nerve III. The vertical gaze centers can also be selectively

injured. Damage to the dorsal vertical nerve nucleus will affect the ability to initiate upgaze

beyond midline, allowing horizontal gaze to be preserved with smooth pursuits and

saccades intact (Parinaud's Syndrome).

Vertical gaze palsies caused by a lesion of the upper midbrain in the area of the superior

colliculus can result in three signs known, collectively, as Parinaud’s Syndrome or Dorsal

FIGURE 6.12

Inputs to horizontal gaze center.

Midbrain Syndrome. This is comprised of a loss of vertical gaze ability and pupillary light

reflex, with preservation of near reflex and the presence of an eye movement disorder

called convergence retraction nystagmus. Convergence retraction nystagmus is triggered by

an upward saccade, either voluntary or in response to a downward rotating optokinetic

drum, which causes simultaneous firing of both the medial and lateral rectus muscles

resulting in convergence and retraction of globes into the orbit. Examination of the pupil

shows light/near dissociation with normal-to-mild dilation of pupils and poor or absent

light response but, with an accommodative target, the pupil will constrict to a near

reaction. A person with this condition has the ability to make rapid horizontal saccades

but abilities for voluntary up and down gaze are lost and the person attempts a head

posture change to compensate. A Doll’s Head rotation may show that vertical movement

can be produced with vestibular input when pontine reflexes are intact and only a supra

nuclear pathway lesion is present.

Early lesions in the region of the posterior commissure can affect upgaze preferentially,

particularly vertical saccades. Lesions can press on the

midbrain aqueduct leading to

hydrocephalus and papilledema. A lateral extension of such a lesion can involve the optic

radiation, while a posterior extension of a lesion can produce ataxia from cerebellar

compression. Pineal tumors are the most common of such lesions, although emboli, vas

culitis, arteriovenous malformations, or arteriosclerosis may also be causal factors. An

upper midbrain CVA, by branches from the posterior cerebral artery, can also result in

impairment of vertical gaze with retraction of both upper eyelids, called Collier’s sign.

These symptoms usually recover over 2 to 3 weeks.

As has been stated, ocular deviation or misalignment can result from cranial nerve

palsies. Deviation is often initially incomitant or variable in different directions of gaze.

There is often more deviation in looking to the side of the affected muscle than when

looking away from its field of action. This condition may resolve in time with return to

normal function or the condition may become more comitant, or even and consistent, in

the different fields of gaze. Sequential measurements are used to study the deviation in

FIGURE 6.13

Supranuclear lesion.

nine cardinal positions. Via sequential measurements, the examiner can more readily make

determinations about whether function is returning to normal or whether deviation is

becoming more comitant.

When ocular deviation is relatively even in primary and reading gaze, prisms can be

used to optically move the image to compensate for the mechanical misalignment. Press

on prisms can be applied to the person’s glasses resulting in increased comfort and

resumption of the ability of the person to see binocularly. Press-on prisms may be changed

at will, unlike ground-in prisms. As the person’s divergence reduces, the amount of prism

can also be diminished to maintain alignment and keep fusional vergence drive active as

an aid to further rehabilitation.

Nystagmus

Ocular stability, the maintenance of fixation and alignment on a target, is the result of

multiple input paths in a carefully balanced feedback loop. Elements of the feedback loop

include a visual stimulus and output from the occipital cortex, vestibular system input,

and proprioceptive information arising from head and neck position A decrease or imbal

ance in any of these systems can lead to spontaneous ocular movements and the failure

of the compensatory mechanisms. These spontaneous eye movements may be asymptom

atic. However, they can be of sufficient amplitude to result in diminished acuity that

people may interpret as blurring or a decrease in vision. Occasionally, people with certain

types of nystagmus can complain of oscillopsia or the sensation of the world moving.

Because nystagmus may be associated with ocular misalignment, the person should be

quizzed with regard to whether he/she does or does not have double vision. Likewise,

vestibular dysfunction may be associated with nystagmus so a problem with hearing or

tinnitus and trouble with balance and vertigo may be associated. This subject is dealt with

further in Chapter 5.

Depending on the degree of movement associated with nystagmus, simple observation

may be sufficient or additional magnification and illumination may be needed, either

with direct ophthalmoscope or during ophthalmoscopy. It is possible to get very precise

oculomotor recordings with an electro-oculogram or other device that will describe the

movements and their characteristics with regard to waveforms and velocities. Clinicians

should note the amplitude and frequency of the movements, the direction of the gaze

that induces nystagmus, and all points where the nystagmus is least evident. The move

ments are commonly recorded with arrows to designate the fast phase of the eye move

ment, both in terms of direction and in terms of amplitude. The movement most

commonly consists of a slow drift to the eye, followed by a corrective saccade, as in a

jerk nystagmus. For instance, a right jerk nystagmus would have a slow movement to

the left with a fast movement to the right. Pendular nystagmus is relatively symmetric

in that there is not an identifiable slow phase and shows relatively equal amplitude in

speed in separate directions. Nystagmus may be horizontal, vertical, or have a torsional

or rotatory component.

In the early onset category, congenital nystagmus is usually recognized in the first few

months of life. There is often a family history and the acuity may be good. People with

congenital nystagmus are not bothered by the eye movements. In young children, it is

important to detect any impairment of visual tracking or optic atrophy. The presence of

either should encourage neuro-imaging as congenital nystagmus most often occurs in

isolation but may be seen in conditions such as albinism, achromatopsia, Leber’s congen

ital amaurosis, and aniridia. The nystagmus is almost always conjugate and horizontal.

It may be continuous or intermittent. It may appear as jerk or pendular in character. Null

points are common and the person may adopt a head turn or posture in an attempt to

improve vision. Visual fixation often amplifies the nystagmus, which is not the case with

peripheral vestibular nystagmus. Two characteristic signs are reversal of the normal pat

tern of optic kinetic nystagmus in which the slow phase of the eye movement moves in

the opposite direction of the rotation of the drum and in electro-nystagmography when

a pattern is observed in which the velocity of slow phase movement increases exponen

tially with distance from fixation. Nystagmus is also associated with 15% of people having

a strabismus. It is abolished by sleep and, in addition to being accentuated by fixation, it

is diminished by convergence.

Latent nystagmus is another form that appears early in life and is a horizontal jerk

nystagmus that is seen in conditions of monocular viewing. The fast phase tends to be

toward the viewing eye, away from the occluded eye. The uncovered eye tends to drift

toward midline. Its fast phase reverses each time the eye is alternately covered. To obtain

the best acuity, one must blur the nontested eye with a plus lens or other filter and not

simply occlude the eye which will unleash the nystagmus and result in greater optical

blurring. Latent nystagmus is very commonly associated with esotropia. Another variation

is manifest latent nystagmus in which the characteristics of latent nystagmus are present

even when both eyes are open. Both these forms of nystagmus are typically benign.

An important subset is a monocular nystagmus in childhood. This is typically vertical

and relatively small in amplitude. The eye may have an afferent pupillary defect, optic

atrophy, or decreased vision and is commonly associated with chiasmal glioma. A spasmus

nutans may resemble a monocular nystagmus of childhood. It consists of a nystagmus in

both eyes that is intermittent, horizontal, low amplitude, rapid, and often dysconjugate.

There may be associated head nodding and/or an abnormal head posture. It can be

monocular and, thus, would be confused with the more ominous monocular nystagmus

of childhood and, therefore, also warrants neuro imaging. It typically is spontaneously

resolved after several years.

In the category of acquired nystagmus, the first is gaze-evoked nystagmus in which

people have difficulty in maintaining eccentric gaze. The eye drifts back toward the center

and a corrective saccade to reposition the eyes more peripherally is required. Thus, the

fast phase is in the direction of the gaze. It is caused by an imbalance in the neural

integrator located in the nucleus propositus hypoglossi adjacent to the medial vestibular

nucleus in the pontomedullary junction that is responsible for matching neural activity

to maintain eyes in the eccentric position. The nystagmus is often symmetrical right to

left. Advanced age is the most common cause, although metabolic and toxic etiologies are

more common in younger adults, either from ethanol or anticonvulsant drugs. Whenever

gaze-evoked nystagmus is asymmetric, it can be presumed that there is a lesion of the

brainstem or the cerebellum. Perhaps stroke, demyelination, or tumor has asymmetrically

affected the vestibular nuclei. Gaze-evoked nystagmus may occur in normal subjects at

the extremes of gaze and this should be assessed by examining the stability of fixation at

roughly 40 to 50 degrees from primary position.

Disassociated nystagmus may result from lesions of the medial longitudinal fasiculus

(MLF), causing nystagmus of only the abducting eye when the gaze is directed to the side

opposite the lesion. The person is often diplopic because of the limited adduction of the

ipsilateral eye. It may be associated with demyelinating disease in younger people or

vascular insufficiency in more advanced age. Most acquired jerk nystagmus in primary

position is due to asymmetric vestibular input which may be related to peripheral pathol

ogy affecting the vestibular end organ, semicircular canals, or the vestibular nerves or to

the central pathology affecting the vestibulocerebral connection. Because tonic input

regarding eye position is mostly vestibular, which feeds directly to the contralateral hor

izontal gaze center located in the sixth cranial nerve nucleus, asymmetric loss of input

results in a conjugate ocular drift. The correcting fast phase is away from the affected side.

Peripheral vestibular lesions are typically not discrete and affect all three semicircular

canals in the otolith organs. This results frequently in mixed (horizontal, torsional, and

vertical) nystagmus. The horizontal component often dominates. Visual fixation tends to

dampen the peripheral nystagmus. This can be seen by observing the fundus with direct

ophthalmoscope while the alternate eye is covered and uncovered to see the difference in

amplitude that fixation on a distant target has on the nystagmus. A peripheral nystagmus

is often accompanied by tinnitus, hearing loss, and vertigo or disequilibrium.

Central nystagmus, in which the fast component is directed toward the side of gaze, is

relatively common, often secondary to medications, such as anticonvulsants, sleeping aids,

sedatives, and antianxiety medications, or alcohol. Visual fixation has little effect on central

vestibular nystagmus. Bruns nystagmus is a characteristic form of vestibular nystagmus

associated with cerebellar pontine angle tumors. Initially, the vestibular nerve is affected;

the eyes drift toward the side of the lesion with corrective phase in the opposite direction.

As the lesion enlarges, the ipsilateral brainstem is compressed, causing problems in main

taining ipsilateral eccentric gaze. As the person looks to the side of the lesion, the fast

phase changes direction to ipsilateral, beating more slowly and with a coarser amplitude.

Some forms of nystagmus and nonnystagmus saccadic oscillations are highly correlated

with lesions and are useful for localization within the central nervous system. Downbeat

nystagmus results from defective vertical gaze holding; the eyes tend to drift up and a

corrective downward saccade is generated. The presumed mechanism is asymmetric loss

of the tonic input from the anterior semicircular canals resulting in an upward drift of the

eyes. Downward nystagmus is almost always present in

primary position. People may

report difficulty in reading and may report oscillopsia. Structural lesions are present in

approximately 50% of people. An Arnold-Chiari malformation, in which the cerebellar

tonsils herniate through the foramen magnum and compress the cervical medullary junc

tion, is the most common structural etiology. Differential diagnosis includes angioma,

cerebellar hemangiomas in the foramen magnum, and demyelination disease. Stroke,

cranial trauma, drugs (alcohol, Lithium, antiseizure medications), syrinx of the brainstem

or upper cervical spinal cord, brainstem encephalitis, or nutrition are some of the etiologies

to be considered.

Upbeat nystagmus may be present in primary position or only in upgaze. It is commonly

associated with lesions of the anterior cerebellar vermis. Common causes include demy

elination, stroke, cerebellar degeneration, and tobacco smoking.

Seesaw nystagmus is a variety of vertical nystagmus that is dysconjugate — as one eye

moves up, the other eye moves down. The upward moving eye also intorts while the

downward moving eye extorts. This occurs with lesions around the diencephalon. Cranio

pharyngioma is the most common cause. Other parasellar tumors and trauma may pro

duce seesaw nystagmus. There is an associated afferent system pathology, including

bitemporal visual field defects.

Periodic alternating nystagmus may be congenital or acquired and is characterized by

an oscillation of cycles of horizontal movements of approximately 4 minutes. The nystag

mus beats in one direction for 2 minutes, slows, then reverses to the other side for the

next 2 minutes. It is most common in posterior fossa disease, especially of the cerebellum.

Common causes include multiple sclerosis, cerebellar degeneration, and Arnold-Chiari

malformation. Etiology is thought to be in the vestibulocerebellum and is manifest as a

shifting in the null point.

Pendular nystagmus of both a vertical and horizontal component may be oblique (if the

components are in phase) or circular or elliptical (if they are out of phase). It is not

localizing and is usually acquired in association with multiple sclerosis.

Microsaccadic refixation movements are an abnormal eye movement resulting from

inappropriate saccade. Most common is square-wave oscillations which is a small move

ment away from, and then back to, fixation. The smaller movements may be seen in

normally aged people. Larger amplitude oscillations may occur in people with progressive

supranuclear palsy, cerebellar disease, or multiple sclerosis.

Ocular flutter is a horizontal small amplitude high frequency movement. Opsoclonus

or high frequency multiple direction movements (or saccadomania) are associated with

a burst of saccades released from the pons without the normal latency between consec

utive saccades. Neoplastic etiology must be excluded in these people. In children, neu

roblastoma is a primary consideration. In adults, small cell carcinoma of the lung and

cancer of the breast or ovaries must be ruled out. These eye movements may be an early

sign of cancer.

Convergence retraction nystagmus commonly occurs as part of a dorsal midline syn

drome of Parinaud (which includes absent upgaze, light–near dissociation, and Collier’s

lid retraction). Anomalous eye movements result from a co-contraction of the horizontal

extraocular muscles on attempted upgaze. It is best elicited by having the person follow

a downward rotating optokinetic nystagmus drum.

Ocular bobbing is a rare sign in which rapid downward movement of both eyes is

followed by a slow return of the eye position to midline. The person is usually comatose

or has severely compromised mental status, usually from bilateral pontine infarction or

hemorrhage. These lesions ablate the paramedian pontine reticular formation on both

sides, thus horizontal movements are lost. Severe metabolic disturbances may, in the

absence of structural lesions, cause ocular bobbing with possible later recovery.

The last form of nystagmus to consider is voluntary nystagmus. It is typically horizontal

in direction, appears as a relatively high frequency convergent saccades, and can rarely

be maintained for longer than 20 seconds. Although it can be induced volitionally in many

normal subjects, it may, occasionally, not be consciously generated and can distress people

because of oscillopsia.

Learning and Therapy

One model for learning and memory includes repetition. Repetitive use of a synaptic

connection causes a broadening and flattening of the endplates with a decrease in resis

tance across the synaptic gap and a preference for using that synapse over adjacent

pathways that have not been so facilitated. 19 Learning has been shown to affect dendritic

spine formation. 20 These concepts are anatomically supportive of many standard teaching

methods from repetition of spelling lists and multiplication tables to rehearsing a speech

to learn a pattern of words.

Repetition may also serve as a foundation for retraining a person with TBI in whom

preferred pathways may have been damaged, resulting in an initial inability to perform

an old, remembered task. The inherent complexity of the central nervous system may be

advantageous in that there seems to be alternate pathways available for bypass of damaged

areas and establishment of new circuits or series of synapses that will allow one to perform

old tasks in perhaps new ways. Therapy can be thought of as a means of helping to identify

some of these previously unused or little used pathways and, through repetition and

building upon prior skills, developing new ways of performing old tasks. Case History 1 A 32-year-old male sustained postconcussion syndrome after being struck in the head by a falling pallet. Initially, he presented with complaints of diplopia and blurry vision. On evaluation, he was noted to have eight prism diopters of exophoria at near and distance, with some difficulty on upgaze. Cogwheeling of saccades was present. It was noted on screening and confrontation fields testing that temporal constriction in the right eye was present. Recommendation was made for saccadic exercises, such as the vertical swinging ball, and convergence exercises. At the next visit, exophoria was decreased to six prism diopters and saccades had improved with therapy. Two months later, exophoria remained about the same and saccades had ceased cogwheeling on left to right gaze and had greatly improved on right to left gaze. The individual continues with vision therapy and has graduated to exercises that are more difficult for him, such as the color bead sorting tray. 21 Case History 2 A 42-year-old male suffered blunt head trauma from metal pipe. Initially, he presented with complaint of decreased vision. On examination, acuity was correctable to 20/25- in the right eye, 20/20 in the left eye. No strabismus was noted. Saccades were slowed, with difficulty moving eyes left to right, and slight exophoria on upgaze. Pursuit was jerky. Worth Four-Dot testing revealed partial suppression with left eye. Visual fields, on confrontation, were constricted bilaterally. Recommendations were for pursuit and saccadic exercises and the individual was started on swinging ball exercise. Two months later, saccades were greatly improved, with almost no cogwheeling. Approximately 6 months after the initial examination, the individual was started on Ritalin for impaired speed of processing. Immediately, he began to complain of more difficulty with tracking and decreased vision. On examination, smooth pursuit had become very jerky, as were saccades. Best corrected acuity had decreased to 20/30- in the right eye and 20/40- in the left eye. He discontinued Ritalin 3 months later and was evaluated after 2 weeks, noting vision still decreased. Smooth pursuits and saccades were still jerky. Acuity had increased to 20/20- in each eye, with difficulty. Final evaluation was done 4 months later. Acuity was 20/20 in each eye, best corrected. Smooth pursuits were improved, but still jerky, and suppression was noted in the left eye via Worth Four-Dot testing. Case History 3 A 31-year-old male suffered a closed head injury

with intracerebral hemorrhages after a motorcycle vs. car accident. Initially, he presented with 20/20 vision, best corrected, bilaterally. Six prism diopters of exophoria with ten prism diopters of left hyperphoria was noted on primary gaze. There was vertical nystagmus on abduction and large lag on abduction. Smooth pursuits were jerky. Recommendations were for saccadic and smooth pursuit exercises, such as the Marsden ball, color bead sorting tray, and accommodative flexibility exercises. Four diopters of prism were applied to present glasses via press-on prism. Six months later, with prism, exophoria was decreased to two prism diopters. Vertical nystagmus had improved, as had saccades. He started the bead sorting tray exercises on a vertical orientation and vertical door jamb reading. 21 Case History 4 A 31-year-old Hispanic male sustained right cavernous fistula post motor vehicle vs. pedestrian injury. His chief complaint was that he was unable to move his eyes laterally to the right. On examination, visual acuity was 20/70-2 right and 20/60-1 left, without correction. Extraocular motility was with restriction to midline with limitation of abduction of the right eye. There was injection and dilation of the vessels, especially temporally on the right eye, similar to venous congestion. Auscultation revealed a bruit that seemed louder on the right side. The man was sent for MRI of the brain, which was not able to be completed due to movement even after 2 mg of Versed. A “very high flow” clotted cavernous fistula was confirmed upon a second MRI and cerebral/carotid angiogram was performed under general anesthesia. Surgical intervention, by placement of three balloons in the right carotid fistula to close it, was performed. The man showed a 25 to 30 prism diopters right esotropia which did not resolve after the cavernous fistula surgery. He was still only able to just achieve mid-line with maximum effort, but had no abduction. Recommendation was for muscle transposition procedure to obtain alignment in primary gaze. This would require several surgeries to achieve the best result, and even so, would not allow for full range of motion.

Most therapy consists of taking a task, breaking it down into smaller steps, teaching,

learning, and repeating each one of the steps, and linking them into larger and larger

groups until, finally, a more complex behavior can be performed. Since the goal of therapy

is to minimize disabilities and maximize abilities, this

retraining process is the key at the

heart of the things that we do.

First, the systems or subsystems that have been adversely affected, what things a person

is unable to do, and what things the person can do to a limited extent must be determined.

Next, a means of working from what the person can do in an additive fashion to allow

him/her to regain as much skill as possible must be devised. For example, in treating

diplopia, the first temptation might be to simply patch the more severely affected eye to

relieve the symptom of diplopia. While this does relieve the immediate symptom, it does

very little toward rehabilitation or establishing these alternate pathways that were dis

cussed earlier. Therefore, the act of putting a patch on the eye temporarily blocks the

symptom but does not approach a solution to the problem, which is mistracking of the eyes.

A preferred plan would be to determine whether or not there is any position of gaze in

which the individual does not see double. Treatment would incorporate prisms in glasses

to move the images into alignment so as to allow the person to continue to use both eyes

at the same time. The goal would be to enlarge the area of single vision through a series

of training exercises. These exercises encourage the movement of the eyes and stimulate

the utilization of existing or new pathways to allow smooth tracking of an object or to

acquire its fixation and maintain it in good alignment.

Treatment may start by using a

large amount of prism in the glasses, perhaps a plastic press-on prism so that it can be

easily changed as the individual improves with time under therapy to keep encouraging

the person to move ahead. The areas of first concern should be primary gaze (straight

ahead gaze) and slightly down gaze in a reading position. These may require two different

sets of glasses with two different amounts of prisms.

Programs of visual therapy require coordination of efforts between the physician and

the therapist. The physician conducts serial repetitive measurements to determine baseline

alignment and provide comparison to previous measurements to monitor progression.

The therapist makes suggestions in consultation with the physician regarding what ther

apies might best improve the individual’s condition, keeping in mind tolerance, strengths,

and any other concomitant difficulties. As long as progress is being made, it should be

encouraged and allowed to proceed.

It may take many months for damaged neural tracts to repair themselves or for com

pensation to occur within the neurological system. Nerve repair proceeds at a slow pace.

At some point, the ophthalmological measurements may plateau and the individual may

show no further progress. Depending upon the nature of the deficit at that time, one may

consider surgical intervention to realign the eyes in a more central and aligned position.

Visual therapy may play a role in stimulating binocular vision, either preoperatively in

preparation for surgery or postoperatively in an attempt to stabilize the alignment that

has been achieved by mechanical movement of the muscles. Once again, small bits of

prism may be utilized to complete the alignment process and then be gradually weaned

away as fusional amplitudes increase over time.

A number of people have shown rather dramatic improvement in areas that traditional

medicine will tell us should not have improved. Some, who initially could not tolerate

things moving near their heads because it gave them a feeling of extreme discomfort,

developed a tolerance for having a ball swinging in a circle around their head as they

tracked it back and forth. Others needed a program geared specifically to their areas of

difficulty, such as working from near to far as they changed their fixation. With time and

repeated efforts, they developed an increased facility in this regard. Still other people who

had specific difficulties in their saccadic tracking systems were able, with simple repetitive

exercises such as door jamb reading, to demonstrate increased facility. This was reported

both subjectively, in that they felt they could do the exercises more quickly, more easily,

and with less fatigue, and also objectively, in that their examination scores showed

improvement over time. It is important to understand that (1) the therapist must realize

that the person can get better and (2) the person must be willing to undergo a fairly

rigorous and sometimes uncomfortable therapeutic process in order to develop the syn

aptic relays necessary for improved function.

Summary

Detailed understanding of the visual system is necessary for accurate diagnosis of visual

disorders following TBI. It should be understood that surgical and therapeutic interven

tions exist to ameliorate some visual system dysfunction. Rehabilitation of treatable visual

system deficits should be undertaken as a regular component of comprehensive rehabil

itation following traumatic brain injury.

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7

Rehabilitation and Management of Visual Dysfunction Following Traumatic Brain Injury

Penelope S. Suter

CONTENTS

Introduction

This chapter surveys the nonsurgical rehabilitative services available to provide effective

treatment of brain-injured patients with visual sequelae. It should be a useful reference

for those who deal with these patients in intensive rehabilitative environments, as well

as for primary care professionals who sometimes find these patients in their care when a

rehabilitative hospital or center is not accessible. It may also be useful to both novice and

experienced vision care providers working in the area of traumatic brain injury (TBI)

rehabilitation.

The basic structure of this chapter remains the same as in the first edition. However, in

added or expanded upon. Also, the model of vision rehabilitation set forth in the earlier

edition has been altered in order to acknowledge visual thinking and memory as part of

the visual rehabilitation process.

Many of the therapeutic approaches used with TBI patients were developed for other

special needs vision patient populations. For this reason, much of the information pro

vided here is applicable not only to the TBI patient, but also to other patients who have

suffered organic insult to the brain. For the same reason, although they may lack specific

experience with TBI patients, vision care professionals who practice other forms of visual

rehabilitation and vision therapy will often be able to provide appropriate rehabilitation

for TBI patients suffering from visual dysfunction — given a few additional concepts

which are specific to the brain injured population. 1

Physical Substrates of Vision

In the rhesus monkey, which provides an excellent model of the human visual system,

more than 50% of the neocortex is involved in visual processing. 2 To date, researchers

have described approximately 305 intracortical pathways linking 32 different cortical areas

implicated in visual function; 25 of these are regarded as either predominantly or exclu

sively involved in visual function, and seven are considered visual-association areas. 3 The

ganglion cells traveling from the retinas represent approximately 70% of all sensory input

fibers to the brain. In addition to multiple subcortical areas (see Chapter 6), every lobe

of the cortex is involved in visual processing (reviewed by Kaas 4). The occipital lobe

contains primary visual cortex for initial processing of vision as contour, contrast, and

depth. The inferior temporal lobe is involved in object identification, the middle temporal

area in motion processing, and the parietal lobe in processing for spatial organization and

visual attention. 4,5 The frontal eye fields and adjacent areas of the frontal and prefrontal

lobes are involved in motor planning and initiation of self-directed eye movements, as

well as visual search 6 (Figure 7.1). In addition, simple visual awareness requires interac

tions between primary visual cortex, posterior parietal cortex, and the frontal eye fields.

Input from the limbic system (especially the cingulate gyrus) may mediate motivational

relevance of the external stimulus, guiding sustenance of attentional activation in the

visual system. 7

Considering this, visual rehabilitation becomes a sweeping term which ranges from

rehabilitation of the eye and surrounding structures, to rehabilitation and management of

sensory processing, organization of sensory input from the eye into visual percepts, and

use of these percepts to support cognitive or behavioral functions. Visual dysfunction may

affect the ability to carry out daily tasks such as reading, driving, walking, and functioning

in the workplace. Diagnosis and rehabilitation of the eye, eyelids, extraocular muscles and

surrounding bony structure, eye movement and eye teaming disorders, as well as the

higher visual functions such as visual perception, spatial organization, visual memory,

and the ability to integrate visual information with other modalities, all fall under the

umbrella of visual rehabilitation. Multiple professionals may be involved and considerable

networking or case management provides for the most effective care.

The Multidisciplinary Approach

Two types of eye doctors are frequently required in management of the visual conse

quences of TBI — the ophthalmologist and the optometrist. In general, their roles may be

considered analogous to the computer equivalents of hardware and software repair per

sons, respectively. The ophthalmologist will often be needed to provide medical/surgical

treatment of the hardware or anatomical and physiological aspects of the visual system

before the optometrist can provide rehabilitation of the software or functional aspects of

the visual system.

Ophthalmologists are trained to diagnose and manage damage to the eye and surround

ing structures as well as to diagnose lesions of the visual pathways and ocular-motor

system. They sometimes prescribe exercises for eye movement disorders which are often

performed with the assistance of an occupational therapist. Occasionally, an ophthalmol

ogist will work with an orthoptist, an ophthalmologically trained therapist, to remediate

eye teaming disorders such as strabismus. However, ordinarily, ophthalmologists are

FIGURE 7.1

Areas of visual cortex and some of the ipsilateral cortical connections in visual cortex of the owl monkey. The arrows

indicate two major cortical pathways of visual processing. The superior path (dotted arrows) to posterior parietal

lobe via the middle temporal area supports “where” processing. The inferior path (hatched arrows) to temporal

lobe supports “what” processing. (From Kaas, J. H., Changing concepts of visual cortex organization in primates,

in Neuropsychology of Visual Perception, Lawrence Erlbaum Associates, Hillsdale, NJ, 1989. With permission.)

mostly concerned with providing the medical/surgical support required in early rehabil

itation, or for later surgical intervention if spontaneous recovery and therapy fail to

produce an acceptable result with a traumatic strabismus.

Neuro-ophthalmologists are ophthalmologists who have specialized in diagnosis and

treatment of neurological dysfunction of the visual system. They are more likely to have

some experience with rehabilitating the visual software or application of nonsurgical or

pharmacological therapies than general ophthalmologists.

Optometrists specializing in vision therapy and/or rehabilitation are trained in diagno

sis and nonsurgical treatment of more complex fixation, eye movement, or eye-teaming

(i.e., binocular) disorders, as well as perceptual dysfunctions in the visual system. Usually,

the treatment of such disorders is performed with the assistance of a vision therapy

technician under the doctor’s supervision. In an inpatient or rehabilitation center outpa

tient situation, occupational therapists working under a doctor’s supervision or prescrip

tion will sometimes assist the patient with vision therapy for perceptual and sensorimotor

dysfunctions, or less complex eye movement and eye teaming dysfunctions. They may

also assist with teaching new living skills to compensate for residual vision deficits.

Optometrists specializing in low vision assessment are trained in prescription of low

vision aids for patients with reduced visual acuity, and “field expanders” which may be

required for patients with visual field defects. These doctors will often work with, or refer

to, a low vision rehabilitation specialist who can assist in teaching the patient new living

and mobility skills to cope with their acquired visual deficit.

Vestibular system damage may cause nystagmus and/or obstruct normal fixation and

pursuit. In such a case, referral for vestibular workup to a professional equipped to

perform eye movement recordings for diagnosis and to make rehabilitative recommenda

tions may be helpful. Neuropsychological examination may help to give a broader per

spective on visual perceptual dysfunctions. Finally, as with other types of rehabilitation

following a TBI, visual rehabilitation may be significantly enhanced by the assistance of

a counselor or psychotherapist to assist patients in understanding their new limitations

and the need to rehabilitate, as well as managing emotional sequelae which can interfere

with effective rehabilitation.

Prevalence and Impact of Visual Dysfunction in TBI Patients

Because of the multifaceted nature of visual dysfunction and the broad distribution of

visual functional areas in the brain, many, if not most, TBI patients suffer from some sort

of visual dysfunction. Transient changes in refractive error which may last for months or

years are common after TBI. 8,9 Accommodative (i.e., focusing) dysfunctions are also

common 10 and may interfere with reading, fine depth discriminations, and rehabilitative

therapies which are performed at nearpoint. Nearpoint tasks, as well as balance, orienta

tion, mobility, and daily living skills, may be affected by visual field defects and binocular

disorders, as well as by dysfunctions in visual perception and spatial organization. 9,11

Binocular disorders can cause postural changes as the patient finds ways to either maintain

fusion or enhance suppression of one eye by tilting or turning the head or torso.

It is often the case with TBI patients that eye-care professionals, untrained in diagnosing

more subtle visual and ocular-motor dysfunctions, may dismiss patient complaints of

headache, dizziness, inability to concentrate, blurred vision, fatigue, light sensitivity, or

inability to read as due to emotional or other nonvisual etiologies. While many of these

symptoms may have nonvisual causes, a careful assessment of the visual system will often

reveal the physiological or perceptual difficulty underlying the patient’s complaint. 12 Gaetz

and Weinberg have demonstrated deficits in visual event-related cortical potentials in

patients with persistent symptoms from traumatic brain injuries classified as mild head

injuries or concussions. 13 They conclude that patients with postconcussive symptoms fre

quently have persistent brain damage which cannot be visualized using CT or MRI tech

niques, but can be elucidated using visual and auditory event-related potential techniques.

Schlageter et al. 14 found that 59% of TBI patients admitted to an acute rehabilitation center

had eye movement or eye teaming dysfunctions. Therefore, it is important that the TBI patient

be examined by an eye/vision care provider who has a special interest in the area of neuro-, rehabil

itative, or therapeutic vision care. (See Appendix 7A for a partial list of organizations that can

provide educational materials or lists of member doctors who practice in this area.)

A literature survey shows some of the types of visual problems encountered. Cohen et

al. 15 found convergence insufficiency (i.e., difficulty pulling the eyes inward as is necessary

for binocular fixation on near targets) in approximately 40% of both TBI inpatients with

recent injuries and follow-up patients 3 years postinjury. In the follow-up group, conver

gence insufficiency was positively correlated with duration of coma, dysphasia, cognitive

disturbances, and failure to find placement in nonsupported work situations. Lepore 16

examined 60 patients with TBI and resultant strabismus. Among the 51 patients with

nuclear or infranuclear findings, fourth cranial nerve

palsies were the most common (39%),

followed by third nerve palsies (33%), sixth nerve palsies (14%), combined palsies (10%),

and restrictive ophthalmopathy (4%). Convergence insufficiency was the most common

supranuclear dysfunction. Similarly, in 114 patients referred to an ocular motor clinic for

visual disturbances following motor vehicle accidents, Fitzsimons and Fells 17 noted fourth

nerve palsy in 36%, third nerve palsy in 25%, and multiple diagnoses in 25%. Aberrant

regeneration was noted in 78% of third nerve palsies. Padula and Argyris 18 have identified

a constellation of visual deficits which they have termed posttrauma vision syndrome.

These deficits may include high exophoria or exotropia, convergence insufficiency, accom

modative insufficiency, and ocular-motor dysfunction. Common symptoms include dou

ble vision or a perception of motion in stationary objects or printed material, blurred near

vision, photophobia, eyestrain, and headache. Further, clinicians and researchers have

described visual-motor dysfunctions related to judgments of egocentric visual midline

shifts following brain injury. These shifts create symptoms including dizziness and balance

problems similar to those created by vestibular dysfunction.

Groswasser et al. 19 reported bilateral visual field defects in 14% of severe TBI patients.

Ocular-motor defects in these patients were associated with poor recovery as defined by

return to work or school. Bilateral visual field defects

were more common in the poor

recovery group, but this finding was not significant. A 15-year follow-up study of United

States' Vietnam veterans with penetrating head injuries showed that visual field loss and

visual memory loss were negatively correlated with return to work. 20 In an assessment of

successful vs. unsuccessful TBI clients in a supported employment program, Wehman et

al. 21 evaluated the functional limitations of those clients rated most difficult and least

difficult to maintain in employment. The two areas of functional limitations which were

significantly different between these groups were visual impairment and fine motor

impairment. Najenson et al. 22 found that performance on The Raven Matrices Test — which

is heavily loaded for visuospatial performance — was highly correlated with successful

performance in the rehabilitated TBI patient's working life.

Lastly, as reviewed by Murray et al., 23 attentional deficits in TBI patients have recently

been considered in terms of information processing models rather than in terms of con

structs such as sustained attention or distractibility. Shum et al. 24 provide evidence for a

four-step sequential information processing model where attentional processes are con

sidered as the sequential stages of: (1) feature extraction, (2) identification, (3) response

selection, and (4) motor adjustment. Children who had suffered severe TBI showed sig

nificant impairment on complex choice reaction time tasks

designed to test each of these

processing stages, as compared to age- and gender-matched controls. Based on these

findings, diagnosis and treatment of these primary processing disorders may be the most

direct approach to treating attention disorders in TBI patients.

Therapeutic Intervention: What and Why?

Flexibility in the Adult Visual System

The amazing flexibility in modification of the vestibulo-ocular reflex, as well as the visual

perceptual apparatus, has been demonstrated in normal adults by application of inverting

prisms. 25 Initially, when wearing these prisms, the world appears upside down and back

wards, but with continued prism wear, the vestibulo-ocular reflex reverses and the visual

perception reverts to normality. Substantial neural plasticity is present in other areas of the

adult visual system as demonstrated by orthoptic therapy remediation of amblyopia and

strabismus in adults. 26-28 Freed and Hellerstein have demonstrated that the visually evoked

potentials (VEPs) of adults with mild TBI frequently normalize following application of

vision rehabilitation techniques, in contrast to VEPs of matched participants who do not

receive vision rehabilitation. 29 In the non-TBI population, vision therapy has proven effective

for treatment of many visual disorders such as accommodative dysfunctions, eye movement

disorders, nonstrabismic binocular dysfunctions such as convergence insufficiency, strabis

mus, nystagmus, amblyopia, and some visual-perceptual disorders in both adults and

children. 30–32 Most of these visual disorders may be suddenly acquired with a brain injury.

Remediation of Ocular-Motor and Binocular Disorders Following TBI

Vision therapy has also been applied successfully to remediation of vision disorders

secondary to brain injury. 33–38 Ron 39 studied six patients with ocular-motor dysfunctions

resulting from TBI such as saccadic dysmetria and decreased optokinetic nystagmus gain.

Both saccades and optokinetic nystagmus normalized more rapidly with training, as

compared to control patients, and gains were maintained after cessation of treatment.

Convergence insufficiency and strabismus have also been successfully remediated with

vision therapy in brain trauma patients. 34,36,40 In an experiment to test the practicality of

applying therapy to vision deficits in a short-term acute care rehabilitation setting, Schlag

eter et al. 14 failed to show statistically-significant improvements from repeated baseline

measures on pursuits and saccades in six TBI patients who received between 2 and 6 hours

of therapy. However, when quality of eye movements was graphed against treatment, the

slope increased (showing faster improvement) during therapy for both saccades and

pursuits, as compared to the baseline period. Although the occupational therapists and

speech pathologists who administered the therapy were

trained in a number of therapy

techniques for saccades and pursuits, it became apparent during the study that “establish

ing a hierarchy of progressively more difficult exercises required a significant amount of training”

(p. 447), and they may have found even better results had they used staff trained in

orthoptic or vision therapy. Because of multiple demands on patient time in the acute care

setting, treatment for visual disorders will generally not be completed in this setting.

However, progress can be made, and visual dysfunction should be considered when

making recommendations for the patient at discharge from acute care.

When surgical intervention is required for remediation of a residual posttraumatic stra

bismus, patterns of eye movement and teaming must be relearned. Fitzsimons and Fells 17

report that among 92 TBI patients who had extraocular muscle surgery, 50% required more

than one surgery, and 30% more than two. Of these patients, 52% had satisfactory outcomes

as defined by a satisfactory field of single binocular vision with tolerable diplopia (i.e.,

double vision) when shifting gaze to the sides. Another 27% had moderate outcomes

defined as suppression or diplopia with the ability to comfortably ignore one image. Finally,

22% had persistent troublesome diplopia necessitating occlusion. Their success rates may

have been even better had they used functional therapy in conjunction with surgery. Pre

or postsurgical application of therapy can be a useful adjunct to surgery in encouraging

fusion, expanding the range of binocular gaze, and eliminating diplopia. Unfortunately, it

is common that the professionals who treat strabismus are dichotomized into those practitioners

who apply surgery and those who apply functional therapies, rather than having the two work as

a team. Those who apply surgery, alone, rely on the existing visual system to relearn

binocular fusion without any guidance. Often, this does not occur. Those who apply

therapy, alone, risk not offering their patients the full range of services to assist in the best

possible outcome. As more eye/vision care professionals begin to treat TBI patients, hope

fully, an integrated approach will become more widely accepted.

Management of Other Visual Dysfunctions Following TBI

In patients with visual loss as measured by decreased visual acuity or visual field, low

vision devices such as magnifiers, special telescopes (some of which may be spectacle

mounted) or “field expanding” devices can be applied. As our population has aged, more

research and development has gone into rehabilitation for these types of visual loss which

are frequent sequelae of stroke and age-related eye disease. Therapy for homonymous

hemianopia has been shown to increase speed and breadth of visual search and improve

both objective and subjective measures of visual abilities on activities of daily living,

including, in some cases, partial recovery of visual field loss. 41,42 Therapy for visual hemi

field neglect can be similarly effective. 43 Researchers at the Massachusetts Eye and Ear

Infirmary have documented the effectiveness of using a multidisciplinary team including

ophthalmologists, optometrists, occupational therapists, and social workers in increasing

patients' functional ability during visual rehabilitation. 44

Therapies for perceptual dysfunctions other than spatial neglect have been previously

applied in non-TBI populations by some educators, optometrists, psychologists, and neu

ropsychologists. Development of computerized therapies for perceptual deficits have

made perceptual rehabilitation more accessible and applicable by other therapists, includ

ing occupational therapists. As perception is dependent on reception, it is advisable to

test for and remediate or manage any sensory visual deficits prior to testing for perceptual

dysfunction other than neglect. Present evidence (reviewed by Gianutsos and Matheson 45)

generally supports the efficacy of perceptual therapy following brain injury, although one

must be aware that substantial spontaneous recovery occurs during the first 6 months

following the injury.

When to Treat

The timing of therapeutic intervention has been a controversial issue. Some practitioners

argue that patients who are diplopic should have vision

examinations as soon as possible

after they are medically stabilized. Appropriate application of prism, cling patches, or

partial patching (discussed later) in the early weeks postinjury can give the patient some

relief of symptoms as well as preventing maladaptations which must be trained away

later. However, application of either specialized patches or prisms during these early

weeks requires frequent reevaluation and adjustment to keep pace with spontaneous

resolution of visual defects.

While there is evidence that some visual defects, such as muscle palsies and pareses,

may spontaneously recover up to 12 months postinjury, 46 other evidence shows that, in

general, untreated brain-injured persons do not spontaneously recover from binocular

disorders such as convergence insufficiency. 15 The decision about when to intervene is

most appropriately determined by factors other than the hope of spontaneous recovery.

During the initial 3 months postinjury, a rapid resolution may occur in many visual

defects as edema in the brain diminishes. After this time, although spontaneous resolution

may still be ongoing, it is likely to be slower and unwanted compensatory mechanisms,

such as suppression, set in. Further, in patients who are struggling with such deficits as

orientation problems or diplopia, failure to address these difficulties in a timely manner

may lead to depression and a poor attitude toward

rehabilitation when it is finally offered.

Patients who are left to their own devices after the acute phase of medical rehabilitation

is completed will find ways to survive with remaining deficits — often in ways which are

not positive adaptations. Follow-up studies in untreated TBI patients show that they

generally do not make continued functional progress and they may even decline in

function over the long run. 45

Even with the most careful diagnosis, one cannot always tell which patients are going

to respond to treatment. In the areas of ocular-motor and binocular dysfunction following

TBI, reevaluation on a monthly basis can be used to determine whether the patient is

making progress. If therapy has been consistent and intensive and no progress is being

made, then compensatory measures should be prescribed. Gianutsos 47 suggests that, in

cognitive rehabilitation, intensive rehabilitation with an initial goal of restoration of func

tion should be applied for 6 months. If no progress is made, then a different approach

should be tried. This seems to be a good rule for visual perceptual and visual memory

rehabilitation, with the modification that some compensatory strategies are often applied

immediately to help the patient function while pursuing therapy.

A Useful Model for Organizing Visual Rehabilitation

Moore 48 has emphasized the importance of considering functional units in the brain, taking

into account contemporary metabolic maps that show brain function, rather than thinking

of the brain as it has been mapped in the last century into discrete compartments associated

with individual functions. While it is necessary to have an understanding of the neu

roanatomy of the visual system in order to help formulate an appropriate diagnosis,

knowing the neurons does not provide an adequate basis for guiding therapy. It is equally

important to have a working model of visual performance to guide rehabilitation efforts

and higher-order visual testing. Neuropsychological models of information processing or

even of reading will often begin with a box labeled visual input or sensory input. Exposure

to such models may give the nonvision specialist the impression that visual input and its

involvement in information processing is discrete and simple enough to fit into such a

box. Working without a model of visual processing may encourage attempts to rehabilitate

splinter skills such as convergence in cases where a more holistic approach is necessary

to get the patient reading again or reoriented in space. Many therapy oriented optometrists

use a model of visual processing similar to that developed by Cohen and Rein 49 and shown

in Figure 7.2. Figure 7.3 represents a simplified model which may help the practitioner

keep the big picture in mind during testing and treatment.

FIGURE 7.2

A model of visual function developed by Cohen and Rein, similar to that used by many optometrists to help

guide vision therapy. (From Cohen, A. H. and Rein, L. D., J. Am. Optom. Assoc., 63, 534, 1992. With permission).

FIGURE 7.3

A modified model for guiding rehabilitation of the visual system. Functions within each processing area are as

delineated in the original model by Cohen and Rein. 49 Visual processes fall within the triangle. Closed head

arrows indicate the major direction of information flow. Note that all arrows are bidirectional — information

flow is bidirectional in most known pathways in the visual system 2 and other bidirectional influences are

explained in text. INPUT Eye Health-Refraction Ocular Motor Skills Accommodative/Convergence DECODE/ENCODE Visual Perception OUTPUT Ocular Motor System Accommodative/Convergence Visuo-motor integration Visual Perception-motor Eye/Visual System Reception Association Areas of Brain Integration of Visual Information and Other Sensory Data Motor Pathway to Action System Feedback Refinement, Adjustments, Changes Organism Body Orientation

Sensory Input/Reception

Visual system input, or reception, is dependent on formation of a focused optical image

on the retina, healthy eyes, and healthy, intact pathways to primary visual cortex. Accom

modation (the internal focusing of the eye mediated by the ciliary muscle) and vergence

(the ability to make disjunctive or inward and outward movements of the eyes) are also

an important part of getting visual input to the visual cortex without confusion. These

two functions are tied together by neural feedback loops. As one expends accommodative

effort (trying to focus closer), the accommodative effort

drives convergence, pulling the

eyes inward. As accommodation is relaxed, the eyes diverge, or relax outward, as for

viewing distant targets. There is a similar, but lower, amplification loop from convergence

to accommodation; as one exerts convergence effort, it drives accommodation. It should

be obvious that a disruption in the balance between these two interacting systems —

accommodative-convergence and convergence-accommodation — can cause serious dys

function in eye teaming and focusing. There are useful models of such disturbances 50

reviewed by Ciuffreda. 51

Visual reception is also dependent on the ocular-motor skills, that is, full range of motion

of the extraocular muscles, the ability to fixate the target of regard, track it if desired, or

saccade to another target efficiently and accurately. These abilities are dependent on feed

back from areas that monitor head and body orientation and movement, as well as those

areas that monitor feedback from the ocular-motor drivers. Reception ends at primary

visual cortex where the initial binocular combination of input from the two eyes occurs to

allow for fusion and stereopsis. The input is processed as color, contour, contrast, and depth.

Perception/Integration

Visual perception and integration are dependent on intact neural communication within

visual processing areas and pathways between these processing areas, as well as intact

reception. Current trends in cognitive neuroscience implicate recurrent processing in pri

mary visual cortex (i.e., feedback from higher cortical processing areas to primary pro

cessing areas) as critical in awareness of visual input or visual perception. 52,53 Not only

does damage to lower visual processing areas decrease activity in higher processing areas

through loss of feedforward (e.g., occipital to parietal and parietal to frontal areas), but

damage to higher processing areas decreases activity in lower level processing areas

through loss of feedback connections. 7

Integration of visual information is also dependent on pathways to and from processing

areas mediating other sensory and motor functions. Much of the cerebral cortex is involved

in visual processing, with close to 300 intracortical pathways between the visual areas.

Therefore, it is important to maintain a holistic model of the functions of this stage of

processing so that one can test for and address functional loss with some guidance from

available topographic details of the injury.

The major functions of this stage in the model are organization of space and motion,

form perception, and object recognition, 49,54 as well as integration of vision with the other

senses and motor system input. Visual awareness is also included here. Interfaces with

thinking and memory processes are not in the original model (Figure 7.2), but should be

added at this stage in a bidirectional manner as in the modified model in Figure 7.3. Our

percepts feed into our memories and influence how we think and our thinking and

memories influence our perceptions and behaviors.

Two major concurrent vision processing pathways proceed forward from the occipital

cortex — the “where” pathway to the parietal lobe and the “what” pathway to the temporal

lobe (Figure 7.1). The “where” pathway is first identified, anatomically, at the lateral

geniculate nucleus where large magnocellular ganglion cells are segregated from the

smaller parvocellular ganglion cells. Magno-cells are, in general, sensitive to large con

tours, lower contrast, faster temporal frequencies, and are retinotopically distributed more

peripherally than parvo-cells (reviewed by Bassi and Lemkuhle 55). Some magno-cells are

color-sensitive, but at least half have broad-band spectral sensitivity (i.e., are insensitive

to wavelength information). 56 The magno-system is preserved, in a relatively segregated

manner, through primary visual cortex to the middle temporal area for motion processing,

and ultimately ends in posterior parietal cortex for cortical processing of object localization

and visual attention. Parvo-cells generally subserve focal color vision; they transmit more

slowly and are more sensitive to high contrast, detailed stimuli. The parvo-pathway

ultimately traverses to inferior temporal cortex and is involved in object perception (dis

cussed later). The cortical magno- and parvo-processing streams maintain both separate

and interactive functions. “Where” the object is and “what” the object is must be integrated

in order to make sense of the world. However, it is possible to selectively interfere with

memory for either “what” or “where.” 57 Also, it can be demonstrated, electrophysiologi

cally, that spatial attention has a different effect on each of these two pathways. 58

In addition to the cortical magno-pathway, an extrageniculate, midbrain visual

system 59,60 processes information both directly from the retina and from striate cortex to

organize orientation in ambient space. Organization of space and motion by both the

cortical magno-system and the midbrain ambient system requires interpretation of recep

tion from visual sensory substrates, ocular-motor drivers, and from substrates reporting

body orientation and motion in order to ascertain the spatial location of objects in relation

to ourselves. This analysis allows us to determine whether we are moving, the external

stimulus is moving, or some combination of both. The midbrain system is faster than the

cortical magno-system and mediates much of our survival level orienting, head, and

saccadic eye movement.

Feedback from both accommodation and convergence help localize objects in depth. 61

Form perception and object recognition require figure-ground segregation, form con

stancy, visual closure, and some processing of spatial relationships. These functions inter

act with visual reception in that the ability to perform these functions may be limited by

visual field loss or degraded visual acuity, contrast sensitivity, or fixation.

Cross modality integration is dependent on intact pathways to and from the neural

substrates mediating the other senses, as well as cortical processing to make matches

between them. Object perception includes integration with the visual input of information

about the object from our other sensory modalities.

Visual awareness, while most often taken for granted by rehabilitation professionals, is

surprisingly often disrupted in TBI and other pathology of the visual system. Patients with

neural damage to the visual system are often unaware that there has been any change in

their function. It is only when one demonstrates to them, on a visual field printout, a line

bisection or crossout test for visual neglect or a processing speed test that their performance

is grossly subnormal that they begin to understand that there is a visual deficit.

Considering the covert nature of many visual deficits following brain injury, it becomes

clear how such a pervasive system as the visual system can be so frequently ignored in

the rehabilitation setting, as neither patients nor practioners may be aware that the

patient’s symptoms are visual in origin. Those systems which traditionally receive the

most rehabilitation effort tend to be those that are overt in nature (e.g., language reception

and expression, vestibular dysfunction, and motor dysfunction) even though the repre

sentation in the brain (and, therefore, the impact of TBI) is often considerably less for these

systems than for the visual system.

Motor Output/Behavior

Organization of body movements in relation to visual targets is mediated, most directly,

by the posterior parietal areas and angular gyrus. Three major pathways connect these

areas with the motor areas — one via intracortical connections, one via the basal ganglia,

and one via the cerebellum. 62 Individual functions of these three pathways are not well

understood.

The percepts of our visual world that we construct during reception and perception are

used to guide further motor activity, both within the visual system and in visually-guided

motor activity such as mobility or eye-hand coordination. These percepts direct our ocular

motor activity and eye pointing. They influence the frontal lobe areas which generate

executive commands for voluntary eye movements so that we may regard objects at will

rather than in a purely stimulus-driven manner. They are involved in direction of the next

movement, whether for perception or for action. In short, these visual percepts and the

resultant thought processes dependent on them are the foundations for much of the

everyday behavior of a sighted person.

Visual Thinking/Memory

Much of our thinking and memory is processed as part of the visual processing stream.

Visualization of complex problems or forms is one method of problem solving and orga

nizing which does not require language. While visual thinking, in general, is typically

addressed by education in the rehabilitation setting, the skill of visualization — the ability

to generate and manipulate endogenous images — is typically addressed by visual reha

bilitation providers. Memory is a concept with which every person is familiar, and yet it

is poorly understood. Memory has both short-term and long-term components. In neu

ropsychology, long-term memory is often subdivided into procedural, perceptual repre

sentation, semantic memory, and episodic memory. 63 Short-term, or working, visual

memory is encoded and stored separately from auditory and haptic memories 64 and can

be broken down into spatial memory (thought to be processed by the magno-stream) and

object memory (thought to be processed by the parvo-stream). 58 Rehabilitation of visual

memory most often involves rehabilitation of visual aspects of working memory as well

as the ability to transfer this information to long-term perceptual representations.

Assessment and Rehabilitation of the Visual System

Assessment and Rehabilitation of Sensory Input/Reception

In the rehabilitation setting, testing and treatment of visual dysfunction has traditionally

centered on the higher-order perceptual disorders, tending to ignore reception. 65 It is

important to keep in mind that many of the higher-order visual abilities are dependent

on sensory input and ocular-motor functions involved in reception.

Eye Movements

Eye movements can be classified into those which shift the direction of gaze (i.e., saccades,

smooth pursuits, and vergences) and those which hold the direction of gaze steady (i.e.,

the vestibular driven, optokinetic, and fixation mechanisms). 66 Vergences are discussed

below under binocular disorders. Optokinetic nystagmus (OKN) may be used in testing

and therapy for other visual dysfunctions, but deficits in OKN are not generally considered

and rehabilitated in the TBI population as visual deficits. This may be because detection

of deficits in OKN requires more sophisticated eye-movement monitoring than is available

in most vision practices.

Saccades

Saccades are the fast eye movements one makes to change the object of fixation; the eyes

seem to jump from one target to another. They are the movements that take us from

word to word in reading and from object to object in driving. Saccades, during reading,

may be affected in a bottom up manner, that is, the eye

movement controllers have been

damaged (see Chapter 6), or in a top-down manner, that is, the ability to comprehend

text has been damaged causing more regressions and less accurate fixations due to poor

guesses about what is coming next. 67 Patients with acquired primary saccadic dysmetria

(i.e., saccades that overshoot or undershoot the target) will often complain of slow and

inaccurate reading.

Voluntary saccades, which allow us to change our gaze at will, and stimulus-generated

or reflexive saccades, where we correct our gaze or saccade to a target that has attracted

our gaze, are controlled, in part, by separate brain centers and should be addressed

separately. It is also important to assess the ability to inhibit saccades to peripheral targets.

This may be a function of the fixation mechanism discussed below. Simple observation

while the patient makes voluntary saccades between two targets or reflexive saccades to

alternately lit targets gives a qualitative measure of latency, speed, and accuracy of the

saccades. This procedure should be done at least for lateral saccades in right and left gaze

orientation. Each eye should be observed independently. Scoring systems for these obser

vations are reviewed by Griffin. 68

A more quantitative approach, which can provide additional data, is provided by the

Developmental Eye Movement Test (DEM).* This is a timed test in which the patient must

saccade to numbers which are arrayed on a page and name them as quickly as possible.

The DEM is a substantial improvement over earlier saccadic tests of this genre in that

timed baseline measurements are taken with the patient reading columns of evenly spaced

vertical numbers so that difficulties with decoding or verbal expression can be differenti

ated from difficulty with the ocular-motor task. Next, a series of horizontal rows of digits

are read. The number of errors and the time required to read all of the digits are combined

into separate scores for the vertical and horizontal tasks, with a higher score being slower

or less accurate performance. A high ratio of horizontal score/vertical score indicates a

saccadic problem. The DEM does not differentiate between difficulties in speed, latency,

or accuracy, although error scores give some indication of the latter. Normative data by

age is provided for times and error scores on both the vertical and horizontal tasks, as

well as the ratio between them.

A variety of instruments have been designed to objectively monitor and record eye

movements. These eye movement monitors give the most easily interpreted data, but are

less frequently used in the clinical setting due to issues of availability and expense.

Ordinarily, when training saccades, latency, speed, and accuracy are lumped into the

same scores; one trains for accuracy and then for speed, which improves as any one of

the three parameters improves. Therapy may start with something as simple as saccad

ing from one penlight to another as they are alternately lit in a dim room and progress

to complex search tasks, such as finding the next in a series of letters or numbers

scrambled on a page. Instruments, such as the Wayne Saccadic Fixator** or the

* Developmental Eye Movement Test: Available from Bernell Corporation, Mishawaka, IN, www.bernell.com.

** Wayne Saccadic Fixator: Available from Wayne Engineering, Skokie, IL.

Dynavision2000,* with various programs for training saccades in combination with

eye-hand coordination, are both useful and motivational. A number of computer-based

programs have also been developed for orthoptic treatment of ocular-motor and binoc

ular disorders. If difficulty inhibiting saccades or sustaining fixation is noted, one can

apply therapies such as making saccades only on a designated command to each in a

series of targets. The ultimate goal of therapy is to develop fast accurate saccades, both

large and small, which can be sustained and performed with a high degree of automa

ticity. The latter is tested by adding a cognitive load, such as addition or spelling, while

the patient does a saccadic task. This is an important concept in much of the visual

therapy of eye movements. When a cognitive load is added, performance of the ocular

motor task will break down in patients who are allocating

excessive resources to what should

be, for the most part, an automatic task. Griffin 68 and Press 69 have written excellent texts

for vision care providers interested in learning about vision therapy programming and

specific therapeutic techniques. Many of these therapy techniques may be prescribed

by vision care practitioners for application by occupational therapists in the rehabilita

tion setting.

Pursuits

Pursuits are the smooth eye movements used to follow a moving object and hold a clear

image of it stationary on the retina. They are complementary to the vestibulo-ocular reflex

in holding images stationary on the retina when we are moving. Pursuits are limited in

speed to about 30° per second. Attempts to track a faster target cause saccadic intrusions

and “cogwheeling” of the movement. Pursuits are usually tested at the same time that

the range of extraocular muscle motion in each eye is tested. Simple observation gives

qualitative information about the ability to track a target to the full range of motion of

each of the extraocular muscles monocularly, and then binocularly. The ability to track

should be judged on smoothness, accuracy, stamina, and the ability to track without head

movement. As with saccades, a cognitive load should be applied to judge automaticity.

Griffin 68 outlines systems for scoring pursuits.

Therapy for pursuits is often combined with extraocular stretching exercises relieving

restrictions or contractures of the extraocular muscles by following targets to the farthest

peripheral directions of gaze possible. These exercises are also important in the initial

stages of therapy for binocular disorders. If there is any deficit on monocular testing,

extraocular movements are trained monocularly prior to training binocularly so that equal

facility is gained with each eye before adding a fusional load to the task.

For most vision therapy, one goal is to make the patient self-monitoring. Pursuit therapy

is most effective when patients can be made aware of jerkiness or saccadic intrusions in

their pursuits so that they can try to correct them. Many patients will be able to feel their

eyes jump when their attention is directed to noticing interruptions in their smooth pursuit.

However, in many TBI patients, proprioception from the extraocular muscles seems to be

diminished or absent so that they are unable to feel when their eyes jump. In such cases,

cues can be added to assist the patient. One technique is to use afterimages to tag the

fovea by using a camera flash which has been masked off except for a small central target

which the patient fixates while the flash is triggered. The patient tries to maintain this

afterimage on the pursuit target without interruption. A simpler technique which is

sometimes effective is to have the therapist tell patients every time their eyes jump until

the patients can begin to feel it for themselves.

Various instruments, from rotating discs with targets on them to computer-generated

pursuit games, have been designed for facilitating pursuit therapy under both monocular

* Dynavision2000: Available from Dynavision2000, Markham, Ontario, Canada. www.info@dynavision2000.com.

and fused conditions. The ultimate goal of therapy is to be able to sustain smooth pursuits

with either or both eyes in all fields of gaze with a high degree of automaticity, initially

without moving one's head, and then, adding head, and later, body movement.

Vestibular-Driven Eye Movements

Vestibular-driven eye movements, in particular, the vestibular-ocular reflex (VOR), help

hold the visual world steady as we move within it. Patients who do not spontaneously

adapt to damage affecting the VOR may complain of oscillopsia, or rhythmic movement

of stationary objects. One way to test for a VOR problem is to have patients read a

nearpoint acuity card while shaking their head side to side and, then, up and down. In

the case of a VOR dysfunction, the visual acuity will be severely degraded as compared

to an acuity taken with the stationary target. 70 While therapy techniques have not been

specifically developed for VOR dysfunction, applying the after-image techniques dis

cussed above with the patient attempting to stabilize the afterimage, initially, while sitting

still and, later, with head movements, may give enough extra feedback to assist in recovery.

Whether the patient recovers or learns to adjust to the movement, oscillopsia should be

taken into consideration in driving rehabilitation.

Fixation

Fixation, or the act of holding gaze steady on a target, was once thought to be a function

of the pursuit system at zero velocity. This may be why fixation, itself, is seldom evaluated

except in relation to strabismic amblyopia. However, recent evidence implicates an inde

pendent visual fixation system, perhaps located in the parietal lobe. 66 Disturbances in

fixation may be considered in terms of inability to sustain fixation, as well as inability to

fixate centrically and steadily. The former can be easily observed by having the patient

hold fixation on a target for a minute. The ability to fixate steadily and centrically is only

observable with special techniques. The easiest, most objective measure is with a visuo

scope or, similarly, an ophthalmoscope with a central target. The examiner looks into the

patient’s eye with the scope which projects a target onto the retina. The anatomy of the

posterior pole of the eye and the projected target are viewed simultaneously. The patient

is instructed to fixate the target while covering the other eye. The stability of the foveal

reflex and centricity with regard to the target are easily observed in this manner. Other

methods require reliable subjective feedback. For instance,

the Haidinger brush, an entop

tic phenomenon that marks the fovea, may be elicited with an instrument such as the

Macular Integrity Tester* in which the patient fixates a target and reports the location and

stability of the Haidinger brush in relation to the fixated target.

In the case of inadequate ability to sustain fixation, the first step is to rule out refractive,

binocular, accommodative, or other ocular-motor dysfunctions that may lead to asthenopia

(i.e., eyestrain and/or headache) or discomfort. Such dysfunctions may make extended

viewing aversive. They are also remediable, where a primary attention or fixation mech

anism dysfunction might not be.

Unsteady or eccentric fixation is most typically encountered as a developmental phe

nomenon associated with strabismic amblyopia. In this manifestation, they cause

decreased visual acuity but are seldom accompanied by asthenopic symptoms. There is

an effective arsenal of therapeutic techniques to routinely remediate developmental eccen

tric fixation. 28,68 Unfortunately, unsteady fixation which is acquired following TBI may

cause asthenopic symptoms as it may be bilateral rather than unilateral and it may be

more resistant to treatment.

* Macula Integrity Tester: Available from Bernell Corporation, Mishawaka, IN, www.bernell.com.

Binocular Dysfunction

Accommodation

Accommodative dysfunctions are common in the TBI population. 9 They can cause blur

or asthenopic symptoms at nearpoint, as well as slow focus change from distance to near

and back. A simple nearpoint acuity test does not rule out an accommodative problem because

it only indicates whether the patient can momentarily hold focus at near. It does not

indicate either that patients can sustain that focus or that they have any focusing flexibility.

Objective techniques, such as nearpoint retinoscopy performed while the patient processes

visual information (e.g., reading or active involvement in viewing a picture), give an

accurate assessment of the patient's lag of accommodation and ability to sustain accom

modation on a nearpoint task. Use of such tools as convex to concave lens flippers (i.e.,

devices with two pairs of lenses for viewing — one pair of convex lenses which requires

that accommodation relax to clear the target and one pair of concave lenses which requires

accommodative effort to clear the target — set into a holder so that one can flip between

the pairs of lenses) of various powers can give measurements of facility. These can be used

as a subjective test with patients reading small print as they are able to clear it or as an

objective test during retinoscopy. As discussed above, accommodative difficulties can

cause convergence dysfunction, and convergence difficulties can cause accommodative

dysfunction. In many cases, it is impossible to tell which problem is primary.

Typical treatments for accommodative dysfunctions are vision therapy or convex lenses

worn either as single vision reading glasses or bifocals. In a prepresbyopic patient, vision

therapy is an effective way to improve the amplitude and facility of accommodation,

provided that the innervation subserving the function is sufficiently intact. Near-to-far

focusing jumps and concave-to-convex lens jumps with nearpoint targets may increase

both amplitude and facility. Associated vergence difficulties must be treated in conjunction

with the accommodative problem for effective remediation. If rehabilitation of accommo

dative function is not possible in the young patient, compensatory convex reading lenses

should be prescribed, generally in a bifocal format. Treatment of convergence insufficiency

due to the sudden loss of the accommodative-convergence mechanism may be necessary

in these patients.

Nonstrabismic Binocular Disorders

Nonstrabismic binocular disorders are those eye-teaming difficulties which do not result

in a frank strabismus (eyeturn). Convergence insufficiency — difficulty pulling the eyes

inward for near work — may be the most common nonstrabismic binocular finding in

TBI patients. Convergence insufficiency will often be missed by the simple pushup or near point

of convergence test. Krohel et al. 40 found that 6 of 23

TBI patients with convergence insuf

ficiency had a normal near point of convergence but showed abnormal convergence

reserves on prism testing. Prism vergence ranges should be mandatory in the visual

evaluation of the TBI patient. Convergence insufficiency can lead to fatigue, headache,

tearing, blurred vision, and eyestrain. 40 Often, it will cause skipping of words while

reading, or transpositions when reading digits in numbers, as the eyes struggle to converge

after each saccade. High exophoria (i.e., nonstrabismic outward resting posture of the

eyes) is also a common finding in TBI patients. Padula 9 hypothesizes that exo- deviations

of the eyes following TBI are caused by damage to the midbrain structures which integrate

ambient vision and spatial orientation. 60 This would be anatomically consistent with

simultaneous damage to the mesencephalic structures involved in convergence control. 15

Padula et al. have described posttrauma vision syndrome, 18,71,72 a cluster of common

posttraumatic visual deficits which may include high exophoria, convergence insuffi

ciency, and accommodative dysfunction. Using brain response testing (VEPs), Padula et

al. demonstrated visual processing abnormalities in posttrauma vision syndrome, as well

as improvement in the brain response to visual stimuli with application of low amounts

of base-in prism and binasal patching. 71 Their work also provides a clinical protocol for

diagnosing posttrauma vision syndrome using the VEP. If posttrauma vision syndrome

is diagnosed or suspected, early application of base-in prism and/or binasal patches may

be profitable in treatment.

Prior to treating other binocular disorders, monocular eye movement and accommoda

tive dysfunctions should be treated insofar as possible. Treatment of exo- binocular disor

ders may include prism in reading or distance lenses, binasal patches, or therapy. One

difficulty with putting base-in prism in lenses is that patients may prism-adapt over a

matter of days or weeks, developing the same phoria through the prisms as they had prior

to introduction of the prisms. In such cases, the prescription of base-in prism increases the

tonic error in binocular posture — leading some optometrists to argue that prism is poison.

However, in a significant number of patients, base-in prisms provide an immediate reduc

tion of symptoms and the patients do not prism adapt. The difficulty is in determining for

which patients this will be the case. In-office, short-term trials may help in this decision.

In any case, patients wearing base-in prism in their habitual spectacles should be followed

carefully. If they prism-adapt, additional prism should not be prescribed.

Besides use of base-in prism, Padula and Shapiro 10 recommend use of bitemporal or

binasal occluders (i.e., occluders covering only the temporal portion of both lenses or nasal

portion of both lenses, respectively) applied to the patient’s habitual spectacles for non

strabismic visual dysfunctions. They suggest that bitemporal patches may reduce confu

sion by reducing input from the midbrain ambient vision system when the patient is

attempting focal tasks such as reading. Binasal patches may be used in an effort to increase

patients’ awareness of their ambient vision while eliminating physiological diplopia (i.e.,

the normal diplopia for objects in front of or behind the plane of fixation), which may

initially cause confusion in the post-TBI patient. They also argue that this encourages

reorganization of the midbrain-based ambient visual system which is critical for visuospa

tial organization and vision during movement.

Vision therapy for poorly compensated exophoria or convergence insufficiency should

include fusional exercises to improve the amplitude of, and the ability to sustain, conver

gence, as well as the speed of reflex fusion. Convex lenses may be used to work fusional

convergence through the accommodative-convergence loop. Viewing through the convex

lens relaxes accommodative-convergence so that the patient must exert more fusional

convergence to avoid diplopia. Prisms can be used for manipulating images, causing the

fusional vergence system to respond to the displaced image. Polarized or anaglyphic

materials may be used in order to create second- or third-degree fusion targets (i.e., flat

fusion or stereoscopic fusion, respectively) which can be manipulated to expand vergence

ranges. At the same time, matches are developed between the ocular-motor feedback and

position-in-space interpretation. Many specialized instruments have been developed for

treatment of such binocular disorders. Some of these techniques may be prescribed for

application by occupational therapists. Many of these techniques require more experience

in vision therapy or more extensive instrumentation for effective application and, there

fore, need to be performed in the vision care setting.

Esophoric (i.e., nonstrabismic inward resting posture of the eyes) deviations of binocular

vision are less common. This may be due to anatomical considerations or because eso

phorias are more difficult to compensate for and are more likely to break down into a

strabismus. Poorly compensated esophoria will often cause eyestrain or headache around

the eyes or temples. Treatment may include use of convex lenses for near work, base-out

prism, and vision therapy similar to that described for exo- deviations. The same cautions

regarding use of prisms apply here — perhaps even more so, as base-out prism is more

difficult to remove once the patient has become dependent on it.

Strabismus

In strabismic deviations secondary to TBI, diplopia causes disorientation, as well as dif

ficulty with spatial judgments, eye-hand coordination,

mobility, and reading. Patients will

often squint, close one eye, or assume head turns or tilts in order to try to block one eye

or to keep objects in a field of gaze where they are able to fuse. In children, suppression

and amblyopia may result. Patients who are diplopic should have a visual examination

early in their rehabilitative program. Assessment of refractive status, binocularity, and

ocular health do not require verbal communication from the patient. The same objective

techniques that one would use to determine these conditions in a 4-month-old infant can

be applied in the TBI population, when necessary. Prisms or partial patching (as discussed

below) can be prescribed to eliminate diplopia so that other ongoing therapies can be

more effective. Any time that prisms or patches are prescribed, frequent follow-up is

required to keep pace with spontaneous and therapy-related recovery.

Fresnel (flat stick-on) prisms may be applied in an effort to reestablish fusion at the

angle of the deviation. Lenses may also be applied in a therapeutic manner, using the

accommodative-convergence relationship to mediate the angle of the deviation. For

patients who are able, therapy is then applied, as described above for nonstrabismic errors,

creating equal, efficient monocular skills, followed by vergence exercises combined with

fusion, depth, and spatial localization training. Initial attempts at reestablishing fusion in

adjustable instruments or with variable prisms may be met with horror fusionis-like

responses where the images from the two eyes will approach each other and then jump

to the other side, or may be superimposed, but not fuse into one object with the percept

of depth. 73 The prognosis for recovery is best for patients with horizontal strabismus,

uncomplicated by vertical deviations. However, vertical deviations will often resolve with

therapy or as therapy is applied to the horizontal component of the strabismus. Residual

vertical deviations can often be managed with prism ground into the patient’s lenses.

Patients who are not able to perform vision therapy for remediation of their strabismus

are generally managed over the long term with patches and prism. They may also be

managed surgically beyond the time period when spontaneous recovery might continue

to lessen the angle of deviation.

Traditionally, TBI patients have been advised to use constant patching of one eye to

resolve diplopia. However, this has undesirable consequences, such as loss of peripheral

vision on the patched side while patched and disuse of the patched eye which may lead

to suppression and/or diminish the chances of spontaneous recovery of fusion. Partial

patching to eliminate diplopia or patching for limited time periods to facilitate other therapies

is more desirable. If patients are unable to access rehabilitative vision care in a timely

manner and diplopia is a major problem, patching the eyes on a daily alternating schedule

may minimize the detrimental effects of patching until they can access such care.

Partial patches are tailored to the patient’s particular deficit and should encourage

recovery. As discussed above, binasal patches applied to the patient’s spectacles allow for

a full field of vision while eliminating diplopia. They are a particularly good patching

method for treatment of esotropia and may enhance peripheral awareness while encour

aging abduction. If the esotropia is unilateral, a single patch may be applied to the nasal

portion of the patient’s spectacles over the nondeviating eye. This technique encourages

abduction of the esotropic eye, as patients must either abduct that eye or turn their head

to view in the visual field ipsilateral to the deviating eye. Exotropic deviations may

sometimes be treated with translucent bitemporal patches. Thus, each eye must adduct

to view in the contralateral field. However, bitemporal patches limit peripheral vision and

are not recommended for long-term application or during ambulation. For patients who

fuse in some fields of gaze but have noncomitant strabismic deviations, partial patches

may be applied to a portion of one spectacle lens to occlude only the diplopic field of

gaze, allowing for fusion, most of the time. At the same time, vision therapy should be

applied to expand the field of comfortable binocular vision.

Partial patches may be as inexpensive as a piece of translucent tape applied to the patient's

spectacle lenses. Cling patches* are also available commercially. These patches, which stick

to the lenses electrostatically, may be easily removed for therapy and reapplied. These also

come in varying densities to degrade visual acuity to approximately 20/100, 20/200, or

20/400. The less dense patches enhance patient acceptance since they are, cosmetically,

quite good and can hardly be discerned on the spectacle lenses by outside observers.

Binasal, bitemporal, and partial patching may not work well for persons with various types

of field defects.

Because most TBI patients with secondary strabismus had normal fusion prior to their

injury, their prognosis is good for recovering fusion, even if one or more muscles are

palsied. Even in apparent paresis of the muscle, recovery can occur, although the prognosis

is more guarded. If a horror fusionis-like response is elicited on initial testing, peripheral

fusion techniques emphasizing depth and SILO (see text below) may be used until the

patient is able to fuse more central targets. Antisuppression therapy should not be used

on these patients until there is evidence of their ability to attain central fusion.

Suppression

Suppression is the ability to diminish or eliminate the central vision originating from one

eye to avoid diplopia. In children, it may lead to

development of amblyopia in a unilat

erally-suppressed eye. Once suppression develops, antisuppression therapies must be

applied in order to continue with fusional training.

Suppression may be considered either a blessing or a curse, depending on the goal of

rehabilitation. If the goal is to restore central fusion with all of the fine motor and stereo

scopic advantages that come with it, then suppression is to be avoided through proper

application of prisms, patching, or early application of vision therapy. If spontaneous

resolution and 3 months of intensive vision therapy show no progress at all toward fusion,

then perhaps encouraging suppression to develop may be the most effective way of

avoiding diplopia.

If the patient cannot learn to successfully fuse or suppress, then a monovision refractive

correction may be prescribed in which the spectacle or contact lens for one eye is set for

near work and the other lens is set for distance clarity. This creates one clear image at

each distance so that, with practice, the patient learns to easily attend to the clear image,

giving a stable referent at each distance.

Decreased Visual Acuity

TBI patients with decreased visual acuity which cannot be improved by refractive means

or by increased contrast will generally profit from standard low vision rehabilitation

techniques. Unfortunately, the prospect of accepting their

limitations and working hard

to learn to use the remaining vision in the most efficient manner possible is not as

motivating as the prospect of performing other types of therapy to recover lost visual

function. This makes low vision rehabilitation a less positive experience for many patients.

Numerous small telescopes have been developed for magnification of distant objects.

These may be hand held for stationary viewing or for spotting and identification. Increased

magnification results in reduced visual field. Therefore, telescopes used only for spotting

* Cling Patch: Available from Bernell Corporation, Mishawaka, IN, www.bernell.com.

and identification will generally have higher magnification than telescopes used for dis

tance viewing. Telescopes may also be mounted in the top portion of a spectacle lens for

frequent spot reference during such tasks as driving and note taking. A slight downward

tilt of the head allows access to the telescope.

For nearpoint tasks, aids range from high powered convex lenses for nearpoint work,

allowing the patient to hold reading material closer, to video enhancement of images via

closed circuit television. Bar magnifiers may assist low visual acuity patients in keeping

their place during reading. Magnifiers that are handheld or stand-mounted for stability

are also frequently used.

One of the difficulties in prescribing for the patient with moderately reduced acuity

(20/60 to 20/120) is that many magnifying techniques will slow the process of reading.

One must judge whether the patient can be rehabilitated with convex lenses and proper

training or whether a magnifier will be of greater assistance. Trial and error to find the

correction with which the patient is most comfortable will be a large part of the decision.

Decreased Contrast Sensitivity

Contrast sensitivity is the ability to discriminate differences in luminance between adjacent

areas. Low contrast situations occur in fog, darkness, and when viewing through media

opacities in the eye such as cataracts. Reduced contrast sensitivity should be suspected

when patients with good visual acuity complain of not seeing well. Neural damage in the

visual system may also cause poor contrast sensitivity. 74 Damage to the magno-system

results in a reduction of contrast sensitivity for middle to low spatial frequency (larger

contours). Damage to the parvo-system results in loss of contrast sensitivity in detailed

targets and may result in decreased visual acuity. Patients with diminished contrast sen

sitivity in the high frequency range resulting in decreased visual acuity may find magni

fying low vision aids helpful. Those with diminished contrast sensitivity for middle to

low spatial frequencies are not helped by magnification. Printed material for these patients

should be good quality and high contrast. In well lit conditions, contrast enhancing tints

(usually yellow to amber tints that screen out blue light) or overlays may be used. The

selection of tint is usually based on the patient's subjective assessment of the quality of

their vision. Working with special lighting for specific tasks may be helpful.

Visual Field Loss

Many patients with TBI have resultant visual field loss. Knowledge of visual field defects

is important in helping patients adjust their behavior. It is also important for other reha

bilitative therapists working with the patient to adjust their therapy, taking the field defect

into account. Field defects may be either absolute, where there is no sensation of light or

movement from within the scotoma, or relative, where brighter, larger, or moving stimuli

may still be sensed within the scotoma. Assessment may range from simple confrontation

testing, to tangent screen, to automated perimetry with a fixation monitor. Each has

advantages and drawbacks. Confrontation testing can be done with no special equipment

on patients who are unable to sit as required for the other tests. It gives a gross assessment

of the extent of the visual field in each direction with each eye. However, it will not reveal

scotomas within those boundaries. Tangent screen testing allows the examiner to very

closely map small scotomas and islands of vision within the field which may not be

mapped well on an automated perimeter that presents test points in a predetermined

pattern. Automated perimeters with fixation monitoring give a relatively reliable mea

surement against which one may chart change in the visual field through repeated mea

sures across time. However, the testing is often lengthy, taxing both posture and attention.

Probably the most common visual field defect necessitating rehabilitative services is

homonymous hemianopia. Rehabilitation has mainly been concentrated on recognizing

the field defect and working on compensatory scanning patterns, as well as mirror or

prism devices to allow more peripheral areas of the scotoma to be viewed with smaller

excursions of the head or eyes. Patients with hemianopia may also have mild balance

difficulties (with their center of gravity shifted toward the blind field). 75 Yoked prism

(discussed below) may be helpful in reestablishing balance.

Compensatory visual search into the scotomatous field is found to expand as a result

of training and these gains remain stable over time. Patients with hemianopic field defects

who do not receive training do not tend to use adaptive search strategies. 76

Mirrors can be mounted on spectacle lenses 77,78 or Fresnel prisms with their apices

toward the pupil can be added in the peripheral portion of the lens in the scotomatous

field(s). 79 These devices move the images that fall in the periphery of the scotomatous

field closer to the center of vision. Both of these techniques enhance peripheral awareness

because it is easier to view farther into the scotomatous field without head movement and

having the device applied to the spectacles serves as a reminder to do so. Considerable

training and motivation are required for successful application of these devices as, when

one scans into binocularly applied peripheral prism, the visual world jumps. If the prism

is applied monocularly, then patients are diplopic while scanning into the prism and must

turn their head to fixate the object of interest singly after locating it. Rather than using

Fresnel prisms, the prism may be ground with patients' spectacle prescription and

mounted into their spectacle lens, reducing the optical blur induced by the Fresnel type

prism. Limited visual field recovery has been reported in some patients with this type of

peripheral prism system applied monocularly, 42 perhaps from reallocation of cortical

receptive fields. For patients with severe visual field constriction, the prism technique may

be used in all affected fields. 80 Peli 81 recommends application of horizontal strips of Fresnel

prism placed (base toward the visual field defect) superiorly and inferiorly across the

extent of the patient's lens on the side of the field defect; for a left hemianopia, one would

place the prism strips on the left lens. Peli argues that this creates peripheral diplopia,

which is easier to adapt to than a peripheral prism that one scans into, and it cues attention

to the unsighted visual field without regard to the lateral

position of the eyes. Field

expanders or reverse telescopes may be helpful in occasional sighting for orientation, as

when entering a room or locating objects on a table. Distortion and minification when

viewing through field expanders make them difficult to use and, again, considerable

training and motivation are required. 82

Perceptual speed and perceptual span, often trained with tachistoscopic techniques, are

also important. During mobility, the patient with visual field loss must make more fixations

to cover the necessary visual expanse. Perceptual speed and span are also important for

reading as any visual field loss that approaches the midline will tend to slow the reading

process. Patients with left field loss may not see the beginnings of longer words and

misread them as similar words. They also have difficulty returning to the beginning of

the next line. The simplest technique for remediating this problem is to keep a finger at

the beginning of the next line down, or use an L-shaped marker that marks the line being

read and has a bright flag at the beginning of the line to indicate the position of the

beginning of the line. Typoscopes or rulers may also be helpful. A contrasting strip of

ribbon placed vertically along the left margin is a simple, effective technique. Patients

with right hemianopias lose the preview information that allows them to judge the place

ment of the next saccade and guess at the content of the

next word. They also have

difficulty judging where to return at the end of a line of print and will often return to the

next line too early. A finger, hand, or strip of ribbon held at the end of the line serves as

an easy marker. These patients may do better reading upside down or rotating the text

90 degrees and reading vertically so that they can preview the text coming up in their

sound visual field. 83

Lastly, there have been reports in the literature of some partial resolution of hemianopia

through training with lit targets moving from the scotoma toward the intact visual field

and scanning into the scotoma. 84,41 These findings have been questioned by Balliet et al. 85

who were unable to replicate findings of recovery by training with lit targets. They bring

up valid concerns regarding this controversial issue. However, Balliet et al. used smaller

targets in their training than were used in the original studies because the smaller target

led to less intrasubject variability. In therapy, variable responses may be the hallmark of

recovery. In their desire for scientific reproducibility, Balliet et al. may have thrown away

the therapeutic effect. Kerkhoff et al., 41 in a study which had positive results, used a three

step training procedure which included: (1) performing large saccades into the blind field,

(2) improving visual search on projected slides, and (3) transfer of both to activities of

daily living. With this procedure, they were training

skills that the patient needed to

acquire, and partial resolution of the scotoma seemed to be an additional gift for some of

their patients.

Photophobia

Photophobia (i.e., extreme light sensitivity) is a common after-effect of head trauma. 86

Jackowski, 87 using dark adaptation studies, has demonstrated damage to rod mediated

visual mechanisms in brain injury patients with significant photophobia, even though

they seldom complain of their night vision being reduced. The rods (i.e., dim light vision

receptors) mainly feed into the magno-visual subsystem. Cone mediated visual mecha

nisms were also damaged in these patients, but these deficits were small in comparison

to the rod mediated visual loss. The cones (i.e., daylight vision receptors) mainly feed into

the parvo-pathway. The magno- and parvo-pathways are mutually inhibitory. Jackowski

has hypothesized from her findings that damage to the rod system, or magno-pathway,

disinhibits the cone or parvo-pathway, causing this bright light sensing pathway to be

overly responsive; this mechanism may be the cause of posttraumatic photophobia in

many patients.

Patients who have posttraumatic binocular disorders or pupil dilation of one or both

eyes may also complain of photophobia. Successful treatment of the binocular dysfunction

will lessen the photophobia in cases where this is the primary cause. Otherwise, photo

phobia may be handled with any number of tints in the patient’s spectacle lenses — the

color and density of which are mainly prescribed for subjective comfort. Photochromic

lenses, which darken in sunlight and lighten indoors, may be helpful, although they do

not darken well for driving applications. While eye protection from ultraviolet radiation

should be a consideration for everyone, it is even more important to incorporate ultraviolet

protection into tinted lenses for patients with mydriatic pupils. In extreme cases of mydri

asis, it is sometimes possible to prescribe an opaque custom contact lens with a small

transparent pupil to decrease the light entering the eye. However, often, patients with

mydriatic pupils have dry eyes and contact lenses would be contraindicated.

Assessment and Rehabilitation of Perception/Integration

Localization and Spatial Vision

There is little information on effects of brain injury on the magno-pathway until it reaches

cortex. However, it is known that the large axon diameter of the magno-cells makes them

more vulnerable to various types of damage as in glaucoma and Alzheimer’s disease. 55

Disorders of motion perception are rare. 88 Indeed, studies in monkeys show that a lesion

in the middle temporal area produces disorders of motion perception but that most of

these disappear within a few days, presumably because the

function is taken over by

redundant pathways. Damage to the posterior cerebral cortex (usually, right posterior

parietal) often results in spatial inattention to the contralateral visual field known as

unilateral spatial neglect (USN) discussed below.

A number of reception dysfunctions affect perception of spatial localization and orien

tation. For instance, we use the feedback from our vergence system to assist us in judging

distance. If our eyes are more converged, then the target we are fixating is seen as closer.

In persons with good binocularity, this effect, called smaller in, larger out (SILO), 89 can be

demonstrated by the use of prisms. If one fixates a target and places base-out prism in

front of the eyes, the images of the target are moved in a convergent direction and the

eyes must converge in order to avoid diplopia. The target will be perceived as having

moved in toward the observer and will appear smaller than before. Size constancy dictates

that objects get larger as they come closer but, since the target has not really moved, the

image size on the retina remains unchanged. Therefore, since the vergence system says

the object is closer but the image size remains unchanged, the interpretation must be that

the object is now smaller. Base-in prism produces the opposite effect, where the eyes

diverge, the object appears to move out, away from the observer, and appears larger.

Due to the roles of accommodation and convergence in depth

perception, 61 sudden onset

of dysfunctions in accommodation or convergence secondary to TBI can make objects

appear closer or farther away than they actually are, effectively collapsing or expanding

visual space.

Conversely, feedback from the cortical and subcortical spatial processors affects the

vergence system. For example, one type of convergence is driven strictly by proximity to

an object; targets close to the face make us converge even though we may be viewing

through an optical system set at infinity. The TBI patient with a primary visuospatial

disturbance will often have inaccurate eye pointing.

Feedback in visuospatial processing runs both ways, from the binocular system to

visuospatial processors and from visuospatial processors to the binocular system. There

fore, the most effective therapy for disorders of spatial perception in depth must take into

account the binocular response. Similarly, the most effective treatment for eye teaming

will often concentrate not only on achieving the correct motor response but also on creating

correct spatial judgments which can be used to guide the motor response.

Other difficulties in spatial organization may be reflected in inability to properly localize

objects in relation to oneself. Egocentric “midline shifts” of varied etiologies have been

noted in patients following brain injury. These shifts in midline perception can cause shifts

in posture and weight distribution which may cause difficulty with balance and gait. They

may also affect eye–hand coordination. Tests used to detect egocentric visual midline shifts

include line bisection tasks 90,91 and, more commonly, subjective judgment by the patient

of when a wand or pencil, held in a vertical orientation and moved laterally, is directly

on the horizontal midline (i.e., in front of nose). 10 Visual field defects, hemifield visual

neglect, disruption of the midbrain ambient visual system, tonic ocular-motor imbalance,

and imbalances in extraocular proprioception, or efferent copy commands to the extraoc

ular muscles, are all possible causes of midline shift. As described by DeRenzi, 92 tonic

ocular-motor imbalance is an increased tone in the muscles turning the eyes to the side

contralateral to the lesion. During routine testing, it is masked by the fixation mechanism,

but it can be elicited by having the patient attempt to look straight ahead in darkness.

During development, we learn to maintain position constancy of objects in spite of eye

movements by comparing the efferent copy (commands going out to the eye muscles) and

proprioceptive information received from the eye muscles, with the movement of the

retinal image. 66 As the eyes, extraocular muscles, and separation between the eyes grow

and change, slow adjustments in these systems take place. However, in TBI, a sudden

change in any one of these systems may occur, changing the

perceived location of objects

in relation to ourselves.

Therapy for spatial distortions may include therapy for accommodative and conver

gence disorders as described above, with special emphasis on development of SILO and

spatial localization. Lenses and prisms may be applied in either a compensatory manner

or for therapy purposes. Spatial and postural effects of these optical devices are thoroughly

reviewed by Press. 93 Padula 9 advocates use of small amounts of base-in prism in order to

facilitate reorganization of the ambient system by reducing stress on the peripheral

fusional system in cases of exophoria. Yoked prisms (i.e., equal amounts of prism in front

of each eye with both bases in the same direction — up, down, right, or left) are an effective

intervention for many cases of egocentric midline shift. These prisms move images of the

surrounds in the direction of the apex of the prism for both eyes. Low amounts of yoked

prism may be used in a compensatory manner 18,94 to shift images of objects that belong

on the visual midline to the recently misplaced perceived visual center; this relieves the

perceptual mismatch between what actually is and what is perceived — often restoring

balance, normal gait, and the ability to move about easily in the world. More often, large

amounts, such as 15 prism diopters, will be used in therapy to force problem solving and

increase flexibility in the sensorimotor system. Activities

such as walking or tapping a

swinging ball while wearing these prisms involve recalibration and integration of vesti

bular, proprioceptive, kinesthetic, and extraocular efferent copy systems. This is an

extremely effective technique for disrupting habitual patterns in patients who have been

unresponsive to more instrument-based therapies so that, with guidance, they can reor

ganize their visual-motor system in a more adaptive manner. It is important to note that,

in an observer with a normal visual system, prism adaptation would be expected to occur

with long-term wear. Therapeutically, yoked prisms are only worn for periods extending

from a few minutes to a few hours. Presumably, those individuals who experience a long

term compensatory effect wearing yoked prism full time have visual dysfunction which

precludes prism adaptation to this prescription. This reasoning makes sense in that, if

these patients had been able to do the sort of reorganization that prism adaptation requires,

they would probably not have sustained an egocentric visual midline shift.

Unilateral Spatial Neglect

Unilateral spatial neglect (USN) is a phenomenon where an entire hemifield (usually the

left) is simply unattended, as if a hemianopia existed there. Worse, patients are unaware

of the defect. This makes them more prone to accident and more difficult to rehabilitate

than the hemianope without neglect. When neglect affects

only the visual system, it may

easily be mistaken for hemianopia and, indeed, often coexists with true hemianopia.

Recently, split-brain research 95 has provided evidence that the right hemisphere allocates

attention to both visual fields, where the left hemisphere allocates attention to only the

contralateral field (Figure 7.4). This finding in split-brain patients suggests that the right

hemisphere allocation of attention to right visual field is probably mediated through

subcortical mechanisms. It may also help explain why most cases of neglect are secondary

to right brain damage. Although USN is easily mistaken for hemianopia, the mechanisms

and damaged brain substrates underlying USN are quite different from hemianopia.

Hemianopia is a sensory loss, where the damaged neural substrates are in the postchiasmal

visual pathway up to and including primary visual cortex. USN is a perceptual deficit,

where the neural substrates necessary for sight are intact, but the visual substrates or

pathways necessary to attend to or perceive the sensory input are not. These neural

substrates probably lie in two major centers of the brain — the posterior parietal lobes,

which are involved in allocation of visual attention, and the frontal lobes, which are

involved in generating eye movements. 7

Various tests, including drawing, line cancellation, pointing to objects scattered around

the room, reading a newspaper article, and line bisection,

have been developed to deter

mine the presence of USN. USN may vary in degree and appear on some tests but not

others. 96 Inattention may also be differentially distributed along the vertical meridian of

the neglected field. 91,97 As reviewed by Kerkhoff et al. 41 during line bisection tasks, patients

with neglect typically transect the line off to the side contralateral to the field defect.

Patients with hemianopia generally do the opposite, deviating in the direction of the

scotoma. Patients with both are more likely to bisect the line. Compared to patients with

hemianopia without USN, patients with USN have even more abnormal scan paths when

viewing simple figures and with fewer excursions into the blind field. 98

Clinically, three considerations are important during therapy for USN (N. W. Margolis,

personal communication). First, the patient must be made aware of the condition. Second,

compensatory strategies such as scanning and reading strategies should be taught. Last,

these strategies must be generalized to both static, predictable stimuli, such as those

encountered in reading or walking down a familiar corridor, and to dynamic, nonpredict

able stimuli, as encountered in new environments. Gordon et al. 99 present a three-step

program for remediation of perceptual deficits in patients with right brain damage. Step

1 is basic scanning training. Step 2 is somatosensory awareness and horizontal size esti

mation, and Step 3 is complex visual perception training combined with left to right visual

scanning within these tasks. They present evidence that, with extensive training, these

functions generalize to daily living. Gianutsos 45 reviews the literature on perceptual reha

bilitation in USN and concludes that, overall, the efficacy of therapeutic intervention is

supported. However, studies of solely microcomputer-based scanning therapy have not

been shown to generalize. 100,101 For an excellent review of diagnostic and therapeutic

activities, see Margolis. 102

FIGURE 7.4

Allocation of spatial attention by the cortical hemispheres. The right hemisphere allocates spatial attention to

both right and left visual fields, while the left hemisphere allocates attention to only the right visual field. Thus,

USN of the left visual field (following right brain damage) is considerably more common than USN of the right

visual field. (Adapted from Moore, J. C. and Warren, M., Effect of visual impairment on postural and motor

control following adult brain injury, Continuing education workbook by visABILITIES Rehab Services, Inc.

[www.visabilities.com].)

Object Perception

The visual percept we construct from sensory signals supercedes even the concrete sensa

tion of touch. For instance, if an object, such as a square of plastic, is viewed through a

minifying lens and is simultaneously manipulated by the

hand (with the hand covered so

that it cannot be used as a visual cue), the observer reports the square as being smaller

than the real square. This is true whether the method of report is visual (i.e., picking a

matching square out of a range of squares of various sizes), visual and tactile (i.e., drawing

the square to size), or, surprisingly, tactile (i.e., picking a matching square by touch alone). 103

It has been suggested that, visually, we construct perceptual objects via a two-step pro

cess. 104 First, preattentive data-driven filtering produces shapes and registers their features,

as in reception. Then, focal attention is used to select a spatial location and integrate the

features registered there into a perceptual object. This is analogous to figure-ground orga

nization and should be concept-driven processing rather than data- or sensation-driven.

Evidence arguing for this feature integration theory comes from the way that stabilized

retinal images fade feature by feature rather than in small random parts. Principles at work

during the second integration stage may be the Gestalt principles of proximity, good con

tinuation, similarity, closure, and pragnanz (i.e., simplicity, regularity, or symmetry) or local

vs. global processing. In addition to integrating visual features, object perception includes

cross-modality integration (i.e., integrating auditory, tactile, and olfactory sensations with

visual information to complete the perceptual object). Spatial orientation, both the ability to

process the orientation of external objects (extrapersonal orientation) and the ability to

process the orientation of ourselves with regard to other objects (personal orientation), is

discussed here because the treatment modalities are generally more similar to those used

with object perception, rather than other spatial dysfunctions. Personal orientation may be

supported by the frontal lobe (particularly in the left hemisphere); extrapersonal orientation

may be supported by the “where” pathway, particularly the right posterior parietal area.

Assessment and treatment of perceptual/integrative vision must take into account dys

functions in reception. Multiple tests, with some redundancy, are necessary to differentially

diagnose perceptual dysfunction of the visual system. For instance, copy-form tests are

useful and may tell you something about spatial organization, but if the forms are poorly

reproduced, you do not know whether this is due to difficulties in reception, perception,

visual-motor integration, or fine motor coordination. One must have a battery of tests

that probe perceptual functions such as figure-ground discrimination, closure, and spatial

organization, as well as cross-modality and visual-motor integrative functions from dif

ferent perspectives using different modalities. Gianutsos 45 reviews most of the available

perceptual tests in the literature. For a sample test battery, see Aksionoff and Falk. 105 The

perceptual workup will generally take 2 to 3 hours to administer and may need to be

broken up into multiple sessions for TBI patients who fatigue easily.

During therapy, the patient and therapist must constantly keep in mind that it is the

process, not the final answer, that is important. Where possible, the strategies patients are

using to solve a particular problem in therapy should be discussed. This creates awareness

of the process, insight for the therapist, and provides the opportunity for the therapist to

suggest modifications in the patient's problem-solving strategy. As reviewed by Groff

man, 106 perceptual therapies may be considered as falling into a number of treatment

modalities: (1) motor activities, (2) manipulatives, (3) instruments, (4) vision therapy, (5)

lens therapy, (6) auditory therapy, (7) workbooks, toys, and games, and (8) computers.

The modality is tailored to fit the level and perceptual deficit of the patient.

While gross motor activities applied in vision therapy have often been criticized by

those not involved in therapy, they are sometimes necessary to create more optimal

support for the visual system. The eyes and visual system do not exist in isolation; the

eyes are horizontally displaced from each other in the head and the biomechanics are such

that they are intended to work with a horizontal disparity in relation to gravity. Tilting

the head induces ocular torsion. Gross motor activities are also used for creating

visual–proprioceptive and visual–kinesthetic matches in

ambient space. Vision is domi

nant over touch in the normal visual system. However, in therapy, proprioceptive and

kinesthetic feedback can help teach veridical visual perception. In the rehabilitation setting,

many therapeutic activities with these two goals can be taken over by physical or occu

pational therapists.

Manipulatives are objects that can be used on the table top so that they can be handled,

rotated, rearranged, and examined in a very concrete way. They allow for learning higher

order visual concepts such as visual discrimination, form perception, and spatial orientation

and organization with very concrete tools. These include blocks and puzzles specifically

designed to teach perceptual skills. Other common examples of manipulatives are flannel

boards (used with felt shapes of varied sizes and colors), geo boards (i.e., boards with

evenly spaced pegs on which designs are made by stretching rubber bands between the

pegs), or Peg-Boards TM which can be used for reproducing patterns with or without rota

tions in orientation. Manipulatives also provide excellent eye-hand coordination activity.

A variety of instruments have been developed for visual-perceptual training. Instrument

techniques are varied and seem to provide additional motivation to many patients. An

example would be adjustable speed tachistoscopes which are used to increase visual

perceptual speed and span, as well as visual attention and

short-term memory. Tachisto

scope targets may vary from abstract geometric forms to be copied, to digit strings, or

words. They are also useful to demonstrate USN or hemifield loss to the patient as, without

time to scan, they will only see the portion of the word presented in the intact field.

Application of vision therapy to remediate receptive dysfunction often involves visual

perception — both in spatial organization as discussed above and in that many fusion

tasks require figure-ground discrimination. Lens and prism therapy have already been

discussed in terms of shifts in the localization and orientation of local surrounds.

Use of the auditory modality can enhance integration of visual and auditory senses. A

number of tape and record programs are available for development of various perceptual

and perceptual-motor skills including spatial relations, directionality, and visual-motor

integration. 107

Many workbooks, toys, and games are available in educational supply stores, including

popular activities with hidden pictures or words for figure-ground discrimination and

form perception. Worksheets with simple, incomplete figures to be completed by the

patient may be used for development of closure, as well as form perception. These tools

also help develop eye-hand coordination. They are generally two-dimensional represen

tations, but have the advantage that, once they understand

the process, patients may

practice unsupervised with worksheets.

With most of the above activities, the understanding of the visual goals, experience, and

creativity of the therapist are key to the success of therapy. However, through development

of computer programs, perceptual therapy has become more accessible and more easily

administered by other rehabilitation disciplines such as occupational therapy. A number

of perceptual programs which combine the challenge and motivation of a video game

with good perceptual therapy are commercially available. Such programs were reviewed

by Press 108 in 1987. Although more programs have been marketed since then, many of the

same companies are developing them, and Press' review is a good resource for those

interested in applying these techniques. Computer therapy generally requires the ability

to manipulate a joystick or press a limited number of response keys. For patients having

motor control problems, this may be easier than using workbooks or manipulatives.

Visual Agnosias

Agnosia is the inability to recognize objects visually. Object recognition may be appercep

tive, where the perception of the object is faulty, or associative, where the object is per

ceived correctly but cannot be associated with prior memories or past experience. 109 In

apperceptive agnosia, patients might not be able to match similar objects, draw or copy

objects or shapes, or name objects by sight. However, if allowed to use tactile input, they

could both name and match the object, as well as describe its function. Apperceptive

agnosia is rare and is associated with diffuse cerebral damage of the occipital lobes and

surrounding areas.

In associative agnosia, objects and shapes can be matched but the patients are unable

to associate them with past experience or function. For instance, they may be able to draw

a key that is placed before them but be unable to name it or describe its function. When

allowed to handle the key, they could both name it and relate that it is used to unlock

doors. Associative agnosias can be surprisingly specific. The more common types of

agnosia include object agnosia, prosopagnosia (i.e., inability to recognize familiar faces),

and color agnosia.

Diagnosis of visual agnosias is important in deciding the proper course of treatment —

therapy or compensation. Associative agnosias may be due to lesions in the pathway that

connect the visual “what” pathway with memory areas. De Haan, Young, and

Newcombe 110 have shown that covert recognition of objects and faces may exist in the

absence of overt recognition. They suggest that this may provide a foundation for reha

bilitation. Sergent and Poncet 111 report some restoration of overt face recognition under

specific circumstances in one patient. While, in some cases, restoration of function may

be possible, therapy to directly address the agnosia is likely to be a long process and

success is not guaranteed. Compensatory strategies, as for low vision/blind patients, may

be the best alternative for immediate management of agnosia.

Alexia

An important part of text recognition is the decoding of visual percepts into language.

Interruption of visual pathways at the left angular gyrus 112 or splenium 113 prevent this

decoding process from occurring, resulting in acquired alexia or inability to read. Most

case reports of this dysfunction show some residual reading function. Treatment of alexia

using integration strategies and based on the patient's residual reading skills has been

successful. Often, a letter-by-letter reading strategy can be employed by these patients,

although it severely slows reading. Motor rehearsal, in terms of copying or tracing letters

and words, as well as flash card techniques pairing the written with the spoken word

have been applied with some success.

A successful strategy employed with one patient is described by Daniel et al. 112 Initially,

the patient spelled words aloud from flashcards and then said the word (as he recognized

the word from auditory spelling). With practice, the patient was able to substitute covert

spelling. Continued practice in this manner significantly increased his ability in reading

and naming so that he was able to return to work within 4 months postinjury. At the 1

year follow-up, reading was still laborious but the patient was able to read sufficiently to

function in his job.

Assessment and Rehabilitation of Motor Output/Behavior

Visually-directed motor output includes not only the planning and execution of eye–hand

coordination and visually-guided movement through space, but also the planning and

execution of the next eye movement. As in the model (Figure 7.3), reception affects

perception which affects cognition — and both of the latter affect programming of the

next eye movement, feeding back into reception (control of binocularity, eye movements,

and fixation). This is a flexible, but closed, loop.

The Eyes

Most aspects of assessment and rehabilitation of motor output to the eyes have been

discussed in the Assessment and Rehabilitation of Sensory Input/Reception section in this

chapter. The rehabilitation already discussed is generally performed in the vision care

setting. Some specific exercises may be prescribed for application by occupational thera

pists in either inpatient or outpatient rehabilitation settings.

In addition to the aspects of ocular-motor and binocular control which have already

been discussed, ocular-motor planning and integration with the output controllers to the

eyes are involved. Ocular-motor gaze apraxia is the inability to execute purposeful eye

movements (reviewed by Roberts 109). Patients with ocular-motor gaze apraxia may be

differentially affected for various stimuli, e.g., unable to change fixation in response to

verbal commands or peripheral visual, auditory, or touch stimuli. This may be exploitable

in that one may be able to practice saccades to a multimodality stimulus and wean out

the intact modality. An activity such as Letter Tracking* where one underlines rows of

letters until a target letter is reached and then circles the target letter, may allow tactile

proprioceptive feedback to help guide eye movements. Treatment here falls into the realms

of neuropsychology, occupational therapy, and vision therapy.

Compensatory strategies should be trained at the same time that remediation is

attempted. Many compensatory strategies developed for low vision or the blind may be

useful. Other strategies that lessen the necessity of looking in a particular location or

reduce the need to scan can also be taught. For instance, moving the television away or

using a small screen lessens the need to scan the scene in an organized fashion.

The Hands

Eye-hand coordination will be affected by receptive and perceptual problems, as well as

by motor planning and integration of percepts with motor output controllers. Mild diffi

culties that occur developmentally in these areas will often result in clumsiness or difficulty

with such tasks as producing clear handwriting. More severe dysfunction is described by

two terms — optic ataxia and constructional apraxia.

Optic ataxia is an inability to visually guide the hand toward an object. Differentiating

optic ataxia from primary dysfunctions in motor control can be achieved by having

patients touch their index finger on one hand with the index finger on the other. Usually,

in optic ataxia, the misreaching occurs for objects in the peripheral field. However, in more

severe cases, misreaching will occur for visually fixated objects. 109 For milder cases, train

ing the patient to visually fixate manipulated objects may be all that is required.

Constructional apraxia generally results from lesions of the posterior parietal lobe or

the junction between occipital, parietal, and temporal lobes. It may be due to perceptual

deficits, more frequently associated with right hemisphere lesions, or motor function

deficits, more frequently associated with left hemisphere lesions. Walsh 114 lists differential

effects on drawing which may be used to discriminate between perceptual and motor

etiologies. For instance, right hemisphere lesions will tend to result in energetic, scattered,

or fragmented drawings with a loss of spatial relations and orientation; left hemisphere

* Letter Tracking: Available from Academic Therapy Publications, Novato, CA.

involvement tends to result in drawings which are spatially intact and coherent but

simplified and laborious, lacking in detail.

Again, treatment here falls into the realms of neuropsychology, occupational therapy,

and vision therapy. A multitude of hand-eye coordination activities exists in the literature.

For constructional apraxia, the differentiation should be made as to whether it is primarily

perceptual or primarily motor and treatment should emphasize that modality.

The Body

As discussed above, receptive and perceptual dysfunctions can lead to adoption of head

tilts or turns and shifts in posture, creating or complicating problems in balance during

standing and walking. Patients are often unaware of these postural adjustments and, when

asked, will deny any distortion in their percept and usually in their posture, even though

something as easily noticed as a pronounced head tilt may be present. Testing for binocular

dysfunctions and conditions that may contribute to egocentric midline shifts in the vertical

and horizontal directions has been discussed. The vision practitioner must take a careful

history and specifically ask about difficulty with balance, instability, mobility, etc., as most

patients with these symptoms will often not bother to tell an eye doctor about these

difficulties, as they assume the symptoms are unrelated to their eyes.

If a binocular dysfunction exists, the associated postural problems generally resolve as

the binocular problem is remediated or when appropriate patching is applied. Treating

the binocular difficulty not only relieves the diplopia or intermittent loss of fusion which

can cause patients to adopt compensatory head and body postures, it may also involve

teaching patients to reorganize their visual space in which the binocular problem has

created distortions.

In the case of an egocentric midline shift, the specific etiology is often not diagnosed.

Tests for midline shift or observing immediate responses to large amounts of yoked prism

may be the extent of the diagnostic procedures. The effects of yoked prism on spatial

organization and resultant shifts in posture with a normal visual system are well docu

mented (reviewed by Press 93). Yoked prisms move the images of the ambient surrounds

in the direction of the apex of the prism for both eyes. In the normal visual system, this

gives a funhouse effect. It is, initially, rather disturbing during head movements and

walking to have the world shifted to the right or left or, seemingly, stretched upward or

squashed downward before you. Base-up prism will generally cause wearers to shift their

weight backward onto their heels; base-down prism generally has the opposite effect,

causing the wearer to shift weight forward onto the toes. Sometimes, these prisms may

be prescribed to assist the physical therapist in rehabilitation of standing and walking.

Often, with TBI patients, yoked prism applied in one lateral direction will create no

noticeable difference and application in the opposite direction will make them unable to

walk as they try to balance against the shift in surrounds. This type of behavior is a good

indication that yoked prism therapy or compensatory yoked prism in patients' spectacle

lenses can help normalize their posture and balance, either by reorienting their egocentric

visual midline or by moving the image of the outside world to match their new internal

visual midline. Patients who veer in one direction while walking may also benefit. Even

without a visual midline shift, yoked prisms used for short therapy periods may be useful

in breaking down maladaptive habitual postures which are resistant to treatment.

Similarly, visual interventions may be useful in patients with upper limb hemiparesis,

although there is not a visual cause. Practicing visual imagery of movement of the para

lyzed limb in conjunction with physical and occupational therapy can improve outcomes

over therapy alone. 115

Assessment and Rehabilitation of Visual Thinking/Memory

Visual images may be stored in either analog or verbal storage. Therefore, when attempting

to rehabilitate visual thinking and memory, it is important to be sure that the patient is

not merely encoding the information verbally but actually

forming the mental image.

Unlike visual perception, which is largely a bottom-up process, visual imagery is largely

a top-down process. Visual imagery uses visual information that has been previously

organized and stored; therefore, it is often possible to use visual imagery even though,

after a TBI, visual input and perception may be disordered. Thus, sometimes, it may be

trained in parallel with, or even in the absence of, organized visual perception.

Visualization, or use of visual imagery, has long been considered a useful high-end

visual task by therapy-oriented optometrists. Visualization can be used for visual memory

enhancement, such as visualizing the spelling of a word, or for spatial relations and spatial

organization, for instance, visualizing object rotations or visualizing a map of how to get

home from the grocery store. Numerous studies using various biological indices (e.g.,

electrophysiology, cerebral blood flow, and other types of brain activity imaging) as well

as studies of adults with brain damage show that, when internally constructing visual

imagery, we may use many of the same visual representations as in constructing visual

percepts from sensory input (reviewed by Farah 116 and Kosslyn and Thompson 117). Tech

niques based on visual imagery may be used effectively for perceptual therapy for those

patients who do not have manipulative abilities, provided that they are effective at using

imagery. Problem solving with visual imagery occurs both by using visual imagery from

memory and from imagination. These are separate skills and are used differently in

problem solving. 118

Visual memory, particularly visual sequential memory, is frequently impaired following

TBI. Often, when there is post-TBI memory loss, verbal compensatory strategies are

employed, such as list making and writing in a calendar or log. These techniques rely heavily

on left hemisphere mechanisms. Rehabilitation of visual memory, which can be built on

visual imagery, a heavily right-hemisphere function, 119 can provide supportive memory

function and help organize incoming visual information, reducing general confusion.

There are many well-standardized tests that tap visual memory. One such test, which

taps short-term visual memory and visual sequential memory, is the Test of Visual Percep

tual Skills 120 (also available in Upper Level 121). An advantage of the Test of Visual Perceptual

Skills is that it allows the patient to simply point to the correct answer, minimizing the

need to generate complex motor or verbal responses. It also provides separate assessments

of visual memory for figures and visual sequential memory, the latter being critical in

reading comprehension and in creating order from the visual information received.

One representative technique for practicing visual imagery from memory and improv

ing visual memory is to use flannel boards. The therapist and patient have matching felt

forms such as squares, circles, rectangles, and triangles of varying sizes and colors; each

of them also has a flannel board on which to place the forms. The therapist places some

of the forms on a flannel board in a spatial or sequential pattern. The patient is instructed

to form a mental image of the pattern presented without using words to describe it. Then,

the therapist’s board is covered and the patient reproduces the pattern on his/her flannel

board. As the performance improves, the number of forms is increased, the exposure

time is reduced, and the delay between exposure and reproduction is increased in order

to encourage transfer to long-term memory. Distracters may be interposed during the

delay between exposure and reproduction. Flat, three-dimensional blocks, available com

mercially in foam or wood, can be used for patients who have difficulty manipulating

felt forms.

Using visual imagery from imagination is a separate skill and is used in problem solving.

Activities that emphasize this skill would include solving constructional or rotational

problems.

Summary

The term visual rehabilitation is so broad that it often encompasses the services of neurop

sychologists, occupational therapists, and psychotherapists, in addition to ophthalmolo

gists and optometrists, and specially trained orthoptists or vision therapists. Besides

damage to the receptive structures such as the eye and optic nerve, visual dysfunction

may be caused by damage to any lobe of the brain, as well as midbrain structures and

cranial nerves. Functional deficits include photophobia, decreased visual acuity or contrast

sensitivity, ocular-motor disorders, binocular dysfunction (including strabismus), visual

field loss, spatial disorientation, imbalance, unilateral spatial neglect, other visual percep

tual disorders, integration disorders, and problems with visually-guided motor planning

and motor output.

Visual sequelae are quite commonplace in the TBI patient, but often overlooked. There

fore, once the medical/surgical rehabilitation of the visual system is complete, the issue

of functional recovery or compensation must be examined. Vision care specialists who

provide other patient populations with orthoptic or vision therapy or low vision services

will generally be able to adapt many of their techniques to working with the TBI patient.

Treatments often must be innovative and coordinated among the various professionals

providing rehabilitative services. Visual sequelae to TBI can affect the patient’s ability to

perform such varied tasks as reading, walking, and driving. Unrehabilitated functional

visual deficits can interfere with other therapies and with the patient’s ability to perform

activities of daily living, as well as return to work or school. They may also be a source

of emotional turmoil as the patient may experience unexplained feelings of imbalance,

spatial distortion, or visual confusion, and may be unjustly suspected of malingering.

The neuroanatomy of the visual system is so complex that, in order to provide effective

therapy, one must have a working model with which to organize rehabilitation. Such a

model is described in Figure 7.3. The major components of the model to be considered in

diagnosis and therapy are: (1) sensory input/reception, (2) perception/integration, (3)

motor output/behavior, and (4) visual thinking/memory. In this model, each component

affects the other. Our receptive functions affect perception and survival motor outputs.

Our percepts affect our motor planning/output, as well as our thinking and memories.

Our thinking and memories mediate our perceptions, as well as affecting our motor

planning/output; motor planning and output determine where our bodies are and how

we are going to use our eyes next — mediating receptive function. Carefully planned

vision therapy or use of lenses and prisms can intervene in any of these areas in a

constructive way, or disruptively to break down bad adaptations.

The redundancy of the visual system as well as the flexibility of the visual system — demonstrated

by experiments such as adaptation to inverting prisms,

together with clinical experience such as

therapeutic remediation of strabismus and amblyopia in adults — makes recovery of function a

reasonable goal for many visual dysfunctions following TBI. While one cannot always predict

which patients will respond to such therapy, it seems inappropriate to offer less if there

is a chance of recovery. Where therapy is ineffective at restoring function within a reason

able time frame, there are many compensatory devices and strategies that can be applied,

for instance, partial patching, prisms, or low vision devices and techniques. Even these

should be prescribed with an eye toward maximizing function within the limits set by

the patient’s condition. The area of visual rehabilitation for TBI patients is still in its infancy.

However, many visual dysfunctions encountered in TBI patients have been addressed for

other special-needs populations. The multiple deficits in sensation, speech and language,

cognition, and motor control encountered in TBI patients add to the challenge of providing

effective vision care.

Illustrative Visual Case Studies Patient J.G. Patient J.G. was seen for vision evaluation 4 years after sustaining a mild TBI when she slipped and hit her head. Since then, she had been unable to read, sew, or do any near work for more than 10 minutes without getting a headache. She also complained of dizziness and photophobia. She had been through vision therapy previously but on an intermittent basis due to geographic constraints. She was admitted to a postacute inpatient rehabilitation setting for treatment. J.G. was diagnosed with accommodative and convergence insufficiencies, as well as a saccadic dysfunction. Based on her symptoms and these findings, a working diagnosis of posttrauma vision syndrome was indicated. Glasses were

prescribed for full-time wear. As J.G. was orthophoric at distance, base-in prism was not prescribed. However, she received a bifocal (in order to compensate for her accommodative insufficiency) with binasal patches (to help reduce her visual confusion and reorient her in space). J.G. reported immediate relief of many symptoms, with decreased photophobia and increased ability to do near work while wearing this prescription. Because her stay would be limited and her visual complaints were central to her rehabilitation, J.G. was seen weekly in the optometrist's office for vision therapy. Exercises were prescribed for convergence, accommodation, and saccadic dysfunction, which were administered by occupational therapists daily at the rehabilitation center. J.G. responded well to her prescription, binasal patching, and vision therapy. She simultaneously underwent vestibular therapy with the physical therapists. Within 3 months, the binasal patches were removed from her glasses and she was able to read and sew as long as she liked (which turned out to be for hours at a time). She continued to wear the glasses full time. The rehabilitation center arranged for her to spend an evening waitressing in a local restaurant (this was her former occupation) and she performed so well that the owner offered her a job. She returned to her home feeling fully rehabilitated and ready to return to her preinjury work and home life. Two factors may have contributed to J.G.'s dramatic recovery in this case. She was in a rehabilitation setting where she was able to take advantage of coordinated rehabilitation services on a constant, rather than intermittent, basis. Also, placing her in a full-time prescription with binasal patches provided her with consistent, organized, visual input so that she could create a stable visual environment. Patient J.R. J.R. was seen for vision analysis 2 years post-TBI. He suffered a severe TBI in a motor vehicle accident. His chief complaint was double vision. He was referred by a local optometrist for treatment of large constant exotropia. His case is notable because, although he had seen at least two ophthalmologists and an optometrist since his injury, no one had diagnosed him with a right hemianopia with visual neglect. He was unaware that he had a visual field defect. He and his family assumed that his spatial disorientation was simply part of his brain injury. When advised of the diagnosis, his mother asked if that was why he always veered to the left when driving. Fortunately, he had only been driving on their property. J. R. also suffered significant memory loss. J.R. was seen on an outpatient basis, intermittently, for several years. Because he had no previous rehabilitation, working in a half day at the rehabilitation center several times a week and a vision

therapy office visit once weekly proved to be a challenge for the family, and J.R. was inconsistent in his attendance and his homework. Nonetheless, over a period of approximately 18 months, the exotropia for which J.R. had been wearing a pirate patch for over 2 years resolved with vision therapy. Therapeutic techniques included both orthoptic visual therapy and spatial organization. Scanning and visual memory therapy activities were prescribed and administered by occupational therapists and his parents. J.R. learned to scan effectively in familiar environments but had residual difficulty in busy, unfamiliar environments, such as the shopping mall. Unfortunately, while his memory improved, it remained significantly impaired. Although his rehabilitation was extended due to less than ideal compliance, J.R. was happy to be rid of his patch and to have better ability to move about in his space world. He continued to live with his parents and young son. Although he required cueing for many tasks, he was able to help raise his son, participate in sports, and maintain a part-time job as a dishwasher in a restaurant. Patient C.L. Patient C.L. was seen for visual evaluation 13 years after TBI sustained in a motor vehicle accident. Her chief complaints at the time of the vision examination were that her eyes rolled back in her head during seizures and she experienced some eyestrain, although her occupational therapist had noted that C.L. complained of headaches and blurred vision after near work. Examination revealed a convergence insufficiency exotropia (i.e., strabismus when viewing at nearpoint due to inability to converge her eyes). She was diplopic almost constantly when doing tasks within arm's length. When queried about the diplopia, she said that the doctor she saw just after her accident had told her it would go away in time, so she just waited. Although her phorias were not large (9 prism diopters of exophoria at near), she had almost no elicitable base-out reflex fusion and abnormal convergence ranges on prism vergence testing with a negative recovery (i.e., once fusion was broken with base-out prism, it required base-in prism to reestablish fusion). Her nearpoint of convergence on push-up testing was 16 inches. Because she had so little fusion response, we were unable to prescribe any out-patient therapy. C.L. was treated on a daily basis for 2 weeks, 45 minutes per day, using large fusion targets projected on a wall to attain peripheral fusion and SILO. Instrument (amblyoscope) convergence techniques were also applied. After 2 weeks, she was fusing well enough at nearpoint that we were able to prescribe convergence exercises for practice with her occupational therapist at the rehabilitation facility. She continued in-office therapy once weekly and made continued progress with this

regimen. Patient L.R. Patient L.R. was seen 4 months postinjury with chief complaints of poor depth perception and difficulty keeping things level. Examination revealed a mild (approximately 10 prism diopters) right esotropia and a mild left superior rectus palsy which resulted in a noncomitant vertical component to the eyeturn (6 prism diopters in primary gaze, increasing on left gaze). The superior rectus also intorts the eye. Her complaint of difficulty keeping things level probably resulted from a combination of extorsion of the eye and the noncomitancy of the vertical component. Pursuits were jerky. Ductions were full with the right eye and showed a superior temporal restriction with the left eye. Although she appeared to fixate with her left eye during the entire examination, she showed alternating suppression on her stereopsis testing. She also had reduced accommodative amplitude and facility. Therapy progressed from monocular and biocular (i.e., two eyes open, without fusion) skills to antisuppression activities and in-instrument fusion with vertical and base-in vergences. After 12 weekly sessions in office with an hour of home therapy daily, her extraocular range of motion was full with each eye, with smooth pursuits. She showed no vertical or horizontal phoria, at distance or near, and she was comfortable with her vision. Therapy was continued for six additional sessions to improve fusional and accommodative flexibility. At her one year progress check, she had maintained all of her visual gains. Patient B.B. Patient B.B. was seen for examination 4 months postinjury. He had no light perception from his right eye, due to optic nerve atrophy following his injury. His left eye was healthy and intact. He presented with decreased acuity (20/80 when reading a vertical column and 20/30 when reading horizontally). He had reduced contrast sensitivity for medium spatial frequencies. He also had a left hemianopia with macular sparing. He had difficulty reading. He watched his feet when walking and tended to veer leftward. Saccades were slow and pursuits were jerky. He had a reduced amplitude of accommodation and was already wearing a bifocal correction, which he found useful. He read at approximately 8 inches from his eyes for the additional magnification. B.B. was aware that he had a field defect but did little to compensate for it. The physical therapists had already taught him to use a walking stick on the blind side, both for physical support and to protect that side. However, like most hemianopes, he did not scan toward the affected side. During tachistoscopic procedures, he generally missed the first few letters or digits and he, initially, had poor perceptual speed and span. On line bisection tasks, he transected the line at the center or contralateral to the blind field. This is the

expected performance for a patient with hemianopia combined with USN, rather than just a hemianopic defect. On some other tasks, his performance was consistent with a mild case of neglect. For instance, when instructed to scan a wall for target figures, he would scan from right (his intact field) to left. When asked to scan again from left to right, he would become argumentative, stating that he always scanned left to right and then would proceed to scan from right to left again. He showed few other indications of neglect. Copied forms were complete. On crossing-out tasks, he generally covered the entire page, always starting from right to left, but was careful to reach the left margin of the page. Therapy began with monocular skills and tachistoscopic procedures for perceptual speed and span. These skills improved rapidly with therapy. Peripheral awareness techniques for expanding awareness within his intact field were applied with good success. B.B.'s overall reading speed improved along with his saccadic speed, perceptual span, and perceptual speed. A number of techniques were applied for making B.B. more aware of space within his blind field. Some of these met with more success than others. He rejected application of Fresnel prism, saying he would rather move his eyes farther without the prism. He actively participated in both table-top and wall projected scanning activities, trying to adopt an efficient scanning pattern, moving from far left in his blind field, rightward. However, initially, these activities did not seem to generalize outside of the therapy room. He was able to adopt a scanning pattern while walking. He looked left on every fourth step, which helped him walk without deviating leftward. His mobility and reading improved enough through his course of therapy that he was able to return to his life as a student at a junior college.

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of the clinical issues herein.

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Appendix 7A

Organizations to contact for information regarding orthoptic or vision therapy, or referral

to member doctors who may provide or prescribe therapy:

College of Optometrists in Vision Development

243 North Lindbergh Blvd., #310

St. Louis, MO 63141

(888) 268-3770

www.covd.org

Neuro-Optometric Rehabilitation Association

P. O. Box 1408

Guilford, CT 06437

(866) 222-3887

www.nora.cc

Optometric Extension Program Foundation, Inc.

1921 East Carnegie Ave. Ste. 3-L

Santa Ana, CA 92705

(949) 250-8070

www.oep@oep.org 251

0-8493-1362-7/04/$0.00+$1.50

8

Auditory Function Assessment in Posttraumatic Brain Injury Rehabilitation

Juan J. Bermejo

CONTENTS

Introduction

The ability to effectively communicate with fellow human beings assumes great impor

tance in a rehabilitative setting. With the focus of various therapies directed toward

advancing a disabled individual’s recovery, we must ensure that communication among

therapists and patients is unencumbered. For this reason, audition is critical to the reha

bilitation of people with brain injury because it is a vital component of the communication

process. As we shall discover, hearing loss is a frequent sequela of traumatic brain injury

(TBI), and its potential impact on peoples’ quality of

life, as well as their rehabilitation, is

well recognized.

The role of the sense of hearing in daily living is no less important than any of the other

human senses, contrary to popular thought that vision supersedes all others in importance.

Awareness of sound in diverse environments can be critical to survival and the ability to

detect and recognize sound patterns that comprise speech is central to human communi

cation. TBI can alter human performance by disrupting a person’s awareness and recog

nition of, and attention to, sound. At a higher level, processing and comprehension of

speech and execution of other cognitive functions that involve memory, ability to com

municate knowledge, and judgment can be affected by hearing loss. Therefore, the status

of a person’s hearing sensitivity should be known to all clinicians, even before the reha

bilitative process is begun. As with all disabilities, early identification and assessment

provide valuable information useful to rehabilitation.

The following section explores the magnitude of auditory problems in the TBI popula

tion. The discussion of the anatomy and physiology of the auditory system will help clarify

how this sensory system can become impaired. An important role of audiologists is in

helping to evaluate auditory function using conventional and newer audiologic techniques

described below. This information should prove useful to therapists formulating their

clinical interventions.

Demographics

Using national data from 1995 to 1996, the Center for Disease Control (CDC) 1 estimates

that more than 80,000 persons in the United States are discharged annually from hospitals

with disabilities secondary to TBI. Approximately 5.3 million Americans suffer from TBI

related disabilities. 1 Estimating how many Americans suffer TBI-related hearing loss is

much more difficult because of the unavailability of premorbid audiologic information

about many of them and the lack of a national survey seeking this information. A Medline

search for data from 1978 to 2002 regarding the incidence of TBI-related hearing loss

yielded little national data. Instead, many reports appear to be regionalized, based on

small numbers of patients seen at a specific medical center. From these studies, it is clear

that hearing defects are common in people with mild to severe TBI. Abd Al-Hady et al. 2

found that 20% of their subjects with minor head injury had varying degrees of hearing

loss. In a study of 130 individuals with minor head injury, five were found to have temporal

bone fractures that caused greater high-frequency hearing loss than found in those with

no temporal bone fracture. 3 Out of 123 people with temporal bone fractures, Ghorayeb

and Rafie 4 reported varying degrees of hearing loss in all of them. Zimmerman et al. 5

analyzed audiologic data from 50 children suffering from head trauma and noted the

occurrence of hearing loss in 48% of the cases.

Overseas, several similar findings have been reported. Vartiainen, Karjalainen, and

Karja 6 concluded that their head-injured patients with neurosensory hearing loss suffered

cochlear lesions. They based this conclusion on their analysis of audiologic data from 199

Finnish children with blunt head injury. Dorman and Morton 7 studied 40 New Zealand

children treated for minor head injury. Audiologic data from 25% of them revealed mild

hearing loss. A more recent study by Jury and Flynn, 8 also conducted in New Zealand,

found that, in 30 people affected by TBI for 19 months to 27 years, persistent hearing loss

occurred in 33%. In 1989, Wennmo and Svensson 9 found that 75% of their 20 Swedish

subjects with temporal bone fractures suffered hearing loss. Bergemalm and Borg 10 studied

audiologic data from 25 TBI patients admitted to two Swedish hospitals. They concluded

that changes in auditory function are common in TBI, vary in site of lesion, and can become

progressively worse.

From these studies, it is clear that even mild TBI can affect auditory function. For this

reason, hearing loss should always be suspected in a person with TBI until clinically

proven otherwise. That hearing impairment impedes sound awareness and recognition,

as well as effective comprehension of speech, is well known.

In order to understand the potential effects of TBI on auditory structures and, therefore,

the onset of hearing loss, it is essential to discuss and appreciate the anatomy involved.

The Human Auditory System

The conventional approach to a discussion of human auditory anatomy, physiology, and

neurophysiology is the division of the auditory system into external, middle ear, inner

ear, and retrocochlear sections. This compartmentalization will aid in understanding

pathophysiology as well as site-of-lesion testing.

A good starting point is a brief description of the skull. There are four sections of bone

that comprise the skull: the frontal, temporal, parietal, and occipital. Of principal impor

tance to this discussion is the temporal bone. The temporal bone has four sections, the

most important of these being the petrous portion because it houses the sensory organs

for audition and balance. Other bony sections (the tympanic, mastoid, and squamous)

help form the ear canal and middle ear cavity.

External Ear

The external ear consists of the auricle or pinna and the osseous and cartilaginous portions

of the ear canal (Figure 8.1). The auricle is cartilaginous, quite flexible, and helps to collect

sound and direct it inward to the ear canal. The concha, the helix, the antihelix, the tragus,

and the antitragus are principal features of the auricle. Of these, the concha, a large bowl

shaped depression near the middle of the auricle, is important because it helps funnel

sound into the ear canal and is involved in providing slight amplification of high frequency

sounds. Yost and Nielsen 11 point to the auricle’s role in helping to localize high-pitched

sounds and to identify sound sources occurring behind or in front of the head. A more

passive function is to protect the middle and inner ears by maintaining constant temper

ature and humidity and to help in keeping out foreign bodies.

The human external auditory meatus (EAM) averages 28 mm in length and 7 mm in

diameter. 12 The orifice of the EAM is generally oval in shape and is situated slightly lower

than the medial portion near the eardrum; this may help keep water from lodging there. 13

The EAM is divided into cartilaginous and osseous portions. The cartilaginous portion

occupies the lateral 1 / 3 to 1 / 2 while the medial 1 / 2 to 2 / 3 section is osseous. Sebaceous and

ceruminous glands located in the cartilaginous portion produce cerumen or earwax.

Functionally, the EAM appears to respond best (resonate) to sounds whose frequencies

approximate 3800 Hz. 13 Together, the EAM and concha provide increased amplification

in the 3000 to 5000 Hz range. This fact is important to consider in patients with EAM

blockages caused by cerumen, dried or oozing blood, or foreign debris.

Middle Ear

The human tympanic membrane (TM) is the medial terminus for the ear canal, anchored

fast to the annulus and measuring about 55 to 90 mm 2 in area. 11 The stiffness of the eardrum

is provided by the pars tens; a portion of the TM, the pars flaccida or Schrapnell's

membrane, lacks stiff fibers and is, therefore, very flexible. As such, it may allow for some

small degree of pressure equalization between external and middle parts of the ear. 13 On

direct observation, the appearance of tympanic membranes may vary from translucent to

opaque. In most individuals, the manubrium of the malleus in its attachment to the

tympanic membrane can be easily observed during otoscopic examination.

The role of the TM is to propagate sound energy from air to the inner ear. Sound

transmission is accomplished by air-conduction, by bone-conduction, and through reso

nation of the air in the middle ear cavity. 11 Recently, Freeman, Sichel, and Sohmer, 14

studying small mammals, described another mode of sound transmission. They were able

to record auditory neural responses by directly applying a bone conduction stimulus to

exposed brains. They postulated that cerebrospinal fluid may transmit sound pressure

through to the inner ear fluids during bone conduction stimulation.

FIGURE 8.1

Drawing of the outer, middle, and inner ear. (From Durrant, J. and Lovrinic, J., Bases of Hearing Science, 2nd ed.,

Williams & Wilkins, Baltimore, 1984. With permission.)

The air-filled middle ear space or tympanic cavity has a volume of approximately 2 cm 3

and communicates, anteriorly, with the nasopharynx via the eustachian tube and, poste

riorly, with the air cells of the mastoid bone. Suspended in the middle ear space are the

ossicles or middle ear bones: the malleus, incus, and stapes. These are the smallest bones

in the body. Also found in the middle ear space are the stapedius and tensor tympani

muscles, the chorda tympani, and ligaments supporting the ossicles.

The malleus has its manubrium attached to the tympanic membrane. A middle ear

muscle, the tensor tympani, has its insertion on the manubrium and neck of the malleus.

The incus and malleus articulate via a “saddle-type” joint. The incus attaches to the head

of the stapes, forming the incudostapedial joint. Medially, the stapes footplate is fastened

to the oval window. The malleus is supported by the anterior, lateral, and superior liga

ments. Support for the incus is provided by the posterior ligament. The stapes is lodged

in the oval window recess, held in place, but not fixated, by the annular ligament.

The stapedius and tensor tympani muscles are the auditory muscles and have an impor

tant role in stiffening the ossicular chain upon contraction through acoustic or nonacoustic

stimulation. On the posterior wall of the middle ear cavity is the pyramidal eminence that

houses the stapedius muscle. The tendon of the stapedius muscle emerges from the

pyramidal eminence to attach to the head of the stapes. Innervation of the stapedius muscle

is by the facial nerve. On the anterior wall of the middle ear is the semicanal of the tensor

tympani muscle. 12 The tendon of the tensor tympani muscle inserts to the manubrium

and neck of the malleus. The trigeminal nerve innervates the tensor tympani muscle. The

chorda tympani, a branch of the facial nerve, also courses through the superior part of

the middle ear cavity on its path to taste receptors on the tongue.

The role of the ossicles is to facilitate sound transmission. Sound energy in the air must

be delivered efficiently to the cochlea, a fluid-filled chamber. Because of the difference in

the densities of air and cochlear fluids, sound energy will be impeded by the greater

density of the latter, resulting in some loss of this energy. Such impedance mismatch would

be expected to decrease auditory sensitivity. The ossicles rotate in such a way that they

perform a lever action, transferring a greater force to the stapes than that exerted on the

tympanic membrane. This effectively increases the gain of the human auditory system by

about 30 dB. 13

The eustachian tube plays an important role in middle ear function. By opening and

closing during chewing, swallowing, or yawning, the entry of air through the eustachian

tube allows air pressure in the middle ear space to match that of ambient atmospheric

pressure and, subsequently, effective sound transmission.

Bony Labyrinth

Within the petrous portion of the temporal bone are cavities that interconnect to form the

osseous or bony labyrinth. Removal of surrounding bone permits a clear view of the

complex system known as the bony labyrinth: the bony semicircular canals, the bony

cochlea, and the vestibule between them. The orientation of the human osseous labyrinth

is such that the semicircular canals lie posteriorly and to the side while the cochlea sits

anteriorly and medially relative to the vestibule. Posterior and anterior semicircular canals

are aligned almost 90° to one another while the horizontal semicircular canal angles up

30° from the horizontal plane. The semicircular canals have visible bulges or dilatations

known as ampullae that open onto the vestibule.

The cochlea, an extension of the vestibule, 13 is a coiled structure measuring about 32 to

35 mm in length. It is wrapped around a bony structure called the modiolus, the base of

which is the internal auditory meatus through which the cochleovestibular and facial

nerves pass to reach auditory nuclei in the brainstem. There are two cochlear ducts, the

scala tympani and the scala vestibuli, that are partially separated by the bony spiral lamina.

On the bony vestibule’s lateral wall is the oval window

which is covered by the stapedial

footplate. The oval window connects the vestibule to the scala vestibuli. The round win

dow is located in the inferior portion of the vestibule facing the middle ear cavity. It is

the lateral terminus of the scala tympani.

Perilymph, one of two labyrinthine fluids and a filtrate of cerebrospinal fluid, fills the

osseous labyrinth. The cochlear aqueduct, a small passage starting near the round window

and continuing to the subarachnoid space, is believed to facilitate the transport of peri

lymph to the labyrinth. 15

Membranous Labyrinth

Inside the bony labyrinth is a smaller, similarly shaped structure known as the membranous

labyrinth (Figure 8.2). There are three divisions: the endolymphatic duct and sac, the

membranous semicircular canals and the utricle, and the cochlear duct (or scala media)

and saccule. 16 The saccule, utricle, and membranous semicircular canals contain the sen

sory organs for detecting angular and linear head motion. Auditory sensory epithelia

(organ of Corti) reside in the scala media. The membranous labyrinth is filled with

endolymph, a fluid different in chemical composition from perilymph. The endolymphatic

duct and sac regulate the pressure of endolymphatic fluid. 17

Because the focus of this discussion is the auditory system, only a brief discussion of

the membranous semicircular canals will follow. The utricle is a sac-like structure inside

the bony vestibule. The semicircular canals have five openings into the utricle. An enlarged

bulb or ampulla at each opening contains the vestibular sensory epithelia, the crista

ampullaris, supported by connective tissue. The crista contain hair cells whose cilia embed

into a gelatinous structure called the cupula. Angular head movement causing endolymph

to move in one direction across the crista will deflect the cupula and cilia and result in a

receptor potential. This electrical event results in a discharge of the afferent vestibular

nerve fibers. Deflection of the cupula in the opposite direction will fail to generate a

receptor potential.

In the saccule and utricle are areas called maculae that consist of “fan-like” sensory

structures with a covering called the otolithic membrane. This membranous structure is a

FIGURE 8.2

The membranous labyrinth. (From Dallos, P., The Auditory Periphery, Academic Press, New York, 1973. With

permission.)

gelatinous mass with a thin layer of calcium carbonate particles called otoconia. The sensory

receptors are hair cells with stereocilia that project into the otolithic membrane. Movement

of this membrane in one direction will cause stereocilia to bend in the opposite direction,

resulting in a physiologic response. The otolith organs thus respond to linear as well as

angular head movements. 16

The Cochlea

The spiral ligament, a crescent-shaped thickening of periosteum attached to the lateral

wall of the cochlea, projects inward and anchors the basilar membrane laterally (Figure

8.3). On its medial side, the basilar membrane is attached to the spiral lamina, a bony

shelf that partially divides the cochlear scalae. Thus, the basilar membrane is the roof of

the scala tympani and the floor of the scala media. The roof of the scala media is formed

by Reissner's membrane. The basilar membrane, about 32 mm long, is composed of

transverse fibers lying perpendicular to its long axis. Unlike the scala media, the basilar

membrane is wider toward its apex and narrower toward its basal end. This arrangement

has had important implications for the development of the many theories of hearing.

The sensory epithelium for hearing, or the organ of Corti, rests on the basilar membrane.

A single row of receptor cells, the inner hair cells (IHC), and three rows of outer hair cells

(OHC) wind their way from base to apex. Inner hair cells appear "flask-like" in shape and

have two rows of stereocilia. 13 The shape of outer hair cells is more cylindrical and each

sensory cell has three to four rows of stereocilia arranged in a "W" shape. The tips of the

tallest of the stereocilia are embedded in the tectorial membrane. The shorter of the OHC

stereocilia are free-standing while the IHC stereocilia are either free-standing or loosely

attached to the tectorial membrane. 15 In simple terms, the hearing process is initiated by

sound pressure acting on the tympanic membrane. Through a piston-like motion, the

ossicles convey sound energy at a significantly higher gain to the oval window. A pressure

gradient develops across the basilar membrane and organ of Corti creating a pressure

wave that travels apically. Shearing forces act on the tectorial membrane which, in turn,

deflects the hair bundles toward their kinocilium, thereby depolarizing the hair cell and

leading to a receptor potential. This physiologic excitation increases the number of spike

discharges from afferent neurons culminating in a whole nerve action potential. Only IHCs

participate in the generation of an action potential. OHCs are the key elements in a cochlear

amplifier which increases the sensitivity and frequency selectivity of the hearing organ. 18

The Auditory Nerve

As discussed previously, receptor cells depolarize when their stereocilia bend in response

to shearing forces from the tectorial membrane during the traveling wave. Each IHC may

FIGURE 8.3

Structures of the organ of Corti.

be innervated by several afferent neurons while many OHCs may be innervated, through

multiple branching, by a single neuron. Approximately 30,000 nerve fibers comprise the

auditory nerve; about 90 to 95% of these are Type I radial neurons — thick myelinated

fibers that synapse with IHCs. Thin, scarcely myelinated Type II, or outer spiral fibers,

make up a smaller percentage (5 to 10%) of all afferent neurons and these synapse with

the OHCs.

An olivocochlear efferent system exists alongside the afferent neuronal pathway. Efferent

fibers arise from either the lateral or medial superior olivary complex. 18 Lateral efferent

axons tend to be unmyelinated, originate in the vicinity of the lateral superior olivary

complex, and directly synapse with afferent dendrites at the base of the IHCs. From areas

near the medial superior olivary complex are larger neurons whose axons are myelinated

and synapse directly on OHCs. The role of the efferent system appears to involve the

lowering of the sensitivity of the hearing organ in response to high-intensity sounds,

reducing the effects of low-level background noise on moderate intensity acoustic stimuli,

and may serve to facilitate selective attention. 19

Central Auditory Pathways

Primary auditory fibers are the central processes of bi-polar neurons. The peripheral

processes attach to the cochlear hair cells, while the central fibers enter the brainstem to

terminate on diverse cells in the dorsal and ventral cochlear nuclei (Figure 8.4). The latter

is divided into anteroventral and posteroventral sections.

A tonotopic arrangement is

evident in the cochlear nuclei, whereby afferent nerve fibers responsive to high frequency

stimuli and, thus, originating from the basal end of the cochlea, terminate on cells of the

dorsal side of the dorsal cochlear nuclei. The cochlear apex is sensitive to low-frequency

sounds; nerve fibers from this cochlear area connect to cells on the ventral portion of the

dorsal cochlear nuclei and to the ventral cochlear nuclei.

Secondary auditory nerve fibers are those that are arranged into three striae: the dorsal

acoustic stria, the intermediate acoustic stria, and the ventral acoustic stria. Fibers from

the dorsal acoustic stria project from the dorsal cochlear nuclei and cross the midline.

Some nerve fibers terminate on the contralateral superior olivary complex with the major

ity entering the contralateral lateral lemniscus. From there, fibers project to the central

nucleus of the inferior colliculus of the midbrain.

FIGURE 8.4

Central auditory pathways.

From cells in the posteroventral cochlear nucleus arise the intermediate acoustic striae

to connect to cells in the periolivary and retro-olivary nuclei. From there, they cross the

midline and terminate on the contralateral periolivary and retro-olivary nuclei. Afferent

fibers continue contralaterally and join the lateral lemniscus and terminate in the inferior

colliculus. Efferent auditory nerve fibers that attach to

outer hair cells arise in these olivary

nuclei to make up the olivocochlear bundle and, as described above, play a role in altering

the sensitivity of auditory sensory receptors.

The ventral acoustic stria begins in the ventral cochlear nucleus and forms the trapezoid

body. Many of its fibers course to cross the midline and form the lateral lemniscus. This

nerve fiber bundle ascends to terminate on the central nucleus of the inferior colliculus

within the midbrain.

The lateral lemniscus is comprised mainly of crossed secondary nerve fibers from the

three acoustic striae. A few fibers from its nucleus will cross the midline and terminate at

the contralateral inferior colliculus. From the inferior colliculus, ascending fibers continue

on to the medial geniculate body of the thalamus. Fibers originating within the medial

geniculate body form the geniculocortical fiber tract that connects to the transverse tem

poral gyrus in the temporal lobe. 20

Typically, the presence of sound is perceived through air-conduction, whereby the ear

detects and processes sound carried through air. Sound transmission can also take place

through the vibration of bones of the skull or teeth. Hearing sensitivity can become

impaired due to defects occurring at the peripheral level (i.e., from the ear canal to the

auditory nerve inclusive) or at the central level (i.e., from the brainstem to the auditory

cortex). Four types of hearing losses are recognized clinically and are discussed below. In

order to assess an individual's hearing sensitivity, it is necessary to perform preliminary,

yet essential, procedures.

Clinical Examination

Patient History

By careful questioning, a clinician should be able to gather enough information about a

person's hearing status to help guide audiologic testing. Was hearing sensitivity normal

or was hearing loss documented or suspected prior to injury? Was there exposure to

excessively loud occupational or recreational noise, toxic industrial chemicals, or use of

ototoxic medications? Did the person report tinnitus or "ringing of the ears" prior to injury?

Did background noise appear to detrimentally affect the person's ability to comprehend

speech? Were family members becoming sufficiently concerned with the person's hearing

difficulty that hearing aid use was contemplated? During hospitalization, was there bleed

ing from either ear or was trauma to either pinna noted? Did radiologic studies discover

fracture of temporal bone? Was the person found to exhibit hearing difficulty by hospital

staff? Was hearing sensitivity assessed during hospitalization or shortly after discharge?

Standard Audiologic Procedures

Following the taking of a case history, the person is prepared for standard audiologic

procedures. Many people with TBI who are seen as outpatients are capable of cooperating

during testing and providing reliable responses. Standard pure tone and speech audio

metric techniques are the basis for conventional audiologic studies of cooperative patients.

By evaluating air-conduction and bone-conduction sensitivity, the audiologist can deter

mine whether hearing sensitivity is within normal limits or whether hearing impairment

is present unilaterally or bilaterally, and its severity can be established.

Speech audiometric data aid in determining the impact of hearing loss on the person’s

ability to perceive speech at normal intensity levels (sometimes referred to as conversational

speech levels). Along with pure tone data, speech audiometric data can help ascertain com

munication problems likely to be experienced by the individual with hearing impairment.

It should be obvious that hearing testing is best performed in a quiet setting. Controlling

the acoustical environment ensures that all persons receive hearing testing in optimal

listening surroundings and that test data are reliable and accurately reflect hearing status

at the time of examination. For these reasons, quantitative data obtained through standard

audiologic procedures, rather than qualitative measures (e.g., “whisper test,” watch test,

single tuning fork test, etc.), are preferred.

A clinical audiometer is an electronic instrument used to generate pure tones and various

types of noise stimuli. These, as well as recorded or live-voice speech stimuli, are presented

to a listener through circumaural or insert earphones or a bone oscillator placed on the

mastoid bone or forehead. When loudspeakers are used instead of earphones, hearing

sensitivity is assessed in what is known as soundfield testing.

The Audiogram

With a person wearing earphones, pure tones ranging from 250 to 8000 Hz are presented

at different sound intensity levels. Bone-conduction thresholds can also be established in

the frequency range of 250 to 4000 or 6000 Hz. Thresholds are determined at each specific

frequency. Theoretically, a threshold represents the sound intensity level at which a listener

is able to successfully detect a stimulus 50% of the time. Clinically, a pure tone threshold

represents the faintest sound a person can hear. These test results can be depicted on a

form known as an audiogram (Figure 8.5). In this graphical representation of hearing

sensitivity, pure tone thresholds are plotted in terms of frequency vs. intensity level,

relative to normal hearing level.

Whereas pure tones are simple acoustic stimuli, speech is a complex stimulus. Conven

tional speech audiometric testing can be performed with single words, nonsense words

or phrases, short sentences, or continuous discourse. Use of speech stimuli for evaluation

of hearing sensitivity is essential because of the

significant impact of hearing loss on one's

ability to communicate orally.

Together, pure tone and speech stimuli help delineate the patient's hearing sensitivity.

An individual with normal hearing sensitivity will typically have air-conduction and bone

conduction thresholds falling between −10 and 26 dBHL. Air-conduction thresholds may

differ from bone-conduction thresholds by 5 to 15 dBHL. Because the normal hearing

range is fairly wide, pure tone thresholds approximating 25 dBHL (and, therefore, tech

nically within normal limits) may present mild auditory problems. Hearing sensitivity in

the normal range facilitates, for most individuals in quiet surroundings, almost effortless

reception of speech and nonspeech sounds. Of course, this may not hold true in geriatric

cases because of aging effects on sensory and neural function.

Acoustic Immittance

Acoustic immittance encompasses tympanometry as well as measurements of middle ear

compliance or impedance and eustachian tube function. In addition, testing for the pres

ence of stapedial muscle contractions in response to loud acoustic stimuli is included. As

described above, the middle ear serves to effectively transfer as much of the acoustical

stimulus to the inner ear as possible through the action of the ossicular chain. Acoustic

impedance refers to the amount of opposition to sound transmission posed by the middle

ear. In ears with no otologic disease, acoustic impedance is minimal. Ears with tympanic

membrane or ossicular chain defects will demonstrate increased acoustic impedance,

resulting in significant reflection of sound off a stiffened tympanic membrane and out

through the ear canal. This implies a reduction of sound energy flow to the inner ear.

By presenting a pure tone to the ear while varying air pressure in a closed ear canal,

tympanometry quantifies the effect on transmission of that stimulus through the middle

ear. A tympanometer measures how middle ear compliance varies as ear canal pressure

changes to values above and below ambient atmospheric pressure. The data obtained

permit assessment of the integrity of the tympanic membrane, the stiffness of the middle

ear, the operational function of the eustachian tube, and the status of the ossicular chain

(Figure 8.6). Patients with occluded ear canals will demonstrate abnormally low ear canal

FIGURE 8.5

Audiogram depicting loss of high frequency hearing sensitivity.

volume. Perforations of the tympanic membrane will yield larger-than-normal ear canal

volumes, as the measurement is that of the combined volume values of both ear canal

and middle ear space. Ossicular chain fixation will cause abnormally restricted movement

of the tympanic membrane and increased resistance to sound transmission as air pressure

is varied. Discontinuity of the ossicular chain will do the opposite; because of increased

flaccidity, the tympanic membrane is hypermobile, and abnormal high middle compliance

values are recorded by the tympanometer.

Acoustic Reflex Testing

The acoustic reflex is a contraction of the stapedius muscle when a sufficiently loud

acoustic stimulus is presented to a healthy ear. This acoustic reflex arc has been described

by Hall 21 as consisting of afferent auditory nerve fibers that terminate on the ventral

cochlear nuclei, neurons arising from the ventral cochlear nucleus terminating near the

ipsilateral facial motor nucleus as well as ipsilateral and contralateral medial superior

olive (MSO), neurons from the MSO or peri-MSO that end ipsilaterally and contralaterally

at the facial motor nucleus, and, finally, the facial motor nerve fibers that innervate the

stapedius muscle (Figure 8.5).

In the normal ear, acoustic reflexes can be elicited by ipsilateral or contralateral stimu

lation. Pure tones, white noise, or bands of noise in the range of 70 to 100 dB above pure

tone threshold are effective stimuli. The acoustic reflex is a stiffening of the tympanic

membrane that, in turn, increases the resistance to sound energy flow. Instrumentation is

used to detect the sudden increase in acoustic impedance upon eliciting an acoustic reflex.

If conductive hearing loss (discussed below) is present,

testing usually fails to elicit an

acoustic reflex, often because of differing circumstances. For instance, persons with

FIGURE 8.6

Tympanogram. ECV 1.2 cm3 PEAK 0.4 cm3 L GR 90 daPa – 20 daPa ECV 1.5 cm3 PEAK 0.7 cm3 R GR 65 daPa – 15 daPa 1.5 cm3 +200 0daPa +200 0daPa 1.5 cm3 NAME DATE GSI 38 –400 –400

conductive hearing loss due to middle ear disease or trauma usually do not register the

expected change in impedance because middle ear stiffness is already abnormally high.

Thus, it is rare that these individuals would present with acoustic reflexes. On the other

hand, a person with disarticulation of the ossicles has a middle ear with an abnormally

high degree of flaccidity. In such a case, no acoustic reflex may be present because of the

loss of continuity within the ossicular chain itself and between the ossicular chain and the

tympanic membrane.

Individuals with neurosensory hearing loss (discussed later) may or may not present

with acoustic reflexes. If the neurosensory hearing loss (i.e., elevated pure tone thresholds)

is mild, acoustic reflexes may be recorded, suggesting that recruitment is present. Recruit

ment is a clinical symptom in which the ear’s ability to process loudness is impaired. A

person with recruitment usually complains that certain sounds are annoying or even

painful to hear. This is frequently the result of damage to the cochlea. In cases where the

neurosensory hearing loss is moderate to severe, acoustic reflexes are generally absent.

Conductive Hearing Loss

Individuals with bone-conduction pure tone thresholds better than air-conduction thresh

olds exceeding 10 to 15 dBHL are said to have conductive hearing loss. Common causes

of conductive hearing loss include cerumen impactions, perforated tympanic membranes,

middle ear disease, ossicular chain fixation or decoupling, and eustachian tube dysfunc

tion. Less commonly encountered are atresia (i.e., absent ear canal), ear canal stenosis (i.e.,

narrowing of the ear canal orifice), active bleeding or dried blood occluding the ear canal,

fracture across the osseous portion of the ear canal or across the middle ear, hemotympa

num or blood occupying the middle ear space, vascular tumor in the middle ear space,

and foreign debris in the ear canal or middle ear.

A patient with conductive hearing loss typically exhibits difficulty responding to verbal

or nonverbal stimuli unless presented with louder-than-normal intensity levels. Most

conductive hearing losses exist as long as the underlying medical condition persists.

Medical and/or surgical treatment may help resolve most conductive hearing losses, and

hearing sensitivity may return to normal in most cases.

Neurosensory Hearing Loss

Air-conduction and bone-conduction thresholds lying outside of normal and approximat

ing one another indicate neurosensory hearing loss. Most individuals will acquire neuro

sensory hearing loss as a result of the aging process. Temporary or chronic exposure to

dangerously loud sound without hearing protection is one of the leading causes of hearing

loss. Autoimmune ear disease, endolymphatic hydrops, perilymphatic fistula, genetic or

hereditary factors, viral infiltration into the cochlea, metabolic disease (such as hypothy

roidism), and anemia are other bases for neurosensory hearing loss. Most individuals with

typical neurosensory hearing losses are not medically treatable, except through amplifi

cation. Hearing aids, alternative listening devices, and the advent of middle ear, cochlear,

and brainstem implants have made audition possible for many people with neurosensory

hearing loss.

Mixed Hearing Loss

When low-frequency bone-conduction thresholds are in the normal range but those in the

mid-to-high frequency range approximate diminished air-conduction pure tone thresh

olds, the hearing loss is referred to as mixed. Otosclerosis, a disease involving the growth

of bone around the stapes footplate, commonly causes mixed hearing loss. The stapes

footplate becomes increasingly fixated and unable to freely pivot within the oval window,

resulting in diminished hearing sensitivity. Individuals suffering from presbycusis (i.e.,

hearing loss secondary to the aging process) may also

exhibit mixed hearing loss should

an outer or middle ear lesion exist concomitantly. For instance, a person with earwax

blockage of the ear canal, TM perforation, or middle ear disease will exhibit hearing loss

due to conductive as well as neurosensory involvement. The conductive component of a

mixed hearing loss may be resolved through medical or surgical treatment. The neuro

sensory portion of the hearing loss, however, may be permanent.

Fractures of the temporal bone can be longitudinal or transverse. Longitudinal fractures

occur more frequently, usually spare Cranial Nerve VIII, and commonly cause conductive

hearing loss due to damage to middle ear structures and the tympanic membrane. Trans

verse fractures tend to produce total loss of auditory function because of the severe damage

to the labyrinth. 16 Labyrinthine concussions can induce permanent change to hearing

ability, especially to high frequency hearing sensitivity.

Central Hearing Loss

People with central hearing loss generally have difficulty with cognitive processing of

complex sounds while maintaining normal or neurosensory hearing loss. What is striking,

from a clinical perspective, is the person’s apparent ability to perceive sounds in a seem

ingly normal manner, but obvious difficulty or failure to recognize specific sounds. It is

not surprising that these individuals are mistakenly deemed to have functional or “non

organic" hearing loss. For instance, a person may completely fail to attend to, recognize,

or discriminate speech stimuli in light of apparently normal peripheral hearing sensitivity

on audiometric testing. Central auditory processing and associated cortical or subcortical

lesions that underlie central hearing loss are beyond the scope of this chapter. For this

information, the reader is encouraged to review Pinheiro and Musiek's text. 23

Electro-Diagnostic Procedures

Otoacoustic Emissions

The existence of "echoes" emanating from the cochlea and out the ear canal was first

described by Kemp in 1978. 24 Briefly, acoustic stimuli presented to the ear at threshold

were found to generate a return wave or echo detected within the ear canal. These echoes

or emissions are the result of distortions in the traveling wave, and their presence reflects

the health of OHCs. The ability to test for the presence of these otoacoustic emissions has

provided clinicians with another tool for assessing the functional integrity of the human

cochlea.

Testing is accomplished using a probe, having both a microphone and a stimulus gen

erator, which is inserted into the ear canal. Clicks or pure tones are stimuli used to elicit

responses that are then detected by the microphone inside the probe. These otoacoustic

emissions (OAEs) are then analyzed to assess cochlear

function in all patient age groups.

Evoked OAEs are of two types: distortion and transient. The distinction is based on the

type of stimulus used to elicit the cochlear response.

Transient OAEs are evoked using click or tone burst stimuli. Because such stimuli

include a broad range of frequency components, their energy stimulates the basal as well

as apical regions of the cochlea. Distortion-product OAEs are generated by using two pure

tones (by convention, labeled F1 and F2). These stimuli are most effective when separated

in frequency by an F2/F1 ratio of 1.22. 19 For instance, F2 may be a 1600-Hz pure tone

while F1 may be 1311 Hz. Their ratio is thus 1600 Hz divided by 1311 Hz or 1.22. Distortion

product OAE findings are graphed, as in Figure 8.7.

Clinically, OAEs are used to assess the integrity of cochlear outer hair cells through an

analysis of their amplitude. Most individuals with hearing loss exceeding 45 dBHL would

be expected to have absent OAEs. 19 OAE testing thus serves to supplement other behav

ioral audiologic data to ascertain presence or absence of hearing loss and to distinguish

sensory from neural hearing impairment.

Auditory Evoked Responses

There has always been a need to improve identification of hearing loss in difficult-to-test

individuals. Individuals with TBI may be unable or unwilling to cooperate for standard

behavioral audiometric testing. There may be a need to

assess the neural integrity of

cortical structures responsible for cognition, memory recall, speech recognition, language

function, or attention. For these purposes, a battery of electrophysiologic techniques has

been evolving since the 1930s. Known collectively as Auditory Evoked Responses, these

cortical responses to diverse acoustic stimuli have been used to delineate normal from

abnormal cortical function, to identify neuroanatomic generators of these responses, and

to evaluate their potential as clinical diagnostic measures. Over the last 40 years, it has

become clear that some of these techniques are more useful than other evoked potential

methodologies in estimating hearing sensitivity.

The Auditory Evoked Responses include electrocochleography (ECochG), Brainstem

Auditory Evoked Response (BAER), Auditory Middle Latency Response (AMLR), Auditory

FIGURE 8.7

Distortion-product otoacoustic emissions from a patient with normal hearing sensitivity.

Late Response (ALR), and Auditory P300 Response (Figure 8.8). These electrophysiologic

procedures utilize electrodes to measure tiny electrical voltages arising from various audi

tory neural substrates in response to clicks, tone pips, tone bursts, tones, or speech stimuli.

The utility of the tests is in the assessment of the neurophysiologic status of the cochlea

(ECochG), the auditory nerve and auditory centers in the lower and middle brainstem

(BAER), and higher level auditory processing centers (AMLR and ALR). These evoked

responses are known as exogenous because their appearance is not dependent on any

cognitive effort by the listener. That is, the evoked potentials from persons with normal

hearing will appear whether the stimuli are attended to or not. On the other hand, the

Auditory P300 Response is known as an endogenous or event-related evoked response. Its

appearance requires considerable cognitive effort such as attention to specific, randomly

occurring auditory stimuli. These cognitive responses are believed to reflect the listener's

capacity to attend or to ignore.

FIGURE 8.8

Waveforms representing the auditory evoked responses that are presently investigated clinically. (From Hall,

J. W., Handbook of Auditory Evoked Responses, Allyn & Bacon, Boston, MA. © 1992 by Pearson Education. With

permission.) ELECTROCOCHLEOGRAPHY (ECochG) AP SP AUDITORY BRAINSTEM RESPONSE (ABR) AUDITORY MIDDLE LATENCY RESPONSE (AMLR) AUDITORY LATE RESPONSE (ALR) AUDITORY P300 RESPONSE P 3 P 2 N 2 N 1 P 1 P 2 V Pa Na Nb I III II 1μv 0.25μv 0.50μv 2μv 2μv 1ms V 2ms 10ms 50ms 50ms

The ECochg and BAER techniques are used more frequently to complement or supple

ment standard behavioral audiologic findings. The sensory or neural events recorded via

these two procedures represent very fast (i.e., in milliseconds) processing of incoming

auditory stimuli occurring at the periphery of the auditory system. The AMLR and ALR

generally reflect auditory processing as it progresses through the brainstem and onto the

auditory cortex. The auditory P300 response is a cumulative neural event arising from the

involvement of cortical structures and sensory association areas.

ECochg

ECochg testing is performed to evaluate the status of cochlear function. A transtympanic

or extra-tympanic electrode is used to record electrical voltages in response to clicks

presented to the ear. Responses arise within a 3- to 5-millisecond time window following

stimulus onset and consist of the cochlear microphonic (CM), the summating potential

(SP), and the compound action potential (CAP) (see Figure 8.8). The CM reflects electrical

voltages generated at the sensory hair cell level within the cochlea. The SP is also generated

within the cochlea and is, most likely, a product of distortion occurring in the processing

of sound by sensory hair cells. The CAP is actually the collective response from hundreds

of auditory nerve fibers departing the cochlea on their way to the brainstem.

ECochg components are analyzed with respect to amplitude and time of occurrence or

latency. While not a true hearing test, ECochg is useful for determining outer hair cell

function and the integrity of the auditory nerve. Because of its dependence on intact high

frequency hearing sensitivity, ECochg response parameters may be affected by different

cochlear pathologies. For example, ECochg may be reduced in amplitude when sensory

hearing loss above 1000 Hz is present. The relationship between the SP and the CAP may

be larger than normal in cases with endolymphatic hydrops.[21] Thus, ECochg may be an

appropriate component in a test battery for establishing auditory function in a person

with TBI, especially if standard audiometric testing is not deemed possible.

BAER

The BAER is perhaps the most commonly used neurophysiologic technique for evaluating

the auditory nerve and nuclei in the lower brainstem, as well as auditory structures in

the pontine and midbrain regions. Typically, clicks are used as stimuli, although tone

bursts may be used to elicit frequency-specific auditory neural responses. Clicks are

presented at a rate between 10 to 25 per second. Stimulus intensity is varied to elicit

consistent neural responses at the lowest presentation level. Electrodes, placed on the scalp

and on the earlobes or on the mastoid bones, are used to detect subcortical responses.

These are submitted to signal averaging to generate five to seven waveforms (refer to

Figure 8.8). These are patterns of negative and positive voltages occurring within a 10

millisecond time window (i.e., after the ECochg response). Auditory nerve conduction,

interwave latencies, wave amplitudes, and the presence or absence of expected waveforms

are analyzed for departure from data norms. Wave I and Wave II are attributed to the

auditory compound action potential. Wave III is thought to arise from the cochlear nuclei.

The superior olivary complex is believed to generate Wave IV, while Wave V probably

has its origins in the lateral lemniscus and inferior colliculus. 21

BAER testing is usually performed on persons unable to cooperate during routine

behavioral audiologic evaluation. Because BAER recordings are generally unaffected by

sedation or sleep and require only that the patient rest quietly, clinicians have a reliable

technique for estimating hearing sensitivity in this clinical population. Some individuals

with suspected brainstem lesions secondary to head trauma will undergo BAER to help

identify possible site of lesion, although the use of MRI, CT scan, and other more advanced

neuroradiologic studies have, over recent years, become the method of first choice. How

ever, BAER recordings can provide information about the neural integrity of auditory

structures in a compromised brainstem. In addition, serial BAER recordings can be used

to assess improvement in the neural activity of auditory brainstem generators as a person

progresses through TBI rehabilitation.

Middle Latency Response (MLR)

While auditory recordings such as the BAER and ECochg are known as fast electrophysio

logic responses, the MLR occurs after the BAER, but before

the slow cortical responses such

as the ALR and the P300 response (refer to Figure 8.8). Typically, clicks or tone-bursts are

presented at a stimulation rate of 7 to 10 per second. Stimulus intensity is generally held

to below 60 to 70 dB above threshold to minimize the large myogenic (i.e., postauricular

muscle) response discussed below. Electrodes are placed over the lateral temporal aspects

of the scalp to record negative and positive voltage waves in response to auditory stimuli.

Typically, 4 to 5 peaks and troughs with latency of 12 to 15 milliseconds extend out to about

50 milliseconds. A first prominent positive peak (Pa) occurs at about 25 to 30 milliseconds,

a large negative trough (Na) at about 40 to 45 milliseconds, and a second large positive

peak (Pb) at about 50 to 55 milliseconds. The auditory structures responsible for generating

the MLR are believed to be the auditory thalamus and primary auditory cortex. 21,22

Of concern in recording the MLR is the ability to generate large muscle activity through

the use of a high-intensity sound. This myogenic response can be recorded within the 15

to 50 milliseconds MLR time window by an electrode placed near the ear. During ECochg

and BAER testing, this myogenic response does not usually figure prominently in recordings

because it typically appears after 10 milliseconds (i.e., after the BAER time window). How

ever, use of high intensity stimulation can often cause the appearance of a robust tri-phasic

myogenic response that is easily misinterpreted as the neurogenic MLR being sought.

Since its discovery in the 1960s, MLR testing has been performed in hopes of more easily

identifying persons with hearing loss or brainstem and central nervous system disorders.

Specific to TBI rehabilitation, using MLR has proven less useful than the BAER technique.

The person’s arousal state can influence the amplitude of the MLR, with natural or

sedation-induced sleep reducing the amplitude of the waveform. Muscle artifact from

body movement or from the presentation of the stimulus itself, if intense enough, will

appear as a prominent triphasic response that mimics the MLR. MLR parameters are more

easily affected by stimulus duration and latency than are BAER recordings.

Auditory Late Response (ALR)

The origin of the ALR is debated among researchers because different studies have shown

variability in response parameters that is contingent on cephalic vs. noncephalic placement

of the reference electrode. Most researchers concur that the origin of the ALR is the vicinity

of the fissure of Sylvius and the primary auditory cortex in the temporal lobe. 21,22

The ALR is evoked using tone bursts with long duration or plateaus exceeding 3 to 4

milliseconds at very slow stimulus rates in the order of ~0.5 or 1 per second. Evoked potential

recordings are generally obtained within the range of 50 to 250 milliseconds. The nomen

clature used to identify the components of the ALR consists of P1, N1, P2, and N2 waves.

Clinical application of the ALR is very limited because of better, faster, more reliable

electrophysiologic procedures that are used to estimate hearing sensitivity. As a measure

of cortical function, the ALR suffers serious limitations, as it is easily affected by arousal

state, sleep, sedation, and medications that impact CNS function.

Auditory P300 Event-Related Potential

The ability to record the auditory P300 response depends very much on the participation

of the listener. This endogenous or event-related potential (ERP), the P300, owes its appear

ance to attention to the presence, or in some cases, the absence, of a specific auditory

stimulus. In a typical testing paradigm, a listener will have electrodes attached to the

scalp. Clicks, tone bursts, speech stimuli, nonspeech stimuli, or practically any acoustic

signal can be used as the “constant” or “frequent” stimulus. The listener may hear the

constant stimulus 90% of the time. An auditory evoked response waveform is generated

whether or not the listener attends to the constant stimulus (Figure 8.9). The technique

calls for another acoustic stimulus, differing on some predetermined parameter, to be

introduced, infrequently and at random, to the listener. The listener is instructed to attend

(e.g., simply by counting) to the occurrence of the target stimulus. For instance, the letter/

e/may serve as the “constant” stimulus and the letter/o/may serve as the “rare” stimulus.

Completely at random, the letter/o/may be presented 10% of the time. Separate scalp

recordings are then made in response to both the presentation of and attention to this rare

stimulus. It is the listener’s act of attending (a cognitive act) to the presence of the rare

stimulus that generates the P300 waveform.

The P300 response is typically seen in the range of 250 to 700 milliseconds. It is comprised

of P1, N1, P2, N2, P3, and N3 peaks and troughs, with P3 generally occurring at about

300 milliseconds. In general, the appearance of P300 depends on both the random occur

rence of a rare stimulus and the ability of the listener to attend to the rare stimulus.

Efforts are less to identify neural generators of the P300 response than to identify those

producing the auditory evoked responses described above because the P300 response,

itself, is viewed as the product of a cognitive effort, such as attention. Nevertheless, there

is some speculation that the P300 response recorded intracranially may arise from the

hippocampal region and the amygdala. 21

Clinical application of P300 recordings have been performed on persons with mild to

severe TBI. Again, it should be clear that estimating hearing sensitivity has not been the

FIGURE 8.9

Auditory Late Response waveforms from a subject under attending or ignoring test conditions. (From Squires,

K. C. and Hecox, K. E., Electrophysiological evaluation of higher level auditory processing, Semin. Hear., 4(4),

422, 1983. With permission.) FREQUENT RARE IGNORE ATTEND P2 P2 P2 P2 P3 N1 N1 N1 N1 0 0500 500 MSEC

focus of such use. Instead, interest is primarily on establishing the relationship between

P300 latency and amplitude and various cognitive tasks. For instance, several recent

studies of interest to TBI rehabilitation examined P300 recordings to investigate whether

mild TBI caused deficits in attention, 24–28 increased distractibility during attending tasks, 29

or impaired information processing time. 30–33

The role of auditory P300 in TBI rehabilitation continues to be of clinical interest because

of efforts to uncover the relationship between neurophysiologic events at the cerebral level

and a TBI individual’s performance on behavioral scales.

Summary

The person with TBI is typically confronted with a lengthy rehabilitation process. Skills

once performed unconsciously may now require supreme conscious effort, often with the

assistance of various TBI rehabilitation specialists. To ensure that therapeutic goals and

objectives are met as efficiently as possible, effective communication between therapist and

patient must take place. For this to occur, rehabilitation personnel must be cognizant of a

patient’s ability to hear well enough to actively participate in his/her rehabilitation. Audi

ologists serve to provide the comprehensive audiologic

assessments, using various and

diverse audiologic techniques, needed to allow patient participation to be more effective.

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9

Traumatic Brain Injury: Aging and Related Neuromedical Issues

Alan Weintraub and Mark J. Ashley

CONTENTS

Introduction

Neuromedical issues are faced by a rapidly growing population of over 5 million persons

living with traumatic brain injury (TBI) in the United States. 1 As the TBI population ages,

survivors, practitioners, caregivers, and financially responsible parties, alike, must con

sider the neuromedical issues associated with aging and the complex sequelae of TBI.

These parties must attempt to anticipate the issues to be faced by this population and

further attempt to put in place mechanisms that might address those problems.

The highest incidence of TBI is bimodal in nature. Individuals 15 to 24 years of age

constitute the first grouping while the second is comprised of those people aged 75 years

and older. Prevalence is estimated at around 5.3 million individuals in the United States. 2

with incidence reported at 90 per 100,000. 3 Thurman et al. 1 estimates that between 80,000

and 90,000 persons per year become disabled as a result of TBI. As such, TBI presents a

major public health concern, both as a diagnosis in itself and, in particular, as the effects

of aging are applied. 4

Age has been identified as contributory to outcome for persons who sustain TBI, though

in a nonlinear way. It seems logical to assume that TBI inflicted upon a chronologically

older brain would yield more devastating sequela, and perhaps a more disabling outcome,

when compared to a similar injury sustained by a younger brain. 5–8 While this seems to

hold true for cases of severe injury, 9,10 there is less support for injuries of lesser severity.

This may be due to the neurobiology of injury and the potential for greater neuroplasticity

in the younger brain. 11 A prospective study by Rapoport and Feinstein 12 found an inverse

relationship associated with age and mild TBI. Older subjects (60+ years) fared better than

their younger counterparts (18 to 59 years) with higher Glasgow outcome scores, less

physical symptomatology, less psychosocial impairment, and less psychological distress.

A reason for these surprisingly better outcomes in an elderly mild TBI population raises

relevant theoretical considerations. While the younger brain has clear biological advan

tages for recovery of function, the older person usually will have well-established “real

life” knowledge, structures, and routines in their day-to-day experience that may give

them compensatory advantage to facilitate a better functional outcome. Additionally,

environmental demands associated with older adult lifestyles are often diminished in

comparison to the demands placed upon younger adults.

Consequently, it is difficult, at best, to attempt to make definitive statements about likely

long-term neuromedical issues following TBI based “solely” upon the age of the individual

and even the level of severity of a given injury. Clearly, additional factors play into the

long-term neuromedical outlook. It seems logical to consider these two factors together

with other pertinent information that may bear on the long-term scenario. Insight must

be gleaned from review of known, frequently encountered acute medical complications

associated with TBI, rehospitalization experiences for individuals with TBI, the patho

physiology of TBI, neurological conditions associated with aging and/or TBI, and mor

bidity and mortality statistics.

This chapter will review various neuromedical issues associated with TBI, along with

the interplay that may exist between TBI and other neurological conditions/diseases

associated with advancing age.

Acute Medical Complications and Rehospitalization Rates in

TBI

TBI impacts the central nervous system and numerous other organ systems due to the

traumatic mechanistic nature of injury, such as motor vehicle accidents, falls, and so on.

An early review of medical complications and associated injuries provides valuable insight

into different types of intracerebral, extracerebral, and systemic complications in TBI. 13

These authors reported differences in outcome as measured by DRS scores 14 and length

of stay for both acute and rehabilitation hospitalization as they related to severity of

intracerebral and extracerebral injury and observed complications. Intracranial hemor

rhages and other cerebral complications included subdural, epidural, subarachnoid, intra

parenchymal, and other hemorrhages. Of individuals studied, 68% had one or more

intracerebral hemorrhages. Other cerebral complications included intracranial hyperten

sion, cerebrospinal fluid (CSF) leak, hydrocephalus, and seizures. Extracerebral complica

tions included respiratory failure, pneumonitis, urinary tract infection (UTI), soft tissue

infection (STI), coagulopathy, renal failure, and septic shock. Associated injuries included

fractures, cranial nerve injuries, hemothorax/pneumothorax, intra-abdominal injury, spi

nal cord injury, peripheral nerve injury, brachial plexus injury, and amputation. The fre

quency of these complications is shown in Table 9.1 to Table 9.3.

Englander et al. 15 also reported that respiratory complications were seen in 39% of 637

individuals during acute hospitalization. Twenty-one percent of individuals required gas

trostomies and 23% required jejunostomies. More detailed information was available from

this study pertaining to upper extremity fractures (humerus, radius, or ulna), which

occurred in 11% of the study population, and pelvis or lower extremity fractures, which

occurred in 21% of persons studied.

Of the four reported intracerebral acute medical complications, only hydrocephalus and

seizures appear to impact the long-term neuromedical status of people with TBI. Of the

seven reported extracerebral complications, it could be argued that respiratory and coag

ulopathic complications might reasonably bear some long-term neuromedical importance

for persons with TBI. 16 It is less clear that early infectious complications, once resolved,

impact long-term neuromedical status. Finally, of the eight associated injuries reported,

cranial nerve injuries, SCI, peripheral nerve, and brachial plexus injuries might bear some

significance from a strict neuromedical perspective, but only cranial nerve injury and SCI 17

seem to bear on likely neuromedical conditions impacting the central nervous system. TABLE 9.1 Intracerebral Complications Complication Percent Intracranial hypertension 20 Seizure 17 CSF leak 8 Hydrocephalus 5 TABLE 9.2 Extracerebral Complications Complication Percent Respiratory failure 39 Pneumonitis 26 Urinary tract infection 21 Soft tissue infection 16 Coagulopathy 5 Septic shock 3 TABLE 9.3 Associated Injuries Injury Percent Fractures 62 Cranial nerve 19 Hemo/pneumothorax 11

Intra-abdominal injury 7 Spinal cord injury 2 Peripheral nerve injury 2 Brachial plexus injury <1 Amputation <1

A second source of insight into the nature of long-term neuromedical issues associated

with aging in TBI is found in literature that reviews rehospitalization rates and reasons

in the TBI population. People with disabilities, in general, are more likely to be rehospi

talized than the nondisabled population. 18,19 Several studies have examined medical com

plications resulting in rehospitalization a number of years postinjury in TBI. Cifu et al. 20

found that rehospitalization rates were relatively stable over the first 3 years postinjury

when all reasons for rehospitalization were grouped together. An increase in rehospital

izations due to behavioral/psychiatric problems, seizures, and general health maintenance

from years 1 to 3 was observed. Rehospitalization for infectious processes peaked in year

2 and decreased somewhat in year 3 (Table 9.4).

A report of rehospitalizations was conducted 1 and 5 years after TBI for 1547 consecutive

cases 21 enrolled in the NIDRR Model Systems for Traumatic Brain Injury. Of these, 799

were eligible for 5-year follow-up. The authors reported findings that were similar to those

of Cifu et al. 20 in that rehospitalization for seizures and psychiatric problems increased

from year 1 to year 5 (Table 9.4). It is interesting to note that between the two studies by

Cifu et al. and Marwitz et al., 21 rehospitalization rates for general health maintenance

increased over the time periods studied. Clearly, disabled persons are less able to partic

ipate in their own health maintenance at the level seen in the general population and

general health may be an issue of concern in the discussion of aging. In persons who have

sustained TBI, cognitive, social, financial, and physical disabilities may serve as barriers

to self-initiated health maintenance activities and practices.

Psychiatric issues also pose a substantial concern for the aging TBI population. Rehos

pitalization rates for psychiatric issues remained relatively stable between the two studies

from year 2 (15.3%) to year 3 (15%) 20 and year 5 (16%). 21 Burg et al. 22 reported finding an

incidence of self-reported TBI of one or more injuries in psychiatrically hospitalized

individuals of 66%. This increase in psychiatric rehospitalization correlated with substan

tially more aggression toward family members and caregivers between years 1 and 5

postinjury. 23 Specifically, Brooks et al. 23 reported the incidence of threats of violence at a

rate of 15% at year 1. By year 5, these incidents were reported by 54% of caregivers.

Physical assault of a family member was reported by 10% of caregivers in year 1 and 20%

in year 5.

Rehospitalization rates for seizures increased steadily over years 1, 2, and 3 in the Cifu

et al. 20 study, peaking at 15% in year 3. The Marwitz et al. 21 study found seizure rehospi

talization rates at 18.7% at year 5.

TABLE 9.4

Etiology of Rehospitalizations by Year Postinjury Reason Year 1 a (n = 79 [22.5%]) Year 2 a (n = 59 [21.0%]) Year 3 a (n = 40 [20.0%]) Year 5 b (n = 75 [17.0%])

Rehabilitation

Seizures

Neurologic disorder

Psychiatric

Infectious

Orthopedic/reconstructive

General health maintenance

Unknown 3 (3.8%) 8 (10.1%) 4 (5.1%) 5 (6.3%) 9 (11.4%) 35 (44.3%) 11 (13.9%) 4 (5.1%) 0 (0%) 8 (13.6%) 8 (13.6%) 9 (15.3%) 10 (16.9%) 14 (23.7%) 10 (16.9%) 0 (0%) 0 (0%) 6 (15.0%) 2 (5.0%) 6 (15.0%) 3 (7.5%) 10 (25.0%) 9 (22.5%) 4 (10.0%) 1 (1.3%) 14 (18.7%) 2 (2.7%) 12 (16.0%) 6 (8.0%) 10 (13.3%) 27 (36.0%) 3 (4.0%)

a Source: Cifu et al., Etiology and incidence of rehospitalization after TBI: A multicenter analysis, Arch.

Phys. Med. Rehabil., 80(1), 85–90, 1990.

b Source: Marwitz et al., A multicenter analysis of rehospitalizations 5 years after brain injury, J. Head Trauma

Rehabil., 16(4), 307–317, 2001.

Rehospitalization rates for orthopedic/reconstructive procedures remained surprisingly

high in the first 3 years postinjury ranging from 44.3% in year 1 to a relatively stable 23.7

to 25% in years 2 and 3, respectively. By year 5, the rate dropped to 13.3%, still fairly high

for 5 years postinjury. Rehospitalization rates of 8% at 5

years postinjury for infectious

disease are also high and may be a reflection of antibiotic resistant organisms which have

increased in recent years.

In summary, the rehospitalization data up to 5 years postinjury suggests that seizures,

neurological disorders, psychiatric/behavioral disorders, and maintenance of general

health are issues of concern. Acute hospitalization complications and relatively short-term

rehospitalization rates out to 5 years provide limited insight into likely neuromedical

concerns for a population that can be reasonably expected to live from 10 to 55 years

postinjury depending upon age at injury, injury type, injury severity, and functional status. 24

Pathophysiology of Traumatic Brain Injury

To speculate in more detail over the anticipated neuromedical sequela of TBI with aging,

clinicians must appreciate the pathophysiologic complexity and heterogeneity of TBI.

Cytoarchitectural changes associated with chronic TBI logically serve as a basis for poten

tial neuromedical aging-related developments and conditions. As such, consideration of

the nature and type of injury to neural structures may be important in understanding the

nature of long-term neuromedical issues that may develop. TBI can result in focal or

diffuse metabolic, hypoxic, ischemic, or traumatic axonal damage. 25 Focal damage can be

reasonably expected to impact certain motor, sensory, or cognitive functions, depending

upon the neural structures or systems involved.

Diffuse axonal injury (DAI) is recognized as a primary component of neurophysiological

dysfunction in 40 to 50% of all brain injury which arises from forces applied to the head. 26

DAI tends to predictably affect specific regions of the human brain, such as the parasag

gital white matter of the cerebral cortex, the corpus callosum, and the pontine-mesen

cephalic junction adjacent to the superior cerebellar peduncles. 27 At the cellular level,

direct forces of sufficient magnitude breach the neuronal/axonal cytoplasmic cellular

membrane, initiating a cytotoxic, biochemical cascade of events which impacts neuronal

health and function in the immediate vicinity of the primary damage. 28 The damage

inflicted by this cytotoxic biochemical cascade, however, is not restricted to the locality

of the primary site of damage and can reach far distant cellular structures within the

central nervous system. 29

Neurofilamentary changes arising from DAI consist of mechanical failure of the axonal

cytoskeleton and/or the biochemical cascade that brings about Wallerian degeneration. 30

Neurofilamentary changes associated with Wallerian degeneration, however, are not

immediate. Wallerian-type axonal degeneration progresses from axonal swelling to swell

ing of the axonal bulbs, leading to the development of small clusters of microglia. 31 At a

cellular level, this includes residual endogenous brain peptides and small proteins, 32

immunoreactive astrocytes in injured areas, 33,34 beta-amyloid protein deposition, 35 and

neurofibrillary tangles. 36 These changes occur from days to months to years after injury.

Active myelin degeneration occurs as the final stage in the neurodegenerative process in

the first 2 years after DAI. 37

Some evidence also exists for the presence of chronic perivascular iron deposition

(siderosis) associated with previous perivascular hemorrhage in cortical, subcortical,

brainstem, and cerebellar structures. 38 Primary areas of involvement include the parasag

gital white matter, the corpus callosum, the internal capsule, and the deep gray matter.

Cognitive Decline

The relationship between a history of TBI, age or aging, and cognitive decline must be

examined from two perspectives. The first considers whether cognitive decline associated

with normal aging is, in some manner, impacted or accelerated by interaction with some

neurological mechanism associated with the abnormal brain following TBI. The second

considers whether the cognitive impairment often seen following TBI persists throughout

life or worsens over time in comparison to the cognitive performance of persons without

TBI. The clinician considering cognitive decline must be able to differentiate normal age

related cognitive decline from early signs of dementia,

especially in attempting to prog

nosticate and make recommendations to individuals and their families. Several studies

have attempted to examine the reality, persistence, and perception of TBI-related progres

sive cognitive impairments with aging.

Subjects with mild to moderate TBI were evaluated several years postinjury for cogni

tive performance and compared to two groups of age-matched normals. Middle-aged

persons and older persons with, and without, TBI were also matched and compared. The

TBI subjects reported the belief that they suffered no long-term sequela associated with

the TBI, though test results demonstrated cognitive performance to be impaired. The

authors reported TBI sustained early in life, which results in permanent sequela in specific

domains of cognitive functioning, did not interact with changes in cognitive function

arising from normal aging. In fact, middle-aged persons with TBI actually performed at

the level of older, non-TBI subjects. 39

Goldstein et al. 40 reported that deficits in cognitive performance persisted over time for

persons with TBI when compared to a normal population. Additionally, these authors

found that the magnitude of the difference in cognitive performance between persons

with and without TBI remained stable over time. These findings suggest that the effect of

TBI on cognitive performance is additive to declines in cognitive performance associated

with normal aging.

Thus, it appears that individuals with TBI may accommodate to some level of decre

ment in cognitive performance over time. Without reference to potentially escalating

neurobehavioral sequelae with aging, these studies show that differences exist between

individuals with TBI and those without. These differences persist, but seem to remain

stable in magnitude.

Dementia and Alzheimer's Disease

Along the continuum of cognitive decline associated with normal aging comes a point at

which the level of cognitive decline interferes with normal function and becomes demen

tia. The prevalence of the "dementia syndrome," in and of itself, increases with advancing

age. 41 There is also some degree of intellectual and cognitive dysfunction affecting about

15% of the population over the age of 65. 42 This makes it difficult to investigate whether

TBI directly causes dementia and/or Alzheimer's disease (AD). The research issue is

further clouded by difficulty in proper characterization of normal cognitive decline and

early onset dementia.

The contribution of TBI to the development of AD and other dementias has been a topic

of considerable focus in the literature. The literature has revealed an intriguing relationship

between a history of TBI and AD, in particular. The linkage of TBI to AD will be examined

but it is important to consider the scientific limitations in research design and methodology.

Much of the literature provides retrospective reviews of coincidental diagnoses such as

stroke or TBI and the development of AD or other dementia. 43 Correlational studies are

useful in pointing to potential causal relationships; however, attribution of causality due

to the finding of correlation is inappropriate. Care must be taken to avoid such common

error in the application of statistical analysis. 44

The presence of neurofibrillary tangles has been identified in the brains of boxers who

suffered from the syndrome of Pugilistica Dementia. AD-like pathology appeared to arise

from a protracted history of repeated blows to the head. 45 Beta-amyloid protein deposition

was not found, however, in these subjects. Conversely, in a study by Roberts et al., 35

immunocytochemical methodology further clarified the neuropathology of pugislitica

dementia. The use of immunocytochemical methodology allowed identification of both

substantial beta-amyloid protein deposition and development of neurofibrillary tangles

in pugilistica dementia similar to that found in AD. Increased expression of beta-amyloid

precursor protein is found as an acute-phase response to traumatic neuronal injury. Addi

tionally, such increased expression is a marker of immunoreactivity. The authors suggested

that the extensive overexpression of this response may lead to the deposition of beta

amyloid protein, thereby initiating an AD-type process within days postinjury. 35

Several retrospective and case-controlled studies demonstrated a higher incidence of

AD in individuals with a history of TBI. 46–49 Salib and Hillier 50 examined the relationship

between TBI and AD and other dementias, looking at relative risk/odds ratios. While

there was an association found between a history of TBI and the development of AD (only

in males) and other dementias, greater risk ratios were observed for other dementias rather

than AD. In this study, head trauma was not identified to be a significant risk for AD. The

interval observed between TBI and the development of AD was several decades.

Later research added still further information in determining the relationship between

a history of TBI and the development of AD. Mayeux et al. 51 determined that it was the

presence of apolioprotein-epsilon-4 (APOE-4) that materially increased the risk of AD.

TBI, in the absence of the APOE-4 allele, did not increase the risk of AD and only the

presence of the APOE-4 allele in persons with a TBI did so. 51 While the presence of the

APOE-4 allele increased the risk of AD, cerebral deposition of beta-amyloid with age, a

genetic mutation, or brain injury were felt to further contribute to the pathogenesis of

AD. 52,53 The effects of brain injury and APOE genotype on AD risk was studied by Guo

et al. 54 evaluating 2233 subjects who met criteria for

probable or definitive AD. The study

continued to demonstrate a relationship between TBI injury severity and genetic subtype.

A population-based study conducted by Nemetz et al. 55 investigated the incidence of

persons with TBI who later developed AD. It was concluded that the incidence of AD was

no different than that of the normal population. The onset of AD for persons with a history

of TBI, however, was observed to occur an average of 10 years earlier than for those without

a history of TBI. These findings are substantiated by the work of Mehta et al. 56 In a pro

spective, population-based study of 6645 participants who were free of dementia at baseline,

the authors compared them to a cohort of individuals diagnosed with dementia. Their

findings included no increased risk of AD or dementia associated with a history of trauma

with a loss of consciousness. Multiple head traumas, time since head trauma, and duration

of unconsciousness also did not significantly influence the risk of dementia. Finally, the

presence of the APOE-4 allele was not found to interact with the time to onset of dementia.

Still other factors may bear on the earlier manifestation of AD and the association of

TBI with other dementias. Brain trauma damages the blood-brain barrier permitting

extravasation of serum proteins into the surrounding parenchyma. 57,58 The introduction

of serum proteins into the surrounding parenchyma may portend an activation of an

immunological response later in life in instances where the blood-brain barrier is again

compromised. Since permeability of the blood-brain barrier is not well understood in

normal aging, the issue of potential leakage as a trigger for a secondary immunological

response needs further exploration. 59

Study of regional cerebral blood flow (rCBF) in AD reveals diminution of rCBF in the

posterior temporal and inferior frontal/parietal areas in subjects who developed AD. 60

Therefore, the nature of the TBI itself may yield predictive insight into whether AD will

more likely manifest. For example, focal and multifocal injuries to the brain tend to

predominate in the frontal poles and anterior temporal structures of the brain.

Utilizing positron emission tomography (PET), regional brain metabolism for individuals

with cognitive symptoms of dementia was found to be a sensitive indicator of both AD

and neurodegenerative disease by Silverman and colleagues. 61 A negative PET scan indi

cated that cognitive impairments were unlikely to progress over at least a 3-year period.

A salient neuroimaging feature of AD and the frontotemporal dementias is progressive

brain atrophy, also a characteristic of chronic TBI. Chan and colleagues 62 obtained serial

MRI images in order to quantify rates of cerebral atrophy in individuals with AD, fronto

temporal dementia, and controls. They found the annual rate of atrophy was significantly

greater in demented individuals (2.7%) than in controls (0.5%). While the results of this

study were able to distinguish normals from individuals with dementia, it could not

differentiate between the types of dementia, such as AD or frontotemporal dementia. These

atrophy measurement techniques are presently confined to the research environment. In

the future, brain atrophy measurement techniques may provide a means of assessing the

differential characteristics of post-TBI cerebral atrophy due to aging contrasted with an

index of a more specific separate dementia entity, such as AD or frontotemporal dementia.

The implications of this regional volumetry technology may help in the development of

treatments with the goal of delaying a progressive neurodegenerative process.

The loss of neural structures associated with TBI earlier in life does reduce overall

neuronal availability and thereby diminishes the redundancy of neural structures. As such,

a diminished reserve may contribute to an earlier manifestation of dementias. To the extent

that AD and other dementias may have a genetic basis, persons with TBI may experience

the development of these dementias in concurrence with the TBI sequela, just as they

might other diseases, such as cancer or heart disease.

As one attempts to draw conclusions regarding TBI and its relationship to the develop

ment of AD or other dementias, multidimensional factors need to be considered. The

clinician must evaluate the potential interrelationships between age, various neuropathol

ogies associated with different injury types, idiopathic neuronal atrophy, the potential

contribution of repetitive trauma, genetic predisposition, and immunosusceptibility. These

relationships may all play a role in the timing of the onset of dementia, the rapidity of

progression of dementia, and/or the development of other neurodegenerative disorders.

Other Neurological Disorders

The majority of studies investigating the relationship of TBI and neurological disease have

focused on brain injury as either a precipitating risk factor for the de novo development

or exacerbation of the progression of AD, Parkinson's disease, Amyotrophic Lateral Scle

rosis, and Multiple Sclerosis. 63–68 Given case reports relating post-TBI syndromes that

resemble Parkinson's syndrome, 69,70 the theoretical consideration of trauma as an etiology

of Parkinsonism is necessary. 71 Goetz and Stebbins 72 found that TBI seemed to modify the

course of Parkinson's Disease (PD) in a small series of ten individuals. Following TBI,

they found a transient increase in disability status lasting a few weeks, but after 1 year,

there was no difference in disability compared to age-matched controls.

Williams et al. 68 examined the medical records of 821 people with TBI, between 1935

and 1974, who were more than 40 years old. These people were followed for the devel

opment of dementia and other degenerative neurological diseases. Utilizing a standard

ized morbidity ratio (SMR), there was no evidence that brain trauma was a significant

risk factor for the development of Parkinsonism, Parkinson’s disease, or Amyotrophic

Lateral Sclerosis.

Over the past several years, the issue of injuries precipitating multiple sclerosis (MS) or

promoting new relapses of MS has also been passionately debated in the literature. Well

designed studies have concluded that TBI and other types of injuries do not precipitate

MS nor lead to relapses of MS. Sibley et al. 64 reported a large number of prospectively

studied individuals with MS and identified a subgroup of 67 individuals who incurred a

total of 140 episodes of “closed head injury.” It should be noted that only nine of these

episodes were associated with a period of definite or probable loss of consciousness, with

none lasting more than a few minutes. Siva et al. 66 examined individuals with significant

TBI to determine whether any of these individuals subsequently developed MS. The study

did not consider individuals with MS who incurred TBI.

However, to these authors’ knowledge, there are no other studies describing the inter

action of “significant TBI” with underlying MS. Many clinicians have wrestled with the

issue of a coincidental MS relapse vs. the consequences from the TBI. It has been postulated

that the pathobiologic interaction of TBI with damage to

axons in previously demyelinated

pathways may explain these unexpected clinical scenarios. 28,29

The majority of studies addressing trauma and multiple sclerosis concern the issue of

trauma as an environmental etiologic trigger of MS or relapses of MS. In 1987, Poser

suggested that TBI may exacerbate the underlying disease process of MS. 73 Bamford et

al., Sibley, Siva et al., Sibley, and Kurland et al., 63-67 on the basis of longitudinal studies of

cohorts, found no indication that either the onset or exacerbation of MS was the result of

physical trauma. A major limitation of these studies was that their design did not evaluate

the consequences of “significant TBI” in people with MS.

In general, the effect of preexisting neurological disorders and their attendant neuropa

thology interacting with the pathobiology caused by TBI appear significant, but how this

modifies outcome is unknown. Conversely, how the pathobiology of TBI modifies the

subsequent course of the underlying neurological disease is also unknown. In this regard,

demyelinating diseases such as MS may interact differently than neuronal diseases such

as Parkinson’s Disease in the setting of TBI and with the consequences of aging. This,

again, may be an additive effect related to neuronal loss with increasing brain age, thus

magnifying the pathobiologic effects of the TBI and the neuropathology of other neuronal

diseases such as Parkinson’s disease and demyelinating

diseases such as multiple sclerosis.

Seizures

Seizures are considered to be the clinical manifestation of an abnormal and excessive

discharge of a set of neurons within the brain, including cortical cells. While seizure

phenomena can be associated with an acute insult to the central nervous system or a

generalized systemic metabolic disturbance, this does not necessarily constitute a condi

tion of “epilepsy.” 94 Epilepsy is defined as a condition characterized by recurrent, unpro

voked seizures. 96

Epilepsy occurs within the general population with varying incidence depending upon

age. This topic must consider, independently, seizures associated with “normal aging,”

aging-related diseases, TBI, and their potential interactions.

Normal Aging

Seizure incidence appears to be highest in children, though incidence increases substantially

in people over the age of 70. 74,75 Hauser et al., 74 in a prospective epidemiologic population

based study, followed the incidence of epilepsy and unprovoked seizures in Rochester,

Minnesota, over a 50-year period. Incidence in people over age 70 was found to be two to

three times greater than in children. Incidence at age 40 was 30/100,000 and, by age 80,

increased to 140/100,000. There was no gender difference observed. Generalized seizures

occurred most frequently in children, whereas the elderly had a higher incidence of partial

onset seizures. In people over age 75, partial epilepsy was five times more frequent than at

earlier ages. Approximately two-thirds of seizures in people under age 40 were tonic–clonic

seizures. The rate of tonic–clonic seizures decreased to 54% for the age group 40 to 65 years

and to 40% in people 65 years and older. 74 Overall, the cumulative incidence of epilepsy

ranged from 1.2% from 0 to 24 years, 3% from 25 to 74 years, and 4.4% from 75 to 85 years.

Age-specific incidence is highest in the first year of life. Incidence decreases during child

hood and remains stable up to age 54, when incidence begins to increase again. 74

Hauser et al. 74 determined the three most common etiologies for seizure disorders in people

over age 65 were cerebrovascular disease, degenerative diseases of the CNS, and CNS tumors.

Approximately two-thirds of all cases had a cerebrovascular etiology. Included in this cate

gory are cerebrovascular accident (embolic stroke and intracerebral hemorrhage), hyperten

sion, vasculitis, and arteriovenous malformation. 76–81 Seizures are fairly common within the

first 2 weeks of cerebral infarction and are considered to be an acute effect of the infarction. 82,83

Cerebral cortex involvement, the presence of multiple lesions, hemorrhage, and embolic

infarcts have been identified as risk factors for recurrent seizures following stroke. 84

Degenerative diseases are associated with an incidence of seizures that ranges from 10

to 22%. 85–88 McAreavey et al. 85 found that people with dementia who had seizures were

younger and more cognitively impaired than a control group of people with dementia

only. There did not appear to be any dementia etiologic differences between the two groups.

Hauser et al. 74 found CNS infections, tumors, and neurological defects arising from birth

or trauma to be of equal frequency as antecedents to seizure disorders in people between

15 and 34 years. Neoplasms and trauma were equally frequent antecedents in people 35

to 64 years and cerebrovascular disease emerged as the most frequent. Cerebrovascular

insults preceded the diagnosis of epilepsy in 15% of this age group. In the greater than

65 years group, 28% of all newly identified seizure cases were preceded by cerebrovascular

disease and 20% of seizures had associated degenerative disease.

Management of seizures is impacted by physiological changes in aging. 89 Pharmacoki

netics, routes of administration, drug interactions, pharmacodynamic interactions, and

even drug cost must all be considered as they influence treatment selection. 75 Aging is

associated with decreases in serum concentration of plasma proteins and albumin neces

sary for pharmacological binding, absorption, and bioavailability. 90,91 Inefficiencies in

hepatic and renal function with advancing age also impact metabolism and excretion. 90,91

Swallowing and cognitive decline may contribute to

difficulty with an oral route of

administration. Nasogastric, intramuscular, and rectal options for drug delivery must be

made available. 92 Finally, in people over 60 years of age, the average number of drugs

taken at one time is 7, with up to 13 taken over a year. 93 The risk of pharmacokinetic and

pharmacodynamic polypharmacy interactions is quite high.

Traumatic Brain Injury

Seizures play a relatively prominent role in a discussion of either aging or TBI. Seizures

represent the second most frequent intracerebral complication, occurring at a rate of 17%.

Only intracranial hypertension, as an intracerebral complication, is higher and, then, by

only 3%. 13 Seizures increase in frequency from year 1 to year 5 as a reason for rehospital

ization and become the second most common reason for rehospitalization, following

general health maintenance. 20,21

Studies of seizure incidence and prevalence in the general population logically have

individuals with TBI as a subgroup. Consequently, direct comparison of data sets between

the two groups should be cautiously interpreted. The causes of epilepsy which are ger

mane to the discussion of “aging-related” posttraumatic seizures can be idiopathic, tumor,

trauma, and vascular, which may include hypoxic/ischemic cerebral insult. 95 A thorough

review of the subject can be found in the chapter in this text by Hernandez et al. Also,

Dalmady-Israel and Zasler 96 published a critical review of the literature related to current

concepts of definition, incidence, and risk factors pertaining to posttraumatic seizures.

This review, together with an overview of the topic by Yablon, 97 offers a good literature

review of posttraumatic seizures over the past 50 years, including incidence, natural

history, and predictive characteristics. These articles discuss rehabilitation management

topics, such as anticonvulsant prophylaxis, symptom management, and other problems

encountered in the rehabilitation setting.

Posttraumatic epilepsy (PTE), to some degree, is the result of neuronal biochemical

changes related to the injury process and may play a role in seizures or recurrent ictal

episodes. 98 In addition, differences in types of force, mechanical factors, and anatomic

injury may help determine one’s predilection for developing posttraumatic seizures. 98 A

positive correlation between brain injury severity and the development of one or more

seizures has been identified. When brain trauma results in cortical injury and neurological

deficits without interruption of the dura matter, PTE incidence ranges between 7 and 39%.

Where dural disruption and neurologic abnormalities coexist, the incidence increases

dramatically to between 20 and 57%. Interestingly, however, injury severity and the per

sistence of ictal episodes do not appear to have a correlation. 99

In practical terms, rehabilitation professionals have considered missile penetrating inju

ries, depressed skull fractures, intracerebral/intracranial hematomas, and early epilepsy,

defined as seizures within the first week after brain trauma, as the highest at-risk group

for developing PTE. 100–103 Feeney and Walker 104 developed a mathematical model to esti

mate the probability of posttraumatic seizures. This classic study found individuals with

central parietal injury, dural penetration, hemiplegia, missile wounds, and intracerebral

hematomas to be at greatest risk for development of PTE.

Clinician's experience and Feeney and Walker's 104 work suggesting dural penetration

to be a key risk factor has been substantiated in the literature. While the risk of seizures

is, in fact, very high following penetrating missile injury and has been estimated at 35 to

53%, 105 the risk in diffuse–closed head injury, without contusion or laceration of the cortex,

is much lower, approximately 5%. 106

PTE can occur in the early period following TBI. The early period is defined as occurring

within the first 7 days of injury. 107 PTE can also have its first manifestation many months

or years postinjury, thereby defining late seizures. The risk of PTE after cerebral paren

chyma–penetrating injury remains for up to 15 years. Approximately 95% of individuals

who remain free of seizures in the first 3 years after injury remain seizure-free long

term. 108–110 Approximately 56% of individuals with TBI,

without missile injuries, who

develop late seizures do so within the first year of injury. 111

Age at the time of injury appears to figure into the risk of developing PTE. 100 In a study

by Kennedy and Freeman, 112 risk of early posttraumatic seizures was found to be higher

in children, though fewer developed late seizures, defined as after the first week post

trauma. When late seizures occurred, approximately 40% were noted to have focal features,

70% became unconscious, and 20% had disturbed consciousness, with or without focality,

defined as partial-complex seizures.

In a study of 490 consecutive people with TBI, Asikainen et al. 113 studied factors active

in the development of early and late seizures and their subsequent influence on long-term

outcome. They determined that young children were more prone to early seizures than

adolescents and adults, who were more prone to late seizures. The main risk factors for

late posttraumatic seizures were the known presence of early seizures and depressed skull

fracture. Brain injury severity, as measured by a low Glasgow Coma Scale (GCS) score,

prolonged unconsciousness, and posttraumatic amnesia, without localized brain pathol

ogy, was not found to be a risk factor for the development of late PTE. It was recommended

that people with TBI who developed seizure disorders have appropriate anticonvulsant

therapy and thorough follow-up. Individuals receiving this

level of care were able to attain

higher rehabilitation goals and functional outcomes, such as employment. 113

It is always of great interest to be able to discern whether a seizure will be an isolated

event or whether recurrence is likely or inevitable. This is of concern for operation of

automobiles and mechanized equipment, independence and safety in the community or

living environment, and return to school or work. Haltiner, Temkin, and Dikman 114 studied

the incidence and risk factors for seizure recurrence after the onset of late PTE. This

longitudinal, cohort design showed that, when late seizures developed following severe

TBI, the probability of recurrence was high. The importance of aggressive anticonvulsant

medication management following a first, unprovoked late seizure was emphasized.

While the importance of treating defined seizures and epilepsy is clear, the issue of

suppressive treatment vs. prevention is somewhat controversial. Suppressive treatment is

defined as medication intervention to decrease the occurrence of seizures during the time

in which the individual is at greatest risk. Prevention refers to an approach of ongoing

treatment following the epileptogenic at risk phase. Several older retrospective studies

suggested antiepileptic prophylaxis may prevent the genesis of epileptic foci. 115–117

However, most clinicians now practice in a manner consistent with a study conducted

by Temkin et al. 107 This randomized, double-blind study of phenytoin coverage for the

prevention of posttraumatic seizures was designed on the assumption that seizure pro

phylaxis following brain injuries (i.e., medicating to attempt to prevent the first seizure)

would prevent the development of eventual posttraumatic epilepsy. Convincing evidence

was demonstrated as to the effectiveness of phenytoin-seizure prophylaxis when treating

during the first week following severe TBI. When compared to placebo, treatment with

phenytoin was associated with a 73% decrease in the risk of seizures in the first week.

However, no significant protective effect was detected between day 8 and the end of the

second year of study. Therefore, the early, but not late, effect of phenytoin appears to have

an early suppressive effect (i.e., during the vulnerable epileptogenic phase), but not nec

essarily a true long-term prophylactic or preventative effect. This hallmark study con

cluded that phenytoin reduces the incidence of seizures in the first week after injury, but

not thereafter.

While managing a person with TBI over his/her entire life, the clinician must be cog

nizant of the unique presentations of the types of seizures that present with aging and

the elderly, appropriate methods of diagnosis, and the complexity of different treatment

paradigms. 92,118,119 Care should be taken to avoid over-attribution of seizures to a history

of TBI alone in the aged.

Cerebral Atrophy, Ventricular Size, and Hydrocephalus

Posttraumatic ventriculomegaly is a frequent neuroimaging finding following moderate

to severe TBI. 120,121 Ventriculomegaly following TBI remains a controversial condition as

to what it signifies. Chronic neuroimaging findings of cerebral or subcortical atrophy do

not necessarily have clinical implications.

Chronically-aging TBI reveals a relationship between cortical atrophy and ventricular

volume in neuroimaging studies. Volumetric measures of brain morphology show that

the generalized effects of most traumatic diffuse axonal injuries are more evident via

ventricular dilatation, while the effects of focal and multifocal injury appear to be more

evident in cortical atrophy measures. 122

Computerized tomographic (CT) volumetric studies of the cortical/subcortical mass to

ventricular size ratio 123 have shown that marked encephalomalacia occurs over many years

postinjury. 122,124 As the processes of neurodegeneration and gliosis associated with injury

advance over time, cortical/subcortical volume decreases, while there is an associated

compensatory increase in ventricular size. Over time, the CT pattern in TBI is one of mild

to moderate ventricular enlargement and normal sulcal prominence, except in cases of

focal injury. This process is far greater than that seen in normal aging, though a similar,

less pronounced change in cortical volume and ventricular size is seen in normal aging.

Magnetic resonance imaging (MRI) of aged persons with a history of DAI demonstrates

progressive atrophy within the corpus callosum over many years. 125–127

Normally, cerebrospinal fluid (CSF) is produced by the choroid plexus in the ventricular

system. CSF is extruded into the ventricles and flows from the ventricle of origin to the

sequential ventricle(s) via the Aqueduct of Sylvius, ultimately exiting the ventricular

system to be reabsorbed by the arachnoid villi in the superior sagittal sinus. Noncommu

nicating or obstructive hydrocephalus develops when an obstruction blocks the flow of

CSF and a buildup of CSF occurs behind the obstruction, causing the ventricle(s) behind

the obstruction to enlarge. Obstructive hydrocephalus can occur as a result of hematoma,

subarachnoid hemorrhage, or meningitis. 128 Communicating hydrocephalus occurs when

CSF production continues at a normal rate, but reabsorption in the subarachnoid space is

slowed, causing a buildup of CSF within the ventricular system. Ventricular enlargement

stretches fibers in the surrounding regions, thereby impairing function. Clinically-signif

icant hydrocephalus, whether obstructive or communicating, may be of a high or normal

pressure variant. 129

Differentiation of ventriculomegaly, in which the underlying process is due to subcortical

atrophy, and “hydrocephalus,” which implies an active obstruction of cerebrospinal fluid

or diminished reabsorption, is quite difficult at times. The progression of ventricular

enlargement, which results from cerebral atrophy associated with diffuse axonal injury

and normal aging, can further complicate this clinical differentiation. The importance of

differentiation of the typical symptoms of normal pressure hydrocephalus 130 from symp

toms related to brain trauma, itself, is reviewed by Beyerl and Black. 131 The imaging criteria

of Kishore et al. are still widely accepted for progressive ventriculomegaly with the

distended appearance of the anterior horns of the lateral ventricles, enlargement of the

temporal horns of the third ventricle, with normal or absent sulci, and, if present, enlarge

ment of the basilar cisterns and fourth ventricle. 120 Periventricular decreased density on

CT imaging was also felt to be a diagnostic indicator of communicating hydrocephalus,

as well as enhanced trans-ependymal and periventricular flow patterns on MRI scan.

The classic triad of normal pressure hydrocephalus is impaired gait, incontinence, and

dementia. 130,132,133 In early stages of this phenomena, gait may be unsteady or apraxic and

cognitive decline can be noted, as opposed to an absolute loss of consciousness in more

severe cases. 134

Even though ventricular shunting is frequently regarded as a routine procedure, clini

cians must be cognizant of the possibilities of mechanical, biological, or technical compli

cations. 135 Complications of ventricular shunting for hydrocephalus can include shunt

failure, hemorrhage, delayed wound closure, infection, and seizures. 136 Dan and Wade 135

reviewed the incidence of seizures after ventricular shunting in 180 of 207 consecutive

cases for hydrocephalus arising from various causes. A total of 9.4% developed seizures.

Incidence appeared to be age-related, with a 15.2% occurrence in children younger than

1 year, 10% occurrence in people aged 1 to 49 years, and 6.9% incidence in people over

age 49. Risk of postshunt seizures decreased with time after surgery, from 5% in the first

year to 1.1% after the third year. The incidence of seizures rose with multiple shunt

revisions. Cortical puncture site for ventricular catheterization significantly affected rates

of seizures. In 168 individuals with a posterior parietal insertion, incidence of seizures

was 6.6%. In 11 individuals with frontal catheter placement, 54.5% experienced seizures.

Shunt implantation outcomes were also reviewed in 48 individuals following severe TBI

where implantation was performed a mean of 27 months postinjury. 136 Improvement in

clinical status occurred in 52.1% of cases, whereas 47.9% showed no improvement. Imme

diate seizures occurred within 1 hour of surgery in five cases. Seizures occurred within

the first week of surgery in one case and, after the first week, in 29 cases. Prior to shunt

implantation, 14 individuals had seizures, while 17 developed seizures after shunt implan

tation. Postoperative complications that required shunt revision were shown by 15 indi

viduals. Three individuals had postoperative complications that did not require shunt

revision, one of whom developed marked cerebral edema.

In summary, clinical differentiation between cerebral atrophy due to aging and subcor

tical atrophy due to trauma must be made. The clinical and imaging differentiation is

furthered by determination of the degree to which the observed recovery pattern is or is

not consistent with an expected recovery pattern related to the underlying pathophysio

logic correlates of injury. Where incongruence between the observed and expected recov

ery patterns exists, the interaction of communicating hydrocephalus, with or without

pressure, should be considered. Careful selection for shunt placement should be based on

a realistic appraisal of the risk/benefit ratio for surgical complications vs. better outcomes.

Favorable outcomes from CSF shunting in appropriately selected individuals are reported,

and technical considerations include timing, the type of shunt valve used, seizure pro

phylaxis, and methods of long-term follow-up. 137 A recent technological advance is found

in the development of programmable shunt valves. An improved understanding of intrac

ranial pressure dynamics and their clinical correlates, before and after CSF shunting, may

lead to a more scientific rationale for the application of these valves and their safe use.

Neuroendocrine Dysfunction

TBI has been associated with neuroendocrine dysfunction in both the acute and chronic

states. 138–142 Endocrine abnormalities following brain trauma vary with the comparative

degree of injury to the hypothalamus, the anterior or posterior pituitary, the upper or

lower portion of the pituitary stalk, and the connections of these structures to other

subcortical and brainstem structures. 143 These traumatic neurohypophyseal system injuries

acutely may lead to abnormalities in salt and water metabolism, including syndrome of

antidiuretic hormone (SIADH), temporary or permanent diabetes insipidus (DI), thyroid

function, control of body temperature, abnormalities in ACTH-cortisol levels, and glucose

metabolism, to name a few. Yuan and Wade 143 felt it was unusual to find “classic” features

of hypothalamic or pituitary dysfunction in the TBI population. Koiv et al. 138 found serum

catecholamine and ACTH levels were reduced in people with severe brain injury who

had CT scan evidence of severe alterations in mesencephalic/diencephalic regions. In

these cases, cortisol levels were elevated.

Neuroendocrine dysfunction following chronic TBI has only recently been systemati

cally evaluated as a potential contributor to outcome. Lieberman et al. 140 studied 70 adults

with TBI on average who were 4 years postinjury. Serum TSH, free T 4 , insulin-like growth

factor I, prolactin (PRL), testosterone (males), and cosyntropin stimulation were evaluated.

Abnormal results were followed by dynamic tests of gonadotropin, thyrotropin stimula

tion hormone (TSH), and growth hormone (GH) secretion. The authors reported that 31.4%

of subjects had no abnormalities. A single abnormal axis was found in 51.4% of the subjects

(26 adrenal, 8 thyroid, and 2 GH) and twelve subjects had dual axis abnormalities (5

adrenal and thyroid, 4 adrenal and GH, 1 GH and thyroid, 1 gonadal and thyroid, 1 adrenal

and PRL). There was no correlation with initial GCS. GH deficiency was found in 15% of

subjects and low morning cortisol levels in 46% of these cases. Hypogonadism and diabetes

insipidus were not observed.

Kelly et al. 139 reported some degree of hypopituitarism in nearly 40% of persons who

had suffered moderate to severe head injury. Long-term anterior pituitary dysfunction was

most common, while thyrotroph and corticotroph deficiencies were less common. The

authors suggest that pituitary-hypothalamic axis testing is warranted for people with

moderate to severe brain injury or subarachnoid hemorrhage, particularly those who expe

rienced hypotensive or hypoxic events, evidence of diffuse brain swelling, and/or basilar

skull fractures that involve the sella turcica. While direct trauma to the pituitary gland may

account for dysfunction, the authors feel that vascular causes may be more prominent.

Neuroendocrine function may be important for rehabilitative success, neuromedical

function, and overall health. It is illustrative to consider examples of how specific endo

crine abnormalities may correlate and further contribute to an individual's functional life

challenges. Neuronal growth is regulated by cytoskeletal proteins and depends on thyroid

hormone equilibrium. 144 The highest concentration of thyroid hormone receptors has been

found in the adult rat hippocampus, amygdala, and cerebral cortex. 145 Both thyroid and

estrogen have been demonstrated to impact dendritic tree density in the cerebral cor

tex. 146–150 Thyroid deficiency can result in cerebellar ataxia, leading to instability and a

predisposition to falling and reinjury. Thyroid deficiency can also further contribute to

cognitive and emotional difficulties in the domains of memory and new learning. Gluco

corticoid receptors, like thyroid receptors, are found in concentration in the hippocam

pus. 151 The subsequent paralimbic neurobehavioral consequences of glucocorticoid

insufficiency include apathy, depression, irritability, and psychosis.

The direct result of endocrine dysfunction as it relates to TBI and aging may lead to an

array of chronic physical, neurobehavioral, and functional disabilities. This comorbidity

should be further explored in individuals who display chronic symptoms of fatigue, loss

of muscle strength, decreased energy, cognitive dysfunction, inability to regulate body

temperature, emotional lability, decreased aerobic capacity, and decreased bone mineral

density. Combined with the direct effects of TBI, an endocrinopathy may further result in

a diminished sense of well-being, social isolation, and overall reduced quality of life. 152,153

Endocrine function should be monitored in brain-injured individuals who may be par

ticularly susceptible beyond the postacute phase of management. TBI individuals at par

ticular risk with aging to this comorbidity are those with known basilar skull fracture,

history of severe DAI with dysautonomia, protracted posttraumatic amnesia, or those

with a history of SIADH or diabetes insipidus.

Sleep

Sleep is beneficial for the rejuvenation of human functioning, and animal studies have

shown it necessary for survival. Deprivation and disturbance of this rejuvenating process

can have many adverse effects. With aging, these effects include excessive daytime sleep

iness, fatigue, frustration, depression, poor quality of life, impaired performance,

decreased productivity, and increased health care costs. 154 Sleep disturbance is a relatively

common complication following TBI. Beetar et al. 155 reported that subjects with brain injury

had significantly more insomnia (56%) and pain complaints (59%) than nonbrain-injured

subjects. Poor sleep maintenance was the most common sleep problem. Clinshot et al. 156

reported 50% of brain-injured individuals had difficulty sleeping during inpatient reha

bilitation. Another study reported 30% of individuals with brain injury were found to

suffer from insomnia. 157 Interestingly, they reported that the more severe brain injury was

associated with less likelihood of sleep disturbance.

Many of the sequelae of sleep disturbance may be particularly disruptive to the neurobe

havioral functioning of individuals with TBI. This includes agitation, poor performance,

decreased attention, memory, confusion, somatic complaints, and decreased seizure thresh

old. One study revealed self-reported sleep disturbance in 73% of rehabilitation inpatients

and 52% of outpatients with brain injury, and two other studies reported a correlation

between sleep pattern abnormalities and cognitive deficits following brain injury. 158–160

The particular sleep disorders individuals with TBI are at risk for include posttraumatic

hypersomnia, narcolepsy, central sleep apnea, obstructive sleep apnea, nocturnal seizures,

periodic limb movement disorder (PLMD), and insomnia. 161 In a study of 20 individuals

between 1 and 9 months post brain injury who complained of excessive daytime sleepiness,

eight subjects had sleep apnea/hypopnea syndrome. 162 Sleep apnea was found in 47% of

individuals with brain injury in acute inpatient rehabilitation. 163 In 71 brain-injured indi

viduals in a residential/day rehabilitation program, excessive daytime sleepiness was

reported in 65% of subjects. Eleven percent (11%) had sleep apnea/hypopnea, 25% had

periodic limb movement disorders, and one subject had narcolepsy. 164 Finally, Castriotta

and Lai 165 found seven of ten individuals with brain injury had complaints of excessive

daytime sleepiness, sleep disordered breathing, and narcolepsy. They reported that all

subjects were treated with either continuous positive airway pressure (for sleep disordered

breathing) or Provigil® (for narcolepsy and posttraumatic hypersomnia) which resulted in

subjectively improved quality of life and substantial improvement in daytime function. 165

The incidence of sleep disorders for persons with TBI is much higher than that in the

general population. Sleep apnea/hypopnea is estimated to occur in 2 to 4% of the general

populace. PLMD occurrence is about 5% and hypersomnolence occurs in between 0.3 and

13% of the general population. 164 Sleep disorders clearly contribute to a number of other

neuromedical conditions including reduced seizure threshold, psychiatric and behavioral

disorders, cognitive dysfunction, and overall feeling of reduced psychological well

being. 166–169 From a social perspective, sleep disorders have been associated with increased

incidence of motor vehicle collisions 170,171 and unintentional injuries. 172

Sleep disturbances can be assessed using subjective measures such as self-rating

scales. 173,174 However, sleep disturbance can also be measured using more objective

techniques that range from monitoring changes in select physiologic processes (heart rate,

temperature, cortisol levels, blood/oxygen levels, etc.) to full polysomnography and sleep

lab studies. 175,176

A combination of subjective and objective measures, combined with serial clinical eval

uation throughout the aging process, will assist clinicians in appropriate management

strategies. 177,178 Depending on etiology, management strategies include extension of time

in bed, naps, surgery, various medical devices (e.g., oral appliances, continuous positive

airway pressure), and pharmacotherapy. 178,179

Mortality and Life Expectancy

One of the most frequently asked questions concerns what impact TBI has on life expect

ancy. This issue presents a number of pragmatic concerns for families of people with TBI

and bears on the development of suitable support systems that will be able to effectively

address lifelong issues. 180 Logistical and financial planning for the individual and public

health planning on a larger scale require the most accurate appraisal possible of what will

need to be provided for an individual living with TBI and for how long.

There is a significant amount of literature describing the risk factors, shortened life

expectancies, and causes of death in persons with chronic,

disabling CNS conditions that

may be illustrative in the discussion of such issues in TBI. 181–184 In certain sub-groups of

persons with severe mental and physical disabilities, several studies have shown abbre

viated life expectancies. In a study examining life expectancy of profoundly handicapped

persons with mental retardation, Eyman et al. 185 collected data on mortality and other

factors for 99,543 persons with developmental disabilities. This comprehensive review

between 1984 and 1987 examined subgroups with functional disability related to mobility,

personal activity of daily living abilities (i.e., self-feeding), and incontinence. People with

severe mental retardation were found to have decreased life expectancy, either as children

or adults, if they had severe limitations in mobility, were dependent on nutritional tube

feeds, and were incontinent. This subgroup represented the most medically-fragile group

and had an average life expectancy of less than 5 years. However, as mobility, nutritional,

and bowel and bladder independence improved, so did life expectancy, adding a range

of up to an additional 23 years. This study did not, however, account for differences in

environmental factors, such as the level and intensity of care and how enriched the

environment in which the person was being cared for was, thus allowing them to thrive.

Roboz 186 found that people with mental retardation had the highest mortality when there

was extensive brain damage and a completely bedridden condition was present. This

study in a non-TBI disabled population with mental retardation demonstrated the influ

ence of functional predictors of long-term morbidity and mortality and the contribution

of comorbid neurological factors.

Much of the literature on mortality after TBI in adults has focused on predictors of early

mortality, i.e., less than 1 year after injury. Mortality studies involving hospitalized indi

viduals have found that approximately 90% of those individuals admitted to a hospital

with TBI are discharged alive. 187,188 Risk factors such as age, admission GCS score, asso

ciated injuries, hypotension, hypoxia, and intracranial hemorrhage are associated with

survival. A study by Marshall et al. 189 reported 6-month mortality at 36% among those

with an admission GCS score of less than 8, by itself, or associated with the presence of

subdural hematoma and elevated intracranial pressure. In another study, 1-year mortality

was found to be associated with factors such as age, GCS score, injury severity, and

presence of intracranial hemorrhage. While neither of these studies focused on individuals

who received inpatient rehabilitation, Fiedler et al. 190 examined first rehabilitation admis

sions for TBI in 1998 using data from the Uniform Data System for Medical Rehabilitation.

They found mortality within this population was 1 to 2% 3 months postdischarge. This

study was focused on functional independence as a correlate of mortality. It did not

attempt to determine survival status in those persons lost to follow-up, nor was any

analysis done to identify predictors of mortality.

Most relevant to issues of aging are studies reporting on mortality and life expectancy

beyond 1 year after TBI. In a study of Vietnam veterans with penetrating cerebral injuries,

the cause of death after TBI appeared to have similar patterns to those seen in the general

population as soon as 2 years postinjury. 191 However, earlier studies implicated seizures

as a cause of death unique to the TBI population. 192,193 More recently, seizures appeared

as the third leading cause of death in reviewing a California database analyzing post-TBI

mortality. 16 However, in this study, both circulatory and respiratory causes of death were

more common than seizures and both of these causes appeared consistently over time

and across populations.

A preliminary study utilizing the NIDRR-funded TBI Model Systems National Data

Base has identified a range of possible predictors of future mortality. 194 These include

age, previous TBI, having an injury that was caused by a fall, blood alcohol level (BAL),

posttraumatic amnesia, and discharge disposition. However, only age at the time of

injury and BAL were significant predictors of mortality in this study’s multivariate

analysis. Alcohol was not shown to be a significant risk

factor in a similar study con

ducted in Australia. 195

Overall, a few studies do suggest that life expectancy for individuals with TBI is shorter

than for those in the general population. 24,192,193 However, the evidence explaining why

life expectancy is shorter is very mixed. 16,24,191,194–197 In persons who have sustained severe

TBI and are considered “low functioning” or dependent, life expectancies seem to be much

shorter. Ashwal et al., 198 in a study reporting on the most severely injured of TBI survivors,

found that those who remained in a persistent vegetative state had a mortality rate of 82%

at 3 years postinjury and 95% at 5 years postinjury.

People with TBI who remain in a persistent vegetative state represent a subgroup of

TBI with the least functional status and mobility. There is some suggestion that a distinction

might be made even between life expectancy for persons with the “minimally conscious

state” vs. “persistent vegetative state.” In this vain, Jennett and Plum 199 differentiated the

persistent vegetative state (PVS) from other types of chronic unconsciousness and sug

gested that life expectancy for PVS differed when compared to other types of unconscious

ness. The Multi-Society Task Force on PVS, 200 in a literature review of the medical aspects

of the persistent vegetative state, examined data available on survival. The review con

cluded that a reduction of life expectancy to approximately 2 to 5 years for both children

and adults resulted when neurological injury was severe enough to produce PVS. Exam

ination of the records of 251 individuals diagnosed with PVS resulted in the conclusion

that survival beyond 15 years was rare.

Morbidity and mortality show differences between those people in coma immediately

after a nontraumatic vs. a traumatic injury with the nontraumatic group having a poorer

prognosis. 200 Rates of death and PVS combined are higher at 1 year postinjury for the

nontraumatic group than for the traumatic group. By 1 year, 85% of nontraumatically

injured people who immediately entered coma remained in PVS or died contrasted with

48% for the traumatically injured group. A shortened life expectancy in PVS was noted

to be due to several factors. Reported causes of death include infection (usually of the

pulmonary or urinary tract), generalized systemic failure, sudden death, respiratory

failure, and other disease-related causes, such as recurrent strokes or tumors. It was stated

that age was an important factor both in young infants and children and that the elderly

have a shorter life expectancy than do young or middle-aged adults. It was not well

delineated whether the cause of the vegetative state or the subsequent medical complica

tions were the etiologies of death.

In contrast, two studies of “highly functioning,” ambulatory adults suggested that life

expectancy was reduced by 3 to 5 years. 192,193 Roberts 201 followed approximately 500

individuals with severe disabilities up to 25 years. An estimated reduction in life expect

ancy of 4 to 5 years was found among individuals who became mobile enough to walk

unaided. Strauss et al. 24 reviewed life expectancies across all severity levels of TBI. They

also found diminution of life expectancy to be dependent upon level of mobility. That is,

life expectancy for people with no mobility ranged from 10 to approximately 15 years

depending upon age at the time of injury. The shortest life expectancies were associated

with higher age at injury. This trend remained stable for people with poor mobility and

fair to good mobility. Those with poor mobility ranged from 17.9 to 34.2 years life expect

ancy and those with fair to good mobility ranged from 26.5 to 54.8 years life expectancy,

again depending upon age at injury. The youngest people at injury had the greatest

decrease in life expectancy.

There appears to be some reduction in life expectancy related to TBI associated with

other comorbidities. Weiss et al., 197 in a study examining post World War I head-injured

veterans, found that the occurrence of posttraumatic seizures was a prognostic factor for

a higher death rate after the age of 50 years. While other indicators of injury severity did

not lead to differences in death rates, there were significantly more deaths due to cere

brovascular causes in the head-injured group compared to controls. In post World War II

studies, Corkin et al. 196 found that penetrating head injury, coupled with posttraumatic

epilepsy, shortened life expectancy in persons who survived the initial postinjury period

when compared to head injury alone. Educational level was found to be independent of

the influence of seizures on life expectancy, meaning people with more education survived

longer than those with less. Walker and Blumer 202 also found the death rate of World War

II veterans with posttraumatic epilepsy to be higher than that of normal men. In addition,

wounds involving the right cerebral hemisphere seemed to shorten life span more than

similar injuries of the left hemisphere.

Strauss et al. 24 reviewed the records of 946 persons who sustained TBI, ages 5 to 21, and

were receiving disability services in California between 1987 and 1995. The study explored

risk factors associated with mortality after TBI: male gender, no mobility, poor mobility,

tube fed, fed completely by others, attempts to finger feed, and ADL assistance. Cognitive

skills did not contribute to prediction of mortality. Age at injury was not found to sys

tematically relate to mortality risk either. Time since injury was found to impact relative

risk of mortality. After the initial acute period, time since injury in the first 1 to 2 years

showed less than half the risk of mortality when compared to children with cerebral palsy.

However, in the longer run, mortality rates between the two groups seemed to converge.

The greatest predictor of mortality appeared to be mobility. Known causes of death were

listed as late effect of accidental history (n = 19), subsequent vehicle and other accidents

(n = 3), infections (n = 3), pulmonary (n = 2), epilepsy (n = 2), cerebrovascular (n = 1),

suffocation (n = 1), burning (n = 1), suicide (n = 1), unspecified (n = 2), and missing (n = 3). 24

The findings of causes of death reported by Strauss et al. 24 are similar to those reported

by Roberts. 201 While Roberts reported that causes of death for people with TBI were not

very different from the general population for many causes, some stood out as being

different. These included meningitis, epilepsy, accidents, suicides, and respiratory disease.

The causes of death reported by Roberts and Strauss et al. closely follow the causes for

rehospitalization reported by Cifu et al. 20 and Marwitz et al. 21

The mortality risk factor of “functional status” has also been explored in the literature

related to TBI mortality. In particular, feeding and mobility are reported to be major deter

minants of life expectancy in both children and adults. 24 One study found that mobility

was a stronger predictor of mortality than consciousness in “poorly” responsive individ

uals. 203 Shavelle et al. 16 reported standardized mortality ratios (SMR) for those with TBI

that range from a low of 180% in ambulatory individuals to 196% in those who are partially

ambulatory and as high as 660% in nonambulatory individuals. These studies are beginning

to lend credence to the concept of function as a predictor of mortality. In future prospective,

longitudinal studies, knowledge of objective functional measures at rehabilitation admis

sion, discharge, and in selected time frames postinjury may, themselves, be predictive of

survival, life expectancy, neuromedical complications, and other relevant comorbidities. 184

Finally, medical-legal issues encompassing life expectancy and the need for long-term

planning seem relevant. 204 The logistics and costs of these long-term planning consider

ations are immense. 180 The anticipated progression of communicative, physical, and neu

robehavioral changes over a lifetime is not yet an exact science. Planning for later life

events and end of life can be furthered to a degree by not only the knowledge of neuro

medical complications and long-term issues but also recognition of associated functional

changes arising from either the neurological injury or associated nonneurological inju

ries. 180 It is not possible, at this time, to fully enumerate the exhaustive implications of

aging on such functional skills and limitations since investigation into these arenas has

only just begun for the TBI population. The work done thus far in SCI should serve as an

excellent model for this endeavor. 17,181-183 This will only help to further the understanding

of the efficacy of specific medical rehabilitative

interventions and allow better understand

ing of society’s duty in resource allocation. 205

Procedures for estimating life expectancy in a “specific” person with TBI is a complex

and challenging endeavor. Statistical methods are often valuable in making life expectancy

estimates for persons with spinal cord injury and other neurologic disabilities when

grouped by particular characteristics. However, in a heterogeneous TBI population char

acterized by different injury types and severity with discrepant medical, neurologic, and

functional disabilities, a statistical methodology may be inaccurate. Furthermore, the

impact of pre- and comorbid variables and different rehabilitative and long-term support

ive care paradigms may also have a differential impact on long-term morbidity and

mortality. In an article by Kraus 206 reviewing accuracy of life expectancy estimates in life

care plans, it was felt important to consider nonbiographical and noninjury factors, as

well as the injury itself. This article emphasizes a host of important variables which may

impact life expectancy, such as income, access to healthcare, health behaviors, and psy

chosocial adaptations.

Successful Aging

Successful aging is a wonderful goal for an individual with the disabling physical, cog

nitive, neurobehavioral, and emotional disabilities associated with TBI. Successful aging

is defined as an optimal state of overall functioning and well-being. Successful aging can

be difficult to achieve, even in the general population. In a cross-sectional aging study

that obtained information from 599 participants in Leiden, Netherlands, successful aging

from a public health perspective, was defined as a state of being. 207 All participants were

classified as “successful” or “not successful” based on optimal scores for physical, social,

psychocognitive functioning, and feelings of well-being using validated quantitative

instruments. Although 45% of the participants had optimal scores for well-being, only

13% had optimal scores for overall functioning. In total, 10% of the participants satisfied

all the criteria and could be classified as “successfully aged.” The qualitative interviews

showed that most elderly people viewed success as a process of adaptation rather than a

state of being. The participants recognized the various domains of successful aging, but

valued well-being and social functioning more than physical and psychocognitive func

tioning. Therefore, aging people with TBI are not unlike the elderly population and should

view successful aging as a process of adaptation.

A study is now being conducted by the Rocky Mountain Regional Brain Injury System

at Craig Hospital in Englewood, Colorado. This study includes collaboration with 17 TBI

Model Systems of care as funded by the National Institute on Disability and Rehabilitation

Research. 208 Over 2500 TBI systems national data base cases, starting in the year 1989, will

be evaluated and compared to a cohort of all individuals with TBI rehabilitated at Craig

Hospital over the past 40 years. The study will investigate mortality and life expectancy

in TBI survivors following inpatient rehabilitation, evaluate the causes of death compared

to the general population, and attempt to determine the risk of death in certain neurologic

and clinical subgroups. This study will also evaluate the effects of different types of

improved care and their relationship to long-term survival.

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10

Therapy, Neuroplasticity, and Rehabilitation

Robert P. Lehr, Jr.

CONTENTS

Introduction

Therapists engaged in the rehabilitation of the traumatically brain-injured person are well

aware that their therapeutic skills are effective and can produce significant results. The

techniques that produce these results are those of a repetitive nature that build on previous

therapeutic procedures and are multimodal in nature.

These therapies are what have been described as being activity-dependent. 1 Being activ

ity dependent means the therapy is focused to the point that the recipient of the therapy

is actively engaged in the therapeutic process. These therapies are designed by the therapist

to elicit a key response from the client and this leads to one part of a successful rehabilitative

program. These learned skills have their foundation in the nervous system, and we now

know that there are physical changes that take place at the synaptic level to produce the

rehabilitative results. It is the synapse that is the ultimate target of the therapeutic process.

The purpose of this chapter is to provide therapists with a better understanding of these

neuronal changes and how the human brain is altered by their therapies.

Neuroplasticity is the ability of the brain to change its structure and organization as the

organism encounters its environment. 2 The human brain is composed of a collection of

neurons that have been shown to be pliable and subject to changes in structure, individ

ually, as well as collectively, if the interaction between them is initiated with purposeful

intent. Just because the brain is active does not mean it is learning. Learning comes from

a purposeful activity in which the learner is fully participating. As you will recall, just

sitting in the classroom did not guarantee the acquisition of the material of the lecture. It

was not until you actively studied the material, committed it to memory, or put it to use

that you learned the material. In a like manner, the traumatic brain-injury (TBI) client

must be committed and actively engaged in the therapeutic process.

Let us now look at some of the learning processes therapists initiate and see them on

the cellular level. It is hoped that this insight will stimulate in the reader a better appre

ciation of the processes involved and perhaps lead to some innovative therapies.

The early prediction by Hebb 3 that there would be observable changes in the neurons

or their synapses was further elaborated by neuroscientists to suggest that the behavioral

changes an organism makes in response to the influences of the environment would be

reflected in changes in synapses in the central nervous system. 4 Neurobiologists (Bailey

and Chen, 5 Kandel, 6 and others) followed with elegant

experiments that demonstrated

the importance of this synaptic organization and the interactions that occur between the

neurons. Using very simple animals, such as marine snails and moving on to rodents and

mammals, these investigators were able to clarify the role of the synapse in learning.

Learning is a complex process that has several levels. We will look at learning in terms

of habituation, sensitization, classical conditioning, and operant conditioning. These are

by no means the only concepts involved in learning, but they will allow us to illustrate

some changes that take place at the cellular organization of the brain and to place them

in the context of therapy.

Habituation

Kandel, 6 using the California marine snail Aplysia, has demonstrated the simple form of

learning known as habituation. This form of learning is characterized by the reduced

response to a presentation of a novel stimulus. The experimental setup is demonstrated

in Figure 10.1. When a stimulus is applied to the siphon, the snail responds by reflex

withdrawal of its gill, mantle, and tail. With repeated stimulation to the siphon, there is

a depression of the reflex response. The decreased response is characterized by a decrease

in the synaptic transmission from the presynaptic sensory neurons to the interneurons

FIGURE 10.1

Marine snail Aplysia: experimental setup. (From Kandel, E.R., Cellular mechanisms of learning and the biological

basis of individuality, in Principles of Neural Science, 4th ed., Kandel, E.R., Schwartz, J.H., and Jessell, T.M., Eds.,

Elsevier, New York, 2000, chap. 63, p. 1248. With permission.)

and motor neurons in the reflex circuit (Figure 10.2). There is a decrease, over time, of the

amount of transmitter released. These changes are internal to the presynaptic neuron and

can last for a few minutes or a few hours. This is known as short-term habituation.

When stimulation occurs over several training sessions, there has been demonstrated

an actual reduction in the number of synapses present to the postsynaptic neuron, and

this process is known as long-term habituation. While this has not been demonstrated in

humans, it can be speculated that this is what occurs when we condition a client that has

symptoms of dizziness by constant exposure to a revolving swing. The constant presen

tation of a stimulus that produces the dizziness will, in time, habituate. First, there is a

reduction of neurotransmitter, and then, eventually, a reduction of synaptic connections

so that a stable equilibrium may be obtained, without nausea.

Sensitization

In sensitization, the process involves an additional neuron and is more complex. The

additional neuron is one that “facilitates” the signal by reinforcement (see Figure 10.3). It

is an enhancement of the reflex response after the presentation of a strong stimulus. After

a strong stimulus, the organism is more attentive to all stimulations to itself and the nature

of the synapse physically changes. There is an increase in the size of the synaptic zone 7

(Figure 10.4) and in the number of vesicles containing neurotransmitter in the active zone. 8

These changes in the circuit demonstrate that there is a “memory” of what has happened

to them. These changes last several minutes and are known as short-term sensitization.

FIGURE 10.2

Marine snail Aplysia: gill-withdrawal reflex circuit. (From Kandel, E.R., Cellular mechanisms of learning and the

biological basis of individuality, in Principles of Neural Science, 4th ed., Kandel, E.R., Schwartz, J.H., and Jessell,

T.M., Eds., Elsevier, New York, 2000, chap. 63, p. 1248. With permission.)

Long-term sensitization also occurs following several training sessions. This process pro

duces proteins that enhance the short-term mechanisms and also promotes the growth of

axons with new synapses. These newly produced proteins have been shown to be persis

tently active for up to 24 hours without requiring a continuous signal of any sort. This is

an exciting opportunity for the therapy regimen. These new synapses cause the postsyn

aptic neuron to increase its dendritic branches to accommodate the new synapses from

the axons of the presynaptic neurons. 8

This synaptic plasticity is “activity dependent” and, with the increased axonal sproutings,

increased neurotransmitters, and correspondent dendritic field expansion, there are changes

in the surrounding tissue. There are increases in the glial cell components and an increase

in the vascular supply to the region. These changes are rapid and have been identified to

take place within 10 to 15 minutes. 9 The therapist must move quickly to reinforce the target

behavior when the client demonstrates the acquisition of that sought behavior.

Additionally, exercise has been demonstrated to increase the number of synapses in the

cerebellum of experimental animals that undergo complex motor skill learning, but not

mere motor activity. 10 These demonstrations of the plasticity of the brain at the cellular

level show that a new foundation for the behavior has been formed, and the repetition of

the behavior will reinforce the newly formed synaptic connection. As we repeat the activity

in a therapy setting, we increase the effectiveness of the corresponding synapses and this,

in turn, contributes to the reacquisition of the skills.

FIGURE 10.3

Marine snail Aplysia: gill sensitization. (From by Kandel, E.R., Cellular mechanisms of learning and the biological

basis of individuality, in Principles of Neural Science, 4th ed., Kandel, E.R., Schwartz, J.H., and Jessell, T.M., Eds.,

Elsevier, New York, 2000, chap. 63, p. 1251. With permission.)

FIGURE 10.4

Schematic model for adhesion-mediated changes associated with synaptic modification. The hatched area between cells represents the extracellular matric (ECM). (From Schubert, D., The possible role of adhesion in synaptic modification, Trends Neurosci., 14(12), 128, 1991. With permission.)

Types of Learning

Learning and memory are closely associated and sometimes difficult to separate except for academic purposes. For the therapist, however, they are intertwined in a more specific way.

The rehabilitation process involves the returning to wholeness of the entire person and, as such, makes demands on many systems, from the locomotor to the cognitive. The cellular mechanisms involved in the learning and memory processes we are discussing are the same.

The two types of learning we discussed above, habituation and sensitization, are forms of nonassociative learning where the organism learns the properties of a single stimulus.

In another form of learning, associative, the organism learns about the relationship between two stimuli or between a stimulus and a behavior.[11] For the therapist, it might be more productive to view the learning/memory process as being based on the classification of explicit and implicit memory. It is not our purpose to engage in an extensive discussion of memory but to set the stage for the learning process within the therapeutic setting.

Explicit memory deals with facts and events. This form of memory is recalled by a

deliberate conscious effort. Facts and remembering events are the purview of the entire

rehabilitative team. It is also the area where the cognitive functions of the skills of daily

living are rehabilitated. The skills to plan the day, to shop for groceries, and to make

change for a dollar are some of the items of concern, and these require the reestablishment

of the explicit memory.

Explicit memory has been shown to involve long-term potentiation (LTP) in a part of the

brain known as the hippocampus. In fact, the presence of LTP in the hippocampus was the

first confirmation of Hebb's rule that learning would be based in the physical changes in

the synapse. LTP represents the receptiveness and increased facilitation of the excitatory

synaptic potentials in the postsynaptic neurons that can last for hours, weeks, or months. 8

The relationship, in time, of two presenting stimuli increases the efficacy of the two

synaptically related cells and is a reminder to the cells of that relationship.

This synaptic enhancement can take different forms in different parts of the hippocam

pus. Recent research has shown that the hippocampus is a key component in early memory

and in the final distribution of information to the multimodal association areas of the

cerebral cortex. The left hippocampus seems to be involved with verbal memory, whereas

the right hippocampus seems to be more involved with the representation of the environ

ment and the ability to find our way in it. 8 Suffice it to say that the association of the

hippocampal and multimodal association cortical neurons is established in the synapses

of their respective neurons. The reinforcement with repeated practice is what produces a

successful therapeutic regimen.

Implicit memory, on the other hand, refers to how to perform an act. These memories of

a specific task do not require conscious effort to recall or to reestablish. They require

concentration and a focus on the task at hand but not the conscious effort of recall. Implicit

memory is seen in the training of skilled movements and perceptual skills. These are the

skills of walking, driving a car, or performing other motor tasks. 8

Implicit memories involve habituation and sensitization but they also include two other

processes, classical conditioning and operant conditioning. These processes involve the con

cept of association. In classical conditioning, there are two stimuli presented, which, after

a series of associations with each other, begin to produce a new response. These associa

tions are established in the synapses of the cooperating neurons. This new response then

enables the organism to predict the environment.

In operant conditioning, the associative relationship is between the organism and a

subsequent behavior produced. The organism learns that, for

a specific action, there is a

related reward. Thus, if behavior is controlled, then the individual receives an appropriate

reward for that action. This is the foundation for the wide use of behavioral modification

programs (see Chapter 14).

Classical conditioning relies on an association in which a stimulus that had been previ

ously incapable of producing a response is paired with a strong stimulus that does produce

the response, and the association between the two will eventually produce the response

from the weaker stimulus. Classical conditioning results in a greater and longer-lasting

enhancement. This process is one in which there is a presynaptic facilitation of the synaptic

transmission. It is the pairing, in time, of a meaningful relationship that produces the

result. The internal mechanisms of the process are solidly established and involve several

enzymes and genes. 8 The combinations of enzymes and genes are the same that we saw

in the process of long-term sensitization. The production of the cellular proteins by this

process forms the foundation for the results seen in the therapeutic program.

Hierarchical Learning

Rehabilitation, as a process, requires the work of several respective professions. Among

these, the professions of physical and occupational therapy hold, as a major tenet, the

developmental concepts in neurodevelopmental therapy. 12,13 Neurodevelopmental theory

says that there is a basic developmental sequence in the individual from the time of

conception to adulthood. The function that is expressed is built on previously learned

foundations. We must crawl before we walk. Therefore, it is important that the process of

restoration of function should follow the same sequences that occurred in development.

Kandel's group 6 has shown that the stages of learning mentioned above are sequential.

The infant Aplysia is first capable of only habituation, then, with maturity, dishabituation

occurs, and finally, sensitization. These sequential stages of learning confirm that learning

is a process that builds on previously developed mechanisms and is not complete at birth.

This understanding seen in the simple snail lends support to the foundation of some long

standing therapies of rehabilitation 3,4 that suggest a hierarchy exists in the development

of the individual, and successful therapy must be carried out in the same order.

It is clear that learning is a hierarchical process and has a neuronal basis. It is not so

clear in the cognitive area where we have only begun to investigate the cognitive functions

with modern imaging techniques and cellular neurophysiological experiments. The liter

ature on cognition is rich indeed and has provided a foundation of strategies that has

been successfully incorporated into the rehabilitation environment (see Chapter 12).

Cognitive scientists will tell us that we are first able to

describe objects using very simple

descriptions of color, size, and shape. From this base, we can move to the descriptions of

their usefulness and, eventually, to the features of the object, allowing use of the object

for other extended purposes. 14

Current concepts in the neural sciences are beginning to reveal a neural concreteness to

constructing the visual image from the features of the object. The neural pathway for

vision is known to have two parallel pathways that convey different types of information. 15

One pathway, the P pathway, is concerned with form, size, and shape or what the object

is. The P pathway projects to the temporal multimodal association cortex. The other

pathway, the M pathway, is concerned with movement and depth perception or where the

object is located. This M pathway projects to the parietal multimodal association cortex.

As these two pathways project to separate areas of the cerebral cortex, this helps explain

the selective loss of some features of an object. As an example, object agnosia, the ability

to name an object, is associated with Brodmann areas 18, 20, and 21 on the left temporal

cortex, whereas color anomia, the ability to name a color, is associated with the speech

zones or connections for Brodmann areas 18 and 37. The mechanism of the complete visual

construct is pulled together by a yet unknown binding mechanism.

The binding mechanism takes the properties of form

(rectangle), color (yellow), and

dimensions in depth (box), and says, “We have a long yellow box!” Thus, the binding

mechanism pulls together a single representation of an object from several multimodal

association cortices. Treisman et al. 16 and Julesz 17 have suggested that such associations

require focused attention. They further divide the process into two steps. One is the

preattentive stage in which the object is scanned for the size, shape, color, and movement

by the parallel processing P and M pathways. A serial processing that is responsible for

identifying how to categorize the visually constructed object follows. This categorization

is dependent on the hippocampus and the eventual storage of the information about the

object in the various association cortices. 10

Attention is a function of working memory. Baddeley 18 proposed a model in which

verbal working memory has two components: a subvocal rehearsal system of a phono

logical log accessed by reading words or numbers, and a short-term memory store acti

vated by speech. This “articulatory loop” allows us to retain phone numbers or addresses

for short periods of time. He also demonstrated a nonverbal working memory that he

called a visuospatial scratchpad. Both of these components are greatly dependent on the

multimodal association areas of the frontal lobe and its executive function.

Until recently, we have assigned the basal ganglia to a

simple role in motor behaviors.

Recent work has demonstrated that they also play a key role in cognition, mood, and

behavior. 19 Three circuits have been described that originate in the prefrontal association

and limbic regions of the cortex and interact with specific areas of the basal ganglia. These

areas of the frontal cortex are frequently the ones implicated in the deficits and behaviors

seen in the traumatically brain-injured individual in the rehabilitation setting.

The first circuit is the dorsolateral prefrontal circuit (Figure 10.5) and this is the one

frequently characterized by the term director of executive functions. It is the one most closely

corresponding to the “articulatory loop” described by Baddeley 18 that is important for

working memory. The circuit begins in the prefrontal cortex, projects to the basal ganglia,

then to the thalamus, and back to the prefrontal cortex. This circuit undertakes cognitive

tasks such as organizing behavioral responses and using verbal responses in problem

solving.

FIGURE 10.5

Dorsolateral prefrontal circuit. Thalamus Substantia Nigra G Pallidus Prefrontal Brodman 9 and 10 Head of Caudate

The second circuit is the lateral orbitofrontal circuit (Figure 10.6). This circuit begins in

the lateral orbitofrontal cortex, projects to the basal ganglia and to the thalamus, and

returns to the orbitofrontal cortex. This circuit seems to be involved in mediating empa

thetic and socially-appropriate responses. Injury to this area results in the individual being

irritable and failing to respond to social cues.

The third circuit is the anterior cingulate (Figure 10.7). This circuit is distinguished by its

role in motivated behavior, and it may play a role in conveying reinforcing stimuli to

diffuse areas of cortical and subcortical regions. 20 This circuit begins in the anterior cingu

late gyrus on the medial surface of the cerebral cortex and projects to the ventral striatum,

which, in turn, receives inputs from the hippocampus, amygdala, and entorhinal cortices.

From the ventral striatum, the projection goes to other parts of the basal ganglia, then to

the thalamus, and back to the anterior cingulate gyrus. This particular circuit includes

dopamine-containing neurons in the midbrain that have inputs to the basal ganglia. It has

been suggested that these neurons may deliver reward-predictive signals. This circuit may

be deeply involved in procedural learning and, as such, this circuit may be important in

the behavior modification programs in which reinforcement and reward are utilized.

FIGURE 10.6

Lateral orbitofrontal circuit.

FIGURE 10.7

Anterior cingulate circuit. Thalamus Substantia Nigra G Pallidus Lateral Orbitofrontal Cortex Ventromedial Caudate Cingulate Gyrus Thalamus Amygdala Entorhinal Cortex Hippocampus Substantia Nigra G Pallidus Ventral Striatum

Multimodal Rehabilitation

Multimodal rehabilitation refers to a therapeutic approach that attempts to address the

individual as a whole person. This places a responsibility on the rehabilitative team to

address all of the rehabilitative possibilities. The process must address the physical aspects

of movement and awareness of the environment as well as the cognitive, behavioral, social,

and psychological aspects of the individual.

We have just discussed the role of the multimodal association cortices and their role in

learning and memory. It was shown that the long-term storage of memories was a function

of the hippocampus distributing the component parts of the memory to the parietal, frontal,

and temporal lobes. In a similar manner, we noted the distribution of the visual pathways

to the multimodal, parietal, and temporal cortices. And the three circuits of the basal

ganglia were related to the limbic and frontal association cortices. Saper, Iversen, and

Frackowiak provided an excellent overview of the association areas of the cerebral cortex

and how these structures form the foundations for the cognitive capabilities of the brain. 21

In each of these descriptions of the related pathway, we mentioned the route through

the thalamus. The thalamus is a central structure of ancient origin. Before the development

of the cerebral cortex, there was a thalamus that performed the functions of integrating

the sensory and motor functions of the organism. It acts as

a gatekeeper for information

that is conveyed to the cerebral cortex. 22 In this role, it is central to the integration of all

the sensory modalities, except olfaction. In addition, it plays a role in the extrapyramidal

motor output from the basal ganglia, as well as the three mentioned basal ganglia-cortical

circuits concerned with cognition, mood, and behavior.

The thalamus is composed of several nuclei that have different roles (Figure 10.8). Some

of the nuclei function for specific sensory modalities such as vision and auditory functions.

Others have a motor integrative function such as pathways to the extrapyramidal tract.

FIGURE 10.8

The major subdivisions of the thalamus. (From Amaral, D.G., The functional organization of perception and

movement, in Principles of Neural Science, 4th ed., Kandel, E.R., Schwartz, J.H., and Jessell, T.M., Eds., Elsevier,

New York, 2000, chap. 18, p. 343. With permission.) Anterior Nuclei Reticular Nucleus 1. Lateral Dorsal Ventrolateral Nuclei: Posterior Nuclei Medial Nuclei 6. Ventral Posterior Lateral Dorsal Column Nuclei Somatosensory Cortex 5. Ventral Posterior Medial 4. Ventral Lateral 3. Ventral Anterior 2. Lateral Posterior Retina Lateral Geniculate Nucleus Visual Cortex Medial Geniculate Nucleus Internal Medullary Lamina Intralaminar Nuclei Midline Nuclei Pulvinar

Then, others are of a diffuse nature to serve the organism’s arousal system. In any case,

it is important for the therapist to remember that the thalamus holds the potential to be

involved in many of the observed deficits of the head-injured person.

Neurogenesis in Adult Humans

The old concept that we are born with all the neurons we will ever have and that some

neurons die off over our lifetime was recently found to be false. This long-held belief was

overturned in an elegant experiment. P. S. Eriksson of Goteborg University, Sweden, and

F. H. Gage of the Salk Institute, San Diego, California, demonstrated that new neurons,

as defined by biological markers, are generated from dividing progenitor cells in the

dentate gyrus of adult humans. 23 Further, they indicated that the human hippocampus

retains its ability to generate neurons throughout life. Exciting prospects and intensive

investigations are under way. Their work was built upon that of Elizabeth Gould who

had demonstrated this phenomenon in macaque monkeys. She has subsequently shown

that some of these new neurons have an apparent transient existence of only nine weeks. 24

This transient existence perhaps holds some promise for utilization for future therapies.

Arsenijevic et al. 2 have demonstrated that there are multipotent precursor cells able to

generate neurons, astrocytes, and oligodendrocytes in the human brain. And, further, that

these precursor cells are widely distributed, having been found in many brain regions

studied, including the temporal and the frontal cortex, the amygdala, the hippocampus,

and the periventricular zone. This work demonstrates a possible new platform to study

adult human neurogenesis and potentially generate neural

cells for transplantation.

The possibility of transplantation and the rehabilitation of the individual in an enriched

environment hold promise for development and recovery of lost functions. The synapto

genesis stimulated by the activity-dependent therapeutic setting should give the cellular

basis of learning we have been discussing a strong chance to bring about the rehabilitative

results we want.

However, these prospects remain speculative, but tantalizing, and will require much

further experimental effort to develop to their potential for rehabilitation.

Constraint-Induced Therapy

More recent has been the discovery of constraint-induced (CI) therapy for stroke victims. 25

This therapy restricts the movements of the undamaged appendage in order to make

maximum use of the appendage that has been impaired. This therapy is not limited to

appendage movement but has been seen to be useful in therapy for language disorders,

such as aphasia. 26 Such restriction of movement to the impaired structure causes changes

in the brain, altering the synapses, and enhancing the neuronal connections. These changes

can take several forms such as the assumption of the function by the same region in the

other hemisphere, or a change in the type of sensory processing from one modality to a

new one, or an enlargement of a functional brain region due to its expanded use. 27

In a like manner, it has been demonstrated that exercise, and not just motor activity, can

produce physical changes in the brain structure. 28 Gõmez-Pinilla has demonstrated in

experimental animals that an increase in challenging exercise activity potentiates the

effects of physical activity on trophic factor induction in the cerebellum, and that the

trophic factor involvement in behavior may provide a molecular basis for the enhanced

cognitive function associated with active lifestyles and may guide development of strat

egies to improve rehabilitation. In addition to the experimental animals, changes that take

place in the human motor cortex have been demonstrated with neuroimaging. 29

This change wrought by the action of the therapist on the impaired person brings about

the positive result of rehabilitation. It is the active interaction of the therapist, client, and

the environment that causes physical changes in the structure of the brain that have formed

the basis of all the therapies ever used. It is only in the last decade or so that we have

been able to demonstrate that these changes are taking place at the level of the neurons.

These changes in the brain tissue have been demonstrated conclusively by the new neu

roimaging technology. 30

Summary

These are exciting times for researchers and rehabilitation specialists alike. The prospect

of new possibilities is incentive to press the frontiers of knowledge. However, it should

be remembered that therapies have worked for years without a clear understanding of

the underlying foundations of the changes wrought on the brain itself. The constant

repetition of the target activity has brought about restoration of function. It is with the

deeper knowledge of the changes in the brain that do occur that insights into new therapies

may develop.

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12

Principles of Cognitive Rehabilitation:

An Integrative Approach

Fofi Constantinidou, Robin D. Thomas, and Phillip J. Best

CONTENTS

Abstract

The cognitive system is comprised of a hierarchy of basic and complex cognitive processes.

Depending on the specific task demands, different levels of processes are recruited for

successful task completion. Brain injury causes a disruption of neuronal systems that may

interfere with the efficiency of the cognitive hierarchies. This chapter presents the neuro

pathological mechanisms that affect basic and complex cognitive systems, current theories

for recovery of function, and the effects of brain injury on attention, learning and memory,

and categorization abilities. Furthermore, this chapter integrates principles of modern

cognitive neuroscience in an innovative manner for the treatment of attention and cate

gorization deficits associated with traumatic brain injury (TBI).

Introduction

The survivor of moderate to severe traumatic brain injury is typically faced with an array

of neurobehavioral challenges. These include attention, memory, and learning difficulties,

information processing impairments, and executive functioning deficits that often hamper

his or her ability to function independently in the home, work, and social settings.

There is little disagreement among researchers and clinicians that cognitive rehabilita

tion should maximize the individual’s level of functioning. However, research has not

determined which specific treatment procedures and methods

are most effective for the

treatment of cognitive deficits associated with TBI. There are several approaches to cog

nitive rehabilitation, including works by Ben-Yishay and Prigatano, 1 and their associates. 2–5

These approaches involve developing hierarchical treatment strategies for the treatment

of basic and complex cognitive systems and, also, helping the individual develop self

awareness and acceptance of changed abilities.

Cognitive retraining falls under two primary categories: restorative and compensatory.

Restorative rehabilitation is based on neuroanatomical and neurophysiological models of

learning. These models suggest that neuronal growth and synaptogenesis result directly

from repeated exposure and repetition of stimulation through experience. 6 Consequently,

cognitive training could potentially lead to the development of new neuronal circuits,

which could cause reorganization of partially damaged systems, reduce cognitive impair

ment, and improve functional ability. While rehabilitation programs typically include each

area of cognitive deficit, tasks that target organizational, attentional processing, problem

solving, and abstract skills may have more lasting effects. 7,8

The compensatory rehabilitation approach operates under the assumption that certain

functions cannot be recovered or restored completely. Therefore, the individual needs to

use certain strategies to improve functional performance

without relying on the restoration

of the damaged neurocognitive systems. 7 The restorative and compensatory approaches

could be used together in rehabilitation in order to maximize performance. 9 For instance,

assisting the individual to develop self-awareness regarding his or her cognitive needs by

the use of systematic strategies could have a restorative effect on planning and on delib

erate cognitive processing abilities. 9

Cognitive theory organizes human cognition into a hierarchy of basic and complex

processes. Basic processes include sensory perception, attention, and memory mechanisms

essential for the execution of complex systems. These basic processes underlie categori

zation, reasoning, problem solving, and abstract thought processes.

Neurobiological research in humans and animals provides support for the cognitive

systems generated by cognitive theory. When these networks are disrupted, the results

are predictable cognitive deficits such as attention, memory, and perceptual problems. The

neuropathology of TBI is complex as it consists of both focal and diffuse, cortical and

subcortical lesions. Therefore, unlike unilateral focal brain damage (e.g., damage resulting

from stroke), the cognitive disruption observed in TBI can be bilateral and extensive. The

challenge of cognitive rehabilitation is to implement effective and efficient treatment

modalities in order to enable the individual to maximize

his or her level of functioning

in the home, educational, and work setting in the face of this diffuse systemic disruption.

The purpose of this chapter is to apply cognitive theory and current findings in cognitive

neuroscience and brain research in order to develop principles of cognitive rehabilitation

following moderate to severe brain injury. The following questions will be addressed:

• What are the neuropathological mechanisms that affect basic and complex cognitive systems following injury?

• How does the brain recover from injury?

• What are the general principles of basic and complex human cognitive systems?

• How does TBI interfere with attention, learning and memory systems, and categorization abilities?

• How can clinicians apply principles of cognitive theory to treat cognitive deficits associated with TBI?

Effects of Brain Injury on Neuronal Function

The most common form of traumatic brain injury is a closed head injury (CHI). The

majority of neuropathologies identified in CHI are the result of forces associated with

movement of the brain within the skull. Upon contact, the individual may sustain a focal

injury (coup or contrecoup) and inertial loading due to acceleration/deceleration forces. 10

The higher the velocity at the time of impact, as in the case of high-speed motor vehicle

accidents, the stronger the inertia forces applied to the skull. The frontal and temporal

lobes of the brain, which include structures involved in attention, categorization, strategy

building, memory, and learning, are often compromised as a result of coup or contrecoup

lesions in CHI. In addition to focal coup and contrecoup lesions, the inertial loading (due

to acceleration or deceleration forces) causes linear and rotational acceleration which

typically coexist or follow each other in CHI 10,11 and may cause greater impairment than

do focal injuries at the site of impact.

Rotational acceleration forces may have more devastating effects than linear forces

because rotational forces lead to greater strain on the axons. The type of strain depends

on the direction of the forces applied to the brain tissue. Specifically, tensile forces pull

axons apart; compressive forces push axons together; and parallel deforming forces lead

to shear strains. 10 Rotational forces may result in focal lesions of midline structures like

the corpus callosum and the dorsolateral quadrants of the midbrain. Mechanical forces

can lead to primary or secondary pathologies, particularly in the deep white matter. 12

However, it appears that the displacement of the brain tissue relative to the skull leads to

more devastating results than the acceleration per se (Viano, as cited in Katz). 10 The strain

rate, according to Viano, is a critical variable. That is, a particular group of axons will

suffer more damage if strained (or displaced) with more intensity and longer duration

than if the same axons were strained at a lower rate of intensity and a shorter amount of

time. The straining of the axon fibers is one mechanism leading to microscopic damage

and, subsequently, to diffuse axonal injury (DAI).

Diffuse Axonal Injury (DAI)

There is a gradient of injury that occurs both at the axonal level and grossly at the

distribution of DAI. The distribution of DAI follows a gradient from peripheral hemi

spheres to deeper parts of the cerebrum in more severe injuries. In more severe injuries,

the corpus callosum and dorsolateral midbrain also tend to be involved, often associated

with macroscopic hemorrhages. “The clinical effects of DAI are directly related to the

amount and density of DAI. In other words, the same pathology is seen in mild injuries

as in more severe, just less of it” 10 (p. 4). Axonal damage may be reversible or completely

irreversible. Part of the variability is due to the fact that some phenomena are not as

immediate as once was thought. 13 The early microscopic picture (12 to 24 hours postinjury)

consists of swollen broken ends of axons called retraction balls, and later (days to weeks),

a microglial reaction occurs to “clear the debris.” 10

Studies with animal models, along with human autopsy findings, have been used to

study the pathophysiology of diffuse axonal injury. 13 The animal models simulated stretch

ing or compressing of long tract axons, with maximal stretching or compression at focal

points on the axons’ length. At 12 to 24 hours postinjury,

swollen axoplasmic masses

formed and detached from more distal axonal segments.

Not all axonal swellings result into retraction balls. In an experimental mild to moderate

brain injury with cats, some of the swellings showed numerous reactive neuritic sprouts

in the brainstem area. 14 By the end of the first month, some of these swellings degenerated

and some continued to mature. Some of these neuritic outgrowths were reorganized to

course into the parenchyma (where myelin was absent) or course parallel to distended

myelin sheath. The exact nature of the reactive axonal changes is unknown, but since the

effects are delayed, future research might determine how to prevent certain axonal

changes. The delayed autodestructive cellular phenomena have been linked to surges of

the excitatory neurotransmitter glutamate, especially at N-methyl-D-Aspartate (NMDA)

receptors. These intracellular surges impede neuronal function. Areas of the brain with

large numbers of NMDA receptors, such as the hippocampus, are very vulnerable to the

aforementioned autotoxic changes. 10

In the second and third month postinjury, there is great variability in the regenerative

responses of animals. Some new sprouting originates from the reactive axonal swellings.

The more mature sprouting and growth swellings show further maturation and seem to

gain easy access to the rest of the brain. 14

A large array of processes can occur following damage to the brain which may be

extensive and result in dramatic changes in behavior and cognition. Some of these pro

cesses occur also during normal development, and some are evident in healthy individuals

following experiences that produce learning and memory. 15 When dramatic changes in

behavior or cognition occur following head trauma, it is normally assumed that some

neurons in the brain have been damaged and/or some axons have been severed. Other

cells in the “penumbra” have also been damaged. Immediately following the injury,

phagocytes infiltrate the area and dispose of the nonfunctioning tissue. Frequently, glial

cells will then infiltrate the area vacated by the dead neurons. They either provide nutrients

for regenerating axons or form scar tissue that will retard functional reconnection between

remaining cells.

The long-term outcomes of regenerative processes need to be investigated further, as

well as the generalizability of the findings to more severe injuries and to humans.

Furthermore, the relationship between regenerative processes and neurobehavioral out

comes is of particular importance, as well as the identification of growth factors to

enhance the processes.

Metabolic Dysfunction

Neurons and cells that are undamaged by the initial injury are, nevertheless, vulnerable

to later damage. Even persons with mild brain injury are extremely sensitive to slight

changes in cerebral blood flow (CBF), increases in intracranial pressure, and apnea. The

exact mechanism of this injury-induced vulnerability is not fully understood. However,

it has become a major concern in brain injury management as it can lead to further tissue

damage and contribute more extensively to the neurobehavioral outcomes following TBI

than the initial neurological damage. 16,17

This vulnerable state following injury is thought to be a result of interactive neurochem

ical and metabolic cascade following injury and consisting of several mechanisms that are

described in experimental and human brain injury:

• A massive release of the excitatory neurotransmitter glutamate leads to excitotoxicity and also to an increase in glucose metabolism (hyperglycolysis). The temporal lobe and hippocampal areas are particularly vulnerable to the glutamate surges. 14,18

• Ionic fluctuations increase levels of extracellular potassium (K +). The increase in K + activates the ATP-dependent sodium-potassium pumps and results in considerable metabolic stress and, possibly, hyperglycolysis.

• Elevation in extracellular calcium (Ca ++) has been shown to increase vasoconstriction, which may account for the reduction in CBF and may also activate destructive lipases and proteases. 18,19

• Production of reactive forms of oxygen species causes damage via the induction of lipid and oxygen oxidation.

• Loss of autoregulation, as evidenced by increased demand for glucose (hyperglycolysis) lasting from immediately after and up to 1 week following the injury 18,20 and a reduction in CBF.

• The acute period of hyperglycolysis is followed by a period of metabolic depression that lasts for up to 10 days in experimental TBI. 20 During this period of time, there is a decrease in protein synthesis and oxidative metabolism, which suggests that the glycolysis is not the only metabolic pathway affected in brain injury.

Brain Reorganization and Sprouting Following Injury

In the central nervous system, when neurons are killed or when axons are damaged, the

axon terminals of those cells will degenerate, thus vacating synaptic contacts on postsyn

aptic neurons. The postsynaptic cell will die if enough of its presynaptic contacts are

vacated. If the postsynaptic cell survives, its soma and/or dendrites will have vacant

locations where presynaptic degeneration has occurred. At this point, a number of possible

events can occur that can result in recovery of function. The damaged axons can regenerate

and form new terminals on the cells they previously innervated, or axons from other

neurons can sprout new terminals that form synapses at the vacant locations on the

postsynaptic neuron. This sprouting constitutes a reorganization of the connections among

the surviving brain structures and can serve as a major impetus for recovery of function.

All sprouting is not, however, necessarily adaptive. It is possible for the newly sprouted

connections to result in maladaptive behaviors. 21

The reorganization of the brain by axon terminal sprouting is not unique to the after

math of neuron death in the brain. It occurs naturally in the healthy brain continually

during development and later in life. During development, axon terminals compete for

positions on various somata or dendrites of neurons. Similarly, when an otherwise healthy

neuron loses synaptic contacts on its soma or dendrites, a variety of different afferent

cells will compete for the vacant areas on its surface. The nature of the connectivity of

the “recovered” brain should be very dependent upon the particular pattern of new

synapses that form.

During development, it is clear that the patterns of connections that form and prevail

are severely impacted by the nature of the organism’s experience. For years, it has been

known that there are gross differences in brain structure as a result of different expe

riences. Later studies have shown that the structure of individual neurons in the neo

cortex is dramatically affected by experience. A good example is shown in the studies

of the brains of animals raised in enriched vs. impoverished environments. Animals

raised in an enriched environment have neurons with richer dendrite trees, containing

a larger number of higher order dendritic branches and more synaptic contacts. These

observations were first made in young animals but have been shown to occur in adult

animals as well. In fact, the richness of the connections of various neocortical cells will

rise and fall in very short intervals with changes in inputs to those cells. 22 The particular

pattern of new connections following brain damage should also be dramatically affected

by the experience of the individual during recovery following the lesion. And some

patterns may prove to be detrimental to the organism. The issue for rehabilitative

therapy is to determine the patterns of experience that best optimize posttraumatic

performance.

One of the most frequently used procedures to study synaptic plasticity examines

the effects of repeated stimulation of the presynaptic cell on the excitability of the

postsynaptic neuron. Depending on the parameters of the repeated stimulation, such

stimulation frequently results in “potentiation” or “depression” of synaptic efficacy.

Earlier studies revealed changes in the excitability of the postsynaptic neuron last for

minutes, called short-term potentiation or short-term depression. However, later studies

revealed that, at certain synapses, such changes could persist for longer periods of

time, in some cases, for many days. Changes in synaptic efficacy that are seen follow

ing long-term potentiation and depression can result from an increase or decrease in

the amount of neurotransmitter released from the presynaptic terminal, an increase

or decrease in the number of active postsynaptic receptors, the sprouting of new

synapses, the pairing down of existing synapses, or changes in the structure of existing

synapses, such as changes in the size or shape of dendritic spines or modification of

the synaptic cleft.

At present, theories of the changes in cell interaction induced by experience or recovery

following brain damage focus on changes in the properties of existing synapses or the

sprouting of new synapses between cells that already have direct synaptic contact. How

ever, during development, changes in brain function and organization are attributed to

the formation of new synapses between cells that did not previously interact. Clearly,

before Purkinje cells exist in the cerebellum, there can be no synapses between climbing

fibers or granule cell parallel fibers onto Purkinje cells. Obviously, the birth of new

neurons that form functional synapses with other neurons requires one to address the

issue that synapses must be forming between cells that previously had not interacted.

In spite of the remarkable degree of behavioral and cognitive changes that accompany

adult learning and memory, or recovery of function, most cellular models of neural

plasticity do not consider these changes to be accompanied by synaptogenesis between

previously noncommunicating neurons. The theories generally assume that the new syn

apses that are formed during learning or recovery only strengthen (or weaken) commu

nication between already communicating neurons. This position has not been challenged

because of the dogma that no new neurons are formed in the adult brain.

Exciting experiments in the past few years have demonstrated that new neurons

continually form in the brain of adult animals, including humans. New neurons were

first found in the brains of adult songbirds, in areas of the brain associated with song

production. Then, new granule cells were found in the hippocampus of adult chicka

dees, then in rats and primates. 23 The same pattern of neuronal generation has been

found in the hippocampus of adult humans. 24 Recently, in monkeys, new neurons were

found to be migrating to the neocortex from stem cells in the region of the ventricles. 25

These new results have very important implications for our understanding of the

mechanisms of neural plasticity in general and recovery of function following brain

lesions in particular.

In summary, the aforementioned effects of cell injury and metabolic dysfunction con

tribute to the morbidity and severity of neurobehavioral outcomes. As the metabolic

balance returns to premorbid levels and neuronal reorganization takes place, the individ

ual’s clinical picture begins to evolve and the long-lasting effects of the injury become

evident. The following section will present general principles of cognitive theory and the

effect of injury on those systems.

General Principles of Cognitive Systems

Perhaps the most influential guiding principle of modern cognitive neuroscience is the

concept of modularity. Early in the history of cognitive psychology, modularity referred

to the strong claim that specific faculties could be completely delineated into separate

neural areas. 26 This very rigid view of local representation of function was contrasted with

the neo-Lashley hypothesis that computation is distributed across large neural populations

and that whole patterns of neural activity, modeled in devices referred to as neural networks

or parallel distributed processing systems, constituted states of cognition. 27 When taken to the

extreme, the distributed processing approach spawned a model of brain function that was

holographic in nature. 28 The truth, not surprisingly, lies somewhere in between these two

endpoints, and today, most cognitive neuroscientists adopt a “weak” modularity frame

work to describe cognitive processing in the brain. Weak modularity holds that the simple

computations and their underlying neural substrates are relatively localized and loosely

autonomous. 29 Responses of neurons within these systems are tuned to specific character

istics in the environment but that tuning is broad (i.e., the response of the cell falls off

gracefully when the stimulus departs from the cell’s preferred stimulus). 30 Complex cog

nitive activities are accomplished by the coordination and communication among these

more specialized modules. Basic processing principles governing how processing takes

place appear to hold across systems and these principles may be formulated in terms of

computational styles or strategies. That is, cognitive activities spanning a variety of tasks

may be rule-governed, similarity-governed, or, through extensive experience or preexist

ing propensities, be automatically accomplished. Characteristics of the environment, the

task demands, and the individual all play into which processing strategies and systems

are utilized.

The implication of this framework for cognitive psychology has been to redirect

research to identifying and characterizing functional systems and their basic components.

In addition, investigators now also search for basic processing principles and hold across

different functional systems that may dictate how different situations lead the brain to

recruit different processing strategies. Methodologies from both traditional cognitive

psychology (involving behavioral measures of accuracy and response times) and modern

cognitive neuroscience (utilizing brain imaging and lesion/damage dissociation logic)

have been brought together in identifying major systems and their processing character

istics. The following sections review the basic cognitive systems (executive function and

attention, memory, and language). Each of these may be broken down into even smaller

functional units as well. Examples of their coordinated deployment in higher cognitive

tasks will be described to highlight the interactive processing so central to the weak

modularity hypothesis.

Domains of Cognition

Attention

Clinicians and researchers have used a variety of tasks to assess attentional processes.

Unfortunately, some of the tasks can be easily contaminated by heavy requirements on

memory, verbal, math, and motor abilities in addition to attentional mechanisms. Conse

quently, it is important that the measures used to assess attention mechanisms do just

that. Posner 31 identifies three qualitatively different anatomical and functional attention

networks that are distinct from other cognitive systems: the orienting network, the exec

utive network, and the arousal or alerting network. The existence of these three systems

illustrates the principle of modularity that is central to the cognitive neuroscience

approach; they can operate independently and be selectively influenced (e.g., impaired)

but are usually coordinated in complex cognitive tasks. Also, each system individually

expresses modularity in that each can be further decomposed into distinct computations

subserved by distinct neural substrates.

Orienting Network

The goal of this system is to guide the sensory organs to

relevant locations within the

environment so that processing of information in those locations is enhanced. In vision,

attentional orienting is closely tied to shifting the gaze of the eyes to that part of the visual

field containing stimuli to which the organism must respond. The shift of attention,

however, can be dissociated from the movement of the eyes per se, in that processing of

items in to-be-attended or cued locations has been shown to be facilitated, even when the

eyes do not move or when the items are no longer present in the visual field by the time

the eyes reach their location if they do move. 31 The areas in the brain responsible for

covertly orienting attention in vision (i.e., without eye movements) include the posterior

parietal lobe, the superior colliculus (and possibly other areas of the midbrain), and the

pulvinar. The current model suggests that the parietal lobe disengages attention from its

current focus following which the superior colliculus moves attention to the new location.

The pulvinar then enhances processing at that location. 32 Damage to any one of these

structures leads to deficits in their respective functions. One deficit, termed visual neglect,

is characterized by the inability to attend to parts of visual space contralateral to the

damage (especially, if the damage is located in the right hemisphere). The specific problem

is an inability to disengage focal attention from currently attended targets so that it can

be moved to somewhere else. This failure is attentional in nature (rather than perceptual)

as it can be revealed in tasks requiring the participant to imagine, rather than actually

perceive, scenes from different perspectives. 33

Neglect often resolves into a condition known as extinction in which the individual is

unable to perceive or respond to an object in the visual field that is contralateral to the

damage only when another object is simultaneously present in the opposite visual field

(i.e., on the same side as or ipsilateral to the lesion). It is as if the object has been

extinguished, hence leading to its name. One question that has dominated research on

extinction is to what extent, if any, is the unnoticed stimulus processed? Initially, it was

believed that no perceptual processing of the neglected object took place, a view similar

to the early-selection theories of attention in general. Recently, research has revealed that

a remarkable amount of detail regarding the neglected object is available in the perceptual

system, including semantic information, and that the failure is that this information does

not reach conscious awareness. Volpe, LeDoux, and Gazzaniga 34 and Farah, Monheit, and

Wallace 35 demonstrated that injured individuals could determine whether a stimulus in

the contralateral field was the same or different as a stimulus in the intact, ipsilateral field

though they could not identify the former. This implicit processing has also been demon

strated in a number of studies, 36 including those examining the effects of similarity on the

strength of extinction and in priming studies similar to those used to study memory. In

the former, extinction is found to be greater when the intact object is highly similar to the

neglected object and this accuracy improves with decreasing similarity. Ladavas, Paladini,

and Cubelli 37 asked a person with right-hemisphere damage to identify words, such as

“nurse,” presented in the intact (ipsilateral) field that were sometimes preceded by a

semantically related prime, such as “doctor,” briefly flashed in the neglected field. They

found performance better than when the target was not preceded by a related prime.

Clearly, then, some semantic processing of the neglected word occurred, enough to influ

ence processing of the target word (in the ipsilateral field). In spite of this priming, the

individual was unable to detect, read aloud, or make judgments regarding the lexical

status and meaning of the word presented in the neglected field.

Executive Network

Governing the bulk of cognitive processing, at least that which is consciously available, is

the executive system, also referred to as the central executive in working memory (see text on

working memory), 38 the anterior attentional network, 39 and controlled-processes of short-term

memory (as opposed to automatic processes). 40,41 This system is largely responsible for

activating a dynamic mental representation of the current situation, ensuring that impor

tant relevant features of that situation are amplified 42 and selecting the most appropriate

response from among a set of competing alternatives. To work properly, the executive

network must be flexible enough to switch attention to different aspects of the situation

or change response selection strategies as environmental events change. This system is

limited in that there is difficulty in attending to several mental events simultaneously. This

limitation goes beyond the interference in attending to multiple aspects of a stimulus due

to shared processing pathways in the perceptual system. This capacity varies among and

within individuals at different times. Factors such as age, mood, fatigue, and arousal

contribute significantly to an individual’s effectiveness with controlled operations. 43,44

Not all cognitive processing requires the effortful attention of the executive network.

Automatic operations place minimal demands upon the executive system’s limited pro

cessing capacity and can take place in parallel with other cognitive activities. These

processes are distinct from the controlled operations of executive function and, hence, are

considered preattentive or nonattentional. Automatic processes can be hardwired, such

as the easy perceptual event of detecting a loud sound, flash of light, or change in color.

They can also develop through extensive practice as in the case of reading (for literate

individuals). With normal brain functioning and practice, action sequences become

increasingly autonomous at the subcortical level, and the management role of the executive

system diminishes. Traumatic brain injury can cause diffuse cortical and subcortical lesions

in the brain and may interrupt the efficient and automatic activation of neural pathways

and routines. Activities, which previously required little or no effort, may require delib

erate control and effort, resulting in reduced efficiency. 44 It also appears that injured

individuals with right frontal lobe lesions fare worse than injured individuals with left

frontal and posterior lesions. 45,46

Damage specific to the frontal lobes disrupts executive functioning as this brain region

is thought to subserve it. 5,47 Patients with frontal lobe lesions often exhibit perseveration,

or a difficulty in changing behavior in the short run. Neuropsychological tests of frontal

dysfunction, such as the Wisconsin Card Sorting Test (WCST), are designed to reveal this

specific deficit. Patients learn a series of category structures that can be described as

differing along a single critical dimension (e.g., color, shape, or numerosity). During the

test, the rule that best separates the categories is switched so that learners will have to

abandon the old rule in order to learn the new one. Individuals with damage to the frontal

cortex cannot perform this necessary switch; the old rule cannot be inhibited so that the

new one can be selected.

A relatively famous example of failure of executive inhibition found in normal func

tioning individuals is the classic Stroop effect. 48 A typical Stroop task requires an observer

to identify the color of ink that is used in the printing of various words, which are,

themselves, color names. Performance in this color-naming task is severely diminished

relative to performance using noncolor nouns. The automatic process of reading the words

is difficult to inhibit, thus leading to response interference in the color naming. Persever

ation and inability of inhibition of competing responses can interfere with activities of

daily living. As part of cognitive treatment, structured therapy tasks as well as activities

that foster social awareness should and must be incorporated to improve self-regulation

and self-inhibition and reduce perseverative responses.

Alerting Network

The ability to maintain a state of alertness or arousal is, phylogenically, the earliest of

attentional systems. In humans, it is studied by requiring observers to monitor the envi

ronment for an extensive period of time for the occurrence of a low probability event.

Sustained attention involves the right frontal areas of the brain as well as the midbrain

areas associated with the cortical distribution of norepinephrine, the main neurotransmit

ter required for alertness. Traumatically brain-injured

individuals who also sustain right

frontal damage have difficulty in sustained attention tasks. Robertson et al. 49 looked at a

sustained attention to response target task in brain-injured subjects compared to controls.

The authors found that individuals with TBI showed a significantly reduced tendency to

slow down their responding after an error when compared to controls and had greater

variability in response times. In addition, Robertson et al. found that variance on the

sustained attention to response target task strongly correlated with informant report of

daily life attentional failures in the TBI group.

In summary, following TBI, increased attention requirements result in increased fatigue

and errors, much more so than in the noninjured population. Injured individuals may

experience inability to maintain attention and discriminate in the presence of distractors

(e.g., vigilance) as well as difficulty in shifting between targets. Inconsistencies in func

tioning may leave individuals with TBI with a sense of vulnerability to circumstances that

they do not understand and cannot control. Clinical assessment will often reveal patterns

in functional inconsistencies that have reliable relationships to particular personal condi

tions such as fatigue, pain, distractions, and excessive demands. 44

Cognitive rehabilitation of attentional processes attempts to recognize and control poten

tially adverse personal and environmental conditions and

ultimately trains the individual

to become more resistive to distracting situations. People with TBI could be trained to

recognize particular situations which may affect their performance and can learn to seek

out environments that are more conducive to productivity. In addition to awareness train

ing, another component of attention training is rehearsal. It has been observed that, with

practice, the effort and attentional control required for a task will decrease as the task

becomes more automatic and efficient. 44 Therefore, it is important to train a person to

perform functional tasks, rehearse them in order to improve accuracy and efficiency, and

decrease the amount of mental effort. Attention retraining should also challenge the indi

vidual by systematically increasing the level of distractors to simulate real-life demands.

In their attention process training (APT) program, a component of a hierarchically orga

nized process specific approach to cognitive retraining, Sohlberg and Mateer 50 begin with

sustained attention tasks. The APT program progresses, hierarchically, from sustained atten

tion to selective, alternating, and divided attention activities. Attention training has report

edly resulted in improved memory performance following TBI. 50 The reader is referred to

Sohlberg and Mateer 5,50,51 for further information regarding this training program.

Memory Processes

Our current understanding of memory suggests that it is

organized with respect to both

time and contents. 52 On the basis of behavioral evidence 53,54 and neuropsychological data, 55

the distinction between a short-term and a long-term retention system was the first to be

made. 40 Initially, the nature of the information handled within these time-delineated sys

tems was thought to be unitary, but a variety of neuropsychological and behavioral

findings argued for a content-based subdivision as well (see Schacter and Tulving 56 for a

review). We present this organization here and discuss its implications for cognitive

rehabilitation following TBI. It should be emphasized that the concept of system organi

zation needs to be supplemented with considerations of memory processes operating

across all subsystems such as encoding and retrieval. 57 The executive network described

earlier in the context of attention is deeply involved in these active memory-related

processes. Hence, any disruption to the frontal lobes underlying executive function will

produce impairments in memory tasks in addition to attention tasks as described in the

previous section on attention. Table 12.1 lays out the current view of the organization of

memory in the human (and, possibly, mammalian) brain.

Short-Term/Working Memory

When information arrives via the sense organs (i.e., perceptually encoded) it is deposited

into an immediate working memory system that is divided into three subsystems special

ized for different functions: 58 a control system — the executive network of attention and

two slave systems, each handling different types of information. Visual (e.g., color and

shape) and spatial (i.e., location) information is held and manipulated in a visuospatial

sketchpad. Cortical areas that are involved in visual perception (the occipital lobe) and

spatial orienting (the parietal areas, especially the right parietal lobe) subserve the oper

ations of this sketchpad. 59,60 Sounds, especially auditory speech sounds, are stored and

processed by the phonological or articulatory loop, a term that emphasizes its prototypical

activity of recycling acoustic information to keep it in conscious awareness. Studies of the

capacity of working memory often use a task in which a sequence of items (e.g., letters

or digits) is presented to a subject who must reproduce them immediately from memory

in order. The length of the longest sequence (in terms of number of digits/letters) correctly

produced (termed the letter or digit span) is an index of the size of short-term memory,

which some believe is correlated with IQ measures of intelligence. 61 However, others

suggest that this span reflects the capacity of the phonological loop rather than the entire

working memory system and the role of the phonological loop in general cognitive

function has been called into question. 62 The loop appears to be necessary, however, for

language acquisition, either the early childhood learning

of a native language 63 or in adult

learning of foreign languages. 64,65

Long-Term Memory

Some incoming information undergoes the process known as consolidation which results

in it being stored in various long-term retention systems. The different routes to storage,

together with the distinctions among the kinds of information permanently stored, define

the various hierarchical subsystems of long-term memory. At the top level of the taxonomy

adopted by many cognitive neuroscientists 56,66 is the divide between information which

can be consciously declared to have been learned or experienced (explicit memory) and

information whose learning is only reflected by changes in future behavior as a result of

the prior experience without conscious remembrance (implicit memory). The kinds of

TABLE 12.1

Memory Systems in the Human Brain

System Subsystems Divisions Function Brain Structures

Working

memory Central executive Control Frontal lobes
Visuo-spatial sketchpad Hold visual information
Occipital/parietal Phonological loop Hold acoustic
information Left temporal/parietal

Long-term Explicit Semantic General facts Temporal Episodic
Autobiographical experiences Medial temporal
(hippocampus) diencephalon Implicit Procedural Motor and
cognitive skill Basal ganglia/motor cortex Perceptual
representation Priming/perceptual encoding Sensory cortex
Simple associative/ Classical conditioning General,
throughout CNS; cerebellum

Note: The term working memory has different meanings in different literatures. For example, in animal learning research, working memory describes tasks in which the capacity to hold information across trials within a test session is necessary for performance as in a radial maze navigation task. 142 Baddeley 62 argues that the concept of working memory in this literature probably involves long-term memory as is conceived in human memory research. Yet another approach to the short-term vs. long-term distinction argues that short-term, or working memory, refers to traces that are lost if consolidation via the medial temporal lobe system is prevented due to injury or insult. 69 The time scale for this (on the order of 30 to 40 min) is much longer than the very brief duration of short-term memory (on the order of seconds) 54 as considered in cognitive psychology. Within the consolidation point-of-view, a memory is short-term if its availability still involves the hippocampus, and it becomes long-term as permanent corticocortical connections are formed.

items deemed declarative include general knowledge or facts about the world termed

semantic memory, and personal, autobiographical recollection of experiences, termed epi

sodic memory. The exact locus of stored memories is not known 67 but it has been suggested

that various cortical sites involved in perception may hold perceptual memories regarding

events whereas general factual knowledge is likely to be represented, at least, in the

temporal cortex. 47

Both semantic and episodic memories are thought to require a functioning medial

temporal lobe system (hippocampus, amygdala, and adjacent cortex, but especially the

hippocampus) for their learning. 66,68 Individuals with medial-temporal lesions typically

show very little retrograde amnesia; they have excellent memory for most of the experi

ences that they have had prior to the brain injury, with the exception of events immediately

preceding insult, perhaps due to their lack of consolidation. However, these individuals

show profound anterograde amnesia in that they cannot recall new events that they

experience after the lesion. They perform poorly on the standard measures of declarative

memory such as recognition and recall of previously studied material. The subject can

recall a new experience for a few seconds before it fades, reflecting an intact working

memory. The role of the medial temporal system appears to be one of storage or consol

idation of short-term memories rather than one of retrieval, given that amnesiacs can

retrieve remote memories with little difficulty.

Explicit memories are not only vulnerable to disruption following medial temporal brain

lesions and TBI, but are relatively vulnerable in healthy individuals, and episodic mem

ories are typically more vulnerable than semantic memories. Most people could not

remember the event during which they learned that Tokyo was the capital of Japan. While

semantic or factual memory appears to be strengthened with repeated exposure, especially

in the presence of interfering or distracting information, episodic memory, by its nature,

cannot undergo repeated exposure. It appears that most episodic memories fade unless

they include, or are accompanied by, some emotionally significant experience. 69 Recent

evidence actually suggests that semantic memory may not require an undamaged hip

pocampus while episodic memories do. Vargha-Khadem et al. 70 describe three individuals

with childhood hippocampal pathology who were able to perform normally in schoolwork

and attain average levels of competence, in fact-knowledge and language development,

yet they could not recall their daily experiences. Tulving et al. 71a discuss a case study of

an individual after a traumatic brain injury who experienced a total loss of episodic

memory, both retrograde and anterograde, yet maintained an intact semantic memory

system, as well as other forms of implicit memory. In the future, if more observations such

as these occur, semantic memory may be reclassified as a kind of implicit memory that

neither requires the conscious recollection of the learning event nor an intact medial

temporal lobe system for its operation.

Implicit memory consists of a heterogeneous collection of various kinds of memory

preserved in the loss of declarative memory ability. These systems are quite distinct from

one another and rely on entirely different brain structures. The development of procedural

memory is independent of the hippocampal formation but appears to depend on the basal

ganglia, especially the caudate nucleus. 71,72 Procedural memory is typically divided into

two major subtypes, which, on the surface, appear to be quite different, but appear to

depend on the integrity of similar brain systems. One of the major categories is motor skill

memory; the other is cognitive skill or reference memory. If an individual learned how to ride

a unicycle today, and her episodic memory is intact, tomorrow she will report having

remembered the experience. However, even if she has no explicit memory of the experi

ence (due to hippocampal damage), she will show intact motor skill memory as mani

fested by improved performance on unicycle riding. Subjects with lesions invading the

motor and premotor areas of the neocortex frequently display difficulty in motor skill

learning. Yet, if their hippocampi are intact, they will recall the experience of attempting

to ride the unicycle.

Reference or cognitive skill memory, the memory of the procedures that are necessary

to win a game or solve a problem, including some kinds of category learning (see text on

categorization), constitutes the second kind of procedural memory. This form of memory

does not refer to explicit declarative memory for the rules of the game, but refers to the

acquisition of successful strategies. An individual with medial temporal lobe lesions could

improve his/her skill at board games such as checkers without recalling that he/she had

ever played the game before. Thus, the solution of some complex cognitive tasks does not

require explicit memory, but rather, repeated exposure to a specific situation and rules for

solutions. Quite possibly, the learned strategies are a collection of observations of cause

and effect that are reinforced according to the principles of operant or instrumental con

ditioning. Consequently, individuals with TBI may benefit from the repetitive nature of

certain activities in cognitive rehabilitation and become more adapted and independent

without necessarily demonstrating improvement in explicit memory tasks. While both

forms of procedural learning involve the basal ganglia, motor skill learning appears to be

dependent on the integrity of the motor areas of the neocortex, including the premotor

strip, and cognitive skill learning appears to be more dependent on sensory cortices in

the parietal and occipital lobes. 71

Another type of implicit memory is revealed in studies of priming phenomena. Priming

refers to the facilitation in the processing, detection, or identification of an item as a

consequence of its prior exposure in tasks not requiring conscious recollection. 73 A classic

priming paradigm involves an initial study of items, such as a list of words, under the

guise of some ruse instructions, which is then followed with a nonmemory task, such as

lexical decision (“Is this letter string a word or nonword?”), word identification (“What

is this word?”), or word-stem completion (“wo_ _”). The typical finding is that lexical

decisions and word identifications occur more quickly or require less stimulus energy to

achieve a given level of performance for words previously seen. In the word-stem com

pletion task, subjects tend to supply words seen from the earlier list to complete the partial

words. 74 That priming is subserved by a different system than explicit memory is dem

onstrated by several observations (though a recent brain imaging study suggests some

involvement of the hippocampus in priming). 75 Individuals with amnesia who fail tradi

tional tests of explicit memory exhibit normal priming, 76–79 individuals with damage to

perceptual areas, such as the occipital lobe, show normal performance on explicit measures

of memory but do not evidence priming, 80 and performance on standard recognition and

recall tasks can be dissociated from priming tasks in normal subjects. 81–84 Priming appears

to be perceptual in nature as any surface change of the stimulus (e.g., font changes for

word stimuli or changes in picture orientation for visual stimuli) from prior exposure to

test can reduce it 85–89 and is mediated by the sensory cortices (visual priming in visual

cortex, auditory priming in auditory cortex, etc.). This system responsible for priming is

referred to as the perceptual representation system in Schacter’s framework 90 and is the

system involved in the initial perception and encoding of a stimulus.

A final category of implicit memory includes simple classical conditioning and associa

tive learning of the sort often studied in animal learning

research. These simple forms of

learning, evidenced even in invertebrates, may reflect principles of neuronal plasticity in

general, such as Hebbian learning or long-term potentiation. However, there is evidence

for the special role of the cerebellum in classical conditioning of discrete motor responses,

such as eye-blinks in the presence of air-puffs. 67 It is unlikely that TBI would disrupt this

form of learning if the individual exhibited any signs of consciousness or had any cognitive

functioning at all. Classical conditioning has been demonstrated in decorticate and decer

ebrate laboratory animals. We mention this type of memory here to provide a complete

picture of what is known regarding memory systems.

The Role of Processes and Strategies in Memory

The above sections describe different categories of memories emphasizing the nature of

the memory content as revealed by dissociations of the effects of variables on performance

using different types of tasks and materials. However, understanding memory perfor

mance requires consideration of the active strategies and processes of encoding and

retrieval involved in, and across, memory systems. Most forms of memory assessment,

especially in clinical neuropsychological contexts, rely heavily on explicit measures 91 as

this type of memory is most characteristic of human cognitive performance and seems to

be most influenced by active memory strategies.

Early cognitive studies of memory formation argued that certain ways of organizing

the to-be-remembered material lead to more durable memory traces. 92 If the individual

elaborated upon the deeper meaning of items, emphasizing connections to already learned

material or involving visual imagery, 93,94 those items would be less subject to forgetting

than items merely rehearsed by being recycled in the phonological loop. This idea has

been exploited in various prescriptions of strategies to improve memory performance in

cognitive rehabilitation. 95–98

This active elaboration clearly places demands on working memory, especially the

executive control component responsible for the planning and sequencing of currently

active mental operations. When subjects with CHI were presented with unclustered words

(word lists that were randomly organized), they did not actively organize this information

according to meaning as did normal subjects, indicating a passive or shallow learning

style. 99 While normal immediate recall is observed in these individuals, suggesting an

intact short-term memory span, the reported passive learning style of some CHI subjects

reflects an inability to successfully move information from working memory to long-term

memory, especially in verbal learning tasks such as the Auditory Verbal Learning Test

(AVLT). 91,99–101 These multitrial tasks provide an opportunity to assess various aspects of

working memory processes involving frontal lobe function in addition to learning. Studies

incorporating these tasks indicate that decreased performance can also be due to retrieving

failures as well, 102 especially if the right frontal areas are damaged. 103

Consolidation, or the transfer of information from working memory to long-term mem

ory, can be disrupted by the appearance of distracting or interfering material 104 as well as

failures to appropriately organize information. Patients suffering from TBI seem to be

most vulnerable to the debilitating effects of interference on consolidation possibly due

to insult to the frontal lobes, especially the left frontal areas 103 or the medial temporal lobe

system. Studies following TBI suggest that immediate recall (measured by tasks that assess

span abilities of working memory) appears to be intact. 105,106 However, when interference

is imposed, memory performance is significantly affected, indicative of difficulties in

consolidating declarative information into long-term memory. 102,106 Interference can be

introduced in the form of a delay or in the form of a competing stimulus. 106 Even a 10

second delay between stimulus presentation and response has been reported to affect

recall performance. 107

The current view of the organization of memory and its processes has been developed,

in part, as a result of focal lesions, both in human and in animals, and their resulting

effects on various memory tasks. Traumatic brain injury, however, rarely causes circum

scribed lesions. As a result, individuals experience a variety of problems along the

information processing continuum, including encoding, consolidation, storage, and

retrieval deficits. 101,108 The severity of the impairment is dependent upon several variables,

including the extent of medial temporal and frontal lobe lesions and severity of diffuse

cortical injuries.

Research suggests that individuals with moderate to severe CHI are able to learn new

information, but at a decreased rate compared to normal subjects. Furthermore, the ability

to recognize information is superior to their free recall skills. 100,102,109 While, as a group,

CHI subjects tend to have a more passive learning style, subgroups of individuals that

apply active memory strategies have been reported. Therefore, these results generate the

following questions regarding memory rehabilitation and research:

- Why do only some subjects with moderate to severe TBI use active strategies?

- Do people with TBI no longer have the ability to use active strategies due to semantic retrieval or association categorization problems?

- Or do they fail to recall using them due to attention and/or memory problems?

- Could it be that these strategies require cognitive effort that, along with the task demands, overloads the already compromised cognitive system and the person finds these strategies too fatiguing and so chooses not to use them?

• Furthermore, if a particular person with TBI cannot use semantic strategies such as association and categorization, would training the person to use these strategies be beneficial and improve encoding and retrieval?

Memory strategies that are reportedly successful with other populations are not always

appropriate in TBI. For instance, visual imagery training for persons with left hemisphere

damage resulting in a specific verbal memory deficit may prove to be a useful memory

aid. 110 On the other hand, in severe CHI, visual imagery was not proven particularly useful,

probably due to the increased mental efforts it requires. 95,111–113 Declarative memory is

typically more affected in TBI than procedural memory. Therefore, teaching domain-specific

memory tasks as they pertain to a given job may be successful. 114,115 However, the applica

tion of that knowledge to novel situations and problems requires declarative knowledge

of strategies, as well as intact executive abilities. 116 These aspects of cognition are impaired

as a result of brain injury. The hierarchical perceptual tasks proposed in this chapter are

designed to enhance both storage and retrieval mechanisms. In addition, external memory

strategies, such as the implementation of a memory notebook, may be beneficial for every

day (or prospective) memory functions, such as remembering important dates and appoint

ments (see Sohlberg and Mateer 5,51 for extensive information on this approach).

Verbal Language

The verbal/logical language system, collectively, is another important system that con

tributes to higher cognitive function. Traumatic brain injury can result in focal damage to

brain structures, such as the medial temporal lobes and the frontal and parietal lobes,

resulting in disruption of the attention, memory, and language systems. Furthermore,

diffuse axonal injury observed in brain injury can result in generalized cognitive disruption

that often affects complex linguistic abilities.

Traditional aphasic syndromes are not often associated with TBI (especially in CHI),

although aphasia may be present during the early stages of the recovery process. Word

finding and lexical retrieval deficits are the most common linguistic deficits associated

with TBI and can persist up to at least a year postinjury. 117,118 Difficulties in discourse

organization and other extralinguistic difficulties are a result of cognitive nonlinguistic

processes that support language. Damage, dysfunction, or disorganization of attention,

memory, categorization, and executive functions can result in linguistic breakdown. The

reader is referred to Fromkin and Rodman 119 and Benson and Ardila 120 for further infor

mation on the major brain areas involved in language functions, their processing charac

teristics, and the effects of brain lesions on language functions.

Categorization

In the hierarchy of cognitive function, complex or “higher”

reasoning activities such as

categorization (including object recognition and perception/action), problem solving, and

decision-making are those that require the coordination of several of the basic systems.

Because of the greater complexity inherent in these higher-level tasks, understanding the

alternative processing strategies and subsystems deployed by the executive system

becomes important for modeling individual performance. When we categorize, we assign

objects or events into groups. This may be done to support other types of activities or

decisions that have to be made. That is, categorization, itself, is a process that serves as a

subcomponent to other higher processes. For example, expert problem-solvers must cat

egorize the situation as a particular kind of problem before solutions are made available.

Modern theories suggest that there are two primary areas of categorization: (1) recognition

and categorization of every day objects and situations and (2) recognition and categori

zation of novel situations and category learning.

Recognition and Categorization of Everyday Objects

The visual recognition and categorization of everyday objects involve two anatomically

and functionally distinct pathways specialized for different kinds of information. As seen

in Figure 12.1, the ventral pathway (through the temporal lobes) subserves passive rec

ognition in which the object is perceived as a kind of thing that the observer has seen

before. This recognition includes all aspects of visual memory such as form, function, the

object’s typical location, and many other associated memories. The dorsal pathway

(through the parietal lobes) mediates visually guided behavior, such as reaching and

grasping of objects and self-locomotion. The dorsal perception-and-action system is under

stood in terms of spatial attention, orienting, and motor control. 47

FIGURE 12.1

Pathways for recognition and categorization of everyday objects. Input from the retina traverses two major

visual pathways in the primate brain. Information supporting visually guided action (e.g., reaching) is routed

through the lateral geniculate nucleus (LGN), the primary visual cortex in the occipital lobe, and on to the

posterior parietal regions (the dorsal pathway). Visual attributes that are necessary for the identification and

recognition of an object and its related properties are processed in the ventral pathway, including the LGN and

the primary visual cortex, ending in inferotemporal cortex.

Deficits in the passive object recognition system due to brain injury lead to dissociations

in categorization ability as a function of the type of stimulus material. Most often, indi

viduals lose the ability to recognize living or animate objects while artifactual recognition

is spared, though the opposite dissociation has been observed. Whether this pattern results

from a semantic (memory) system that is organized along domain-specific modules 121 or

in terms of perceptual and function features 122 is still open to debate. There is clear evidence

in vision of a hierarchical recognition process that begins with early feature processing

(such as orientation, motion, and color) and leads to the processing and representation of

objects and object classes in the inferiotemporal cortex. 123 We propose that cognitive

treatment should incorporate a systematic hierarchical protocol beginning with early

feature identification in order to retrain the passive object recognition system. The tasks

should consist of both animate and inanimate classes of objects in order to account for

the possibility of domain specificity in the representation of visual memories.

Recognition and Categorization of Novel Situations and Category Learning

When people are faced with having to learn to categorize novel objects or situations, current

cognitive theory suggests they may be able to recruit one of three specialized systems for

this purpose. 124 Of these, two are “explicit” in the sense that their processes and outputs

are consciously available to the category learner. The most important of these, the rule

based or rule-governed category system, involves the use of explicit verbalizable rules and

hypothesis testing to determine category membership and, hence, relies heavily on exec

utive functioning for its operation. The other explicit system requires significant episodic

memory in that categorization is accomplished by the recall

of previously experienced

category members, or exemplars that are similar to the present novel object. Exemplar

based categorization very likely draws upon brain structures known to underlie episodic

memory performance, that is, the medial temporal lobe, including the hippocampus.

It has been observed that, even in the case of severe deficits in episodic memory and in

the case of nonverbalizable category rules, individuals can still learn to classify objects. 125,126

An example of the latter kind of category learning problem is the complex pattern recog

nition required in such cases as radiology or sonography in which the category boundaries

are quite fuzzy and the elements in the pattern combine in nonlinear or interactive ways

to specify identity. It is because of these observations, a third category system, an implicit

system, has been proposed. It is currently thought to rely on the structures of the basal

ganglia and involve processes similar to that of procedural motor learning (the reader is

referred to the section on procedural memory). Which system is recruited for a particular

problem is a complex interaction of task characteristics, individual differences, and stage

of learning. 127 One interesting hypothesis is that, in the development of categorization

expertise, often essential in many vocations, a progression occurs from exemplar to rule

based to implicit categorization.

Moderate to severe traumatic brain injury seems to

interfere with the individual's

ability to use attributes to describe objects. In a preliminary study by Constantinidou

and Kreimer, 128 subjects with moderate to severe brain injury provided significantly fewer

attributes to describe common household objects compared to matched noninjured sub

jects. Subjects with brain injury were able to learn a list of eight core attributes such as

color, shape, composition, and weight. Finally, they were able to apply these attributes

to describe another set of common objects more effectively, compared to their spontane

ous description. However, their performance was, at all times, significantly poorer than

that of noninjured subjects. These findings support the need for a systematic rehabilita

tion program to improve the categorization abilities of individuals with moderate to

severe TBI.

Abstract Thought

Reasoning, making decisions, and solving problems are among the highest forms of

cognition, and characterize what we think of as human intelligence. These complex pro

cesses emerge from the interaction of many of the more basic cognitive processes that

have already been described. For example, a current model of expert decision-making

combines the executive network of attention, whose function is to amplify the relevant

features of the current situation, and an implicit categorization process that recognizes the

current situation as similar to one that has been experienced before. Hence, a response or

choice for action is automatically selected based on situation awareness. 129 Judgments of

the probabilities of events are governed by heuristics such as representativeness in which

the likelihood of an event is determined by how typical the event is of the category it

represents. 130 Thus, there is a categorization process involved in making probability judg

ments. Similarly, models of problem-solving rely on selective attention, memory, and

categorization capabilities as crucial components. 131 Consequently, a deficit in any of these

more elemental processes will disturb performance on tasks of higher order thinking.

Directions for Rehabilitation

The cognitive system is comprised of hierarchical processes. Depending on specific task

demands, different levels of processes are recruited for successful task completion. At

infancy, the individual begins with basic concrete abilities such as directing attention to

a given object or person. Infants and young children learn features of objects (such as

color, texture, and shape) in a predictable manner. These skills enhance their ability to

learn categories, discriminate, and make generalizations. 132,133 As the cognitive system

matures, attention capabilities become more sophisticated. Cognitively-intact adults are

able to direct attention, discriminate, shift, and sustain response sets in the presence of

distraction. Brain injury causes a disruption of neuronal systems that interfere with the

efficiency of the cognitive hierarchies. Consequently, postacute cognitive rehabilitation

(CR) should implement systematic hierarchical treatment protocols that target attentional,

memory, categorization, and abstract thinking tasks to restore impaired cognitive pro

cesses. 12,117 A systematic hierarchical approach has been suggested in the brain injury

rehabilitation literature as a means to rehabilitate and reorganize cognitive systems and

restore concept formation and cognitive function. 111,134,135

Where should cognitive rehabilitation begin? One needs to consider that even the most

minimal cognitive act, from input to output, involves recognition and categorization.

Therefore, we propose that postacute CR should implement a hierarchical program begin

ning with basic levels of categorization such as feature identification with the ultimate

goal to target higher processes, such as abstract thought, decision making, and problem

solving. The proposed treatment model integrated principles of cognitive theory and

models of category learning, 136,137 language theory, 132,133 and rehabilitation 12,138 for the

design of hierarchical tasks to treat the two aspects of categorization described above: (1)

recognition and categorization of everyday objects and (2) recognition and categorization

of novel situations and category learning.

As seen in Appendix 12A, the first part of such a program should begin at a very basic

level of concept formation and thought productivity, which includes asking and training

the person to express as many attributes as possible about a common object. The person

progresses through the various levels of the Categorization Program (CP) as he/she

achieves criterion at each level. 139 Each level becomes increasingly demanding, requiring

more cognitive effort. The stimuli begin with concrete objects (in order to minimize

cognitive distance) and progress gradually to abstract ideas. Abstract reasoning, mental

flexibility, and problem-solving abilities are the targets of the higher levels of this system

atic perceptual training program.

The remedial systematic hierarchical approaches are based on the fact that our cognitive

system is comprised of systematic hierarchical components. All of these basic and complex

systems tie together in order for the individual to learn and adapt to the environment.

These approaches are different from external compensatory strategies which are often part

of cognitive rehabilitation programs. The combination of remedial (or restorative) and

compensatory techniques could be used together in order to maximize the individual’s

level of functioning.

Efficacy Research

Efficacy research in the area of cognitive rehabilitation

is a relatively new science, less

than 20 years old. As Malec pointed out, scientific inquiry is a “slow process that frequently

begins with uncontrolled naturalistic observations leading to single-case and other limited

experiments that, in the long term, provide a basis for more sophisticated experimental

designs.” 8, p. 232

While it would be desirable for researchers to apply a strict medical model and imple

ment randomized clinical control trials with this population, ethical and practical consid

erations often interfere with this effort. 111 The lack of tight experimental control in research

with TBI has made it difficult to obtain competitive funds from the National Institutes of

Health (NIH) and other federal sources for CR outcome studies. 8 Some authors support

the use of carefully designed multiple-baseline designs in order to allow clinicians in a

competitive fee-for-service environment to assess their treatment effectiveness. 9 In addi

tion, variables, such as the extent and severity of the injury, time from injury, premorbid

educational levels, age at time of injury, duration and intensity of cognitive interventions,

premorbid psychiatric and substance abuse history, medications, and other confounding

variables need to be addressed and controlled in TBI outcome research as they, reportedly,

could affect recovery.

Results from efficacy research in attention, memory, executive functions, and social skills

following brain injury are in favor of treatment (the reader is referred to Coelho et al. 9 for

a comprehensive review). As outcome research in the area of CR following TBI continues

to grow, researchers need to carefully match their dependent and independent variables.

That is, the research protocol needs to use sensitive measures to measure changes that

directly relate to the hypothesis at hand and to the changes (or behaviors) that the study

intends to measure. Furthermore, both functional measures and formal neuropsycholog

ical measures that are not only sensitive, but also have been validated with the TBI

population need to be incorporated to measure changes as a result of specific treatment.

The most dramatic recovery following brain injury occurs during the first year postinjury,

also known as the spontaneous recovery stage. Efficacy research may want to identify treatment

strategies that enhance recovery during the first year postinjury. It is possible that certain

treatment paradigms may yield different results, depending on the time since injury.

In addition to chronicity, injury severity is another factor that needs to be investigated.

The length of impaired consciousness, the length of posttraumatic amnesia, and the Glas

gow Coma Scale scores have been used to determine injury severity. Research has shown

that cognitive abilities upon admission are a predictor of functional gains and neuropsy

chological performance during rehabilitation, and at 1 year

postinjury. 140,141 Efficacy

research may want to investigate whether certain treatment paradigms yield different

outcomes, depending on the injury severity.

Future research in cognitive rehabilitation following brain injury needs to systematically

investigate the efficacy (i.e., Does cognitive treatment yield better results than no treat

ment?) and efficiency of treatment paradigms (i.e., Is Technique A better than Technique B

in treating this population with X characteristics?). To accomplish this task, researchers

need to carefully implement control groups in order to avoid previous experimental pitfalls.

Conclusions

Children learn new skills by attending, discriminating, categorizing, and acting upon their

environment. The essence of cognitive rehabilitation following brain injury is to teach the

individual new skills, remediate old skills, refine existing abilities, and teach compensatory

strategies in an integrative manner in order to enhance and maximize the individual's

level of functioning. Evidence presented in this chapter from cognitive theory, neurobiol

ogy, psychology, and clinical research support the use of remedial techniques using sys

tematic hierarchical programs. Thus, cognitive retraining should be systematic and

hierarchical in nature and should target basic and complex cognitive systems. In postacute

brain injury rehabilitation, cognitive rehabilitation goals that target attentional, organiza

tional, visual processing, problem solving, and abstract skills may have lasting effects in

people with TBI. 117 The categorization tasks included in the appendix are being used as

examples of how a treatment model might be developed and are not a comprehensive

treatment plan for all cognitive abilities.

Neurobiological research on learning suggests that repetition enhances learning. We

could assert that systematic, hierarchical restorative training as part of a CR program could

facilitate adaptive neuronal sprouting that occurs during spontaneous recovery. Further

more, CR would provide environmental support and stimulation that will facilitate central

nervous system functional reorganization as part of the recovery process.

Successful rehabilitation following brain injury is a complex process. The focus of this

chapter was to apply cognitive theory and neurophysiological principles of learning and

recovery as they relate to the restoration of attention, memory, and perceptual skills

following TBI. However, cognitive rehabilitation is part of the large umbrella of neuro

psychological rehabilitation. As part of that, the person’s psychosocial functioning, self

awareness, and self-acceptance are necessary components for successful rehabilitation.

When all of these processes function in synergy, the outcome is greater than the sum of

its parts, resulting in a well-adapted individual.

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Appendix 12A: The Categorization Program

The Categorization Program (CP) 139 is comprised of two parts and eight levels which are

designed to retrain a series of categorization abilities. Each level in both parts builds on

the skill set trained and applied in the previous level; therefore, a range of concrete to

abstract thinking abilities is targeted. The purpose, specific aspect of categorization trained,

and the ultimate goal of each level are outlined below.

Part A: Object Categorization and Concept Formation

Level 1: Perceptual Feature Identification and Application

The purpose of this section is to train perceptual feature identification, thereby building

a framework for cognitive structures. The retraining of basic categorization abilities will

build the foundation for more abstract functions and will facilitate communication during

word-finding difficulties. The goal is to have the individual learn eight perceptual features

and then consistently apply all the features to describe common objects. Objects are

presented via a range of stimulus types including real objects, color photos, line drawings,

written words, and spoken words.

Level 2: Similarities and Differences

The purpose of this level is to apply the eight perceptual features trained in Level 1 to

compare objects. Identification of similarities and differences between two objects of the

same and of different categories using the eight perceptual features is utilized in order to

train conceptual thinking. The process of applying the trained perceptual features is the

next layer of the continuum of concrete to abstract functional abilities. Stimulus types

include color photos, written words, and spoken words.

Level 3: Functional Categorization

The purpose of this task is to identify functional categories and maintain the delineations

within that category. There are two specific foci in this level which require the consideration

of the features of the objects trained and applied in Levels 1 and 2: the application of

retrieval strategies to generate novel items that belong in a given category and the mental

flexibility required to generate alternate uses for the objects in a given category. This task

enhances functional problem-solving abilities and mental flexibility.

Level 4: Analogies

The purpose of this level is to apply both the categorization abilities trained in Levels 1

to 3 and inductive reasoning skills in order to identify and match the concepts represented

in analogies. The analogies progress from concrete to abstract in order to train word

abstraction. Stimulus materials include multiple-choice responses for each analogy that

will aid in the training process of word abstraction, as needed.

Level 5: Abstract Word Categorization

The purpose of this level is to further develop concept formation and abstract conceptual

thinking. The goal is to identify similarities and differences in abstract verbal concepts.

The generation of similar word pairs using synonyms that represent the relationship

between the words is incorporated to enhance cognitive and linguistic flexibility.

Part B: Category Learning

The exercises in Part B are constructed to examine and train learning rule-based classifi

cation strategies. A core set of five conditions or rules is utilized in Levels 6 to 8. The

conditions, which stem from cognitive psychology, are: affirmative, conjunctive, disjunc

tive, exclusive, and conditional. The stimulus for Part B range from concrete to abstract

and include shapes (Level 1), gauges (Level 2), and written word groups (Level 3). The

goal of Part B is the formulation of the rule that governs the classification of each stimulus

into either Category A or Category B. Errorless learning is implemented as a cueing

technique to counter frustration and aid rule formulation. Ultimately, the tasks in this part

will enhance decision-making and problem solving abilities.

Level 1: Progressive Rule Learning 1

The stimuli for Level 1 of Part B vary along two dimensions: shape and color. The nine

stimuli include squares, circles, and triangles that are red, white, and black. Each stimulus

is presented individually and a formulation of the rule that classifies each stimulus into

either Category A or Category B follows.

Level 2: Progressive Rule Learning 2

The stimuli presentation for Level 2 of Part B are gauges that include two dials which

must be interpreted as a single unit. This level forces generalization into a real-world

situation by simulating the reading of gauges at a power plant. The determination of

operational or not operational for each stimulus is utilized and the cumulative interpre

tation of each judgment leads to the formulation of the rule that classifies the stimuli for

each of the five conditions.

Level 3: Progressive Rule Learning 3

The final explicit rule task contains the same underlying structure as the earlier two levels;

however, this time, a judgment is made using stimuli constructed from dimensions of

language. This further abstracts the rule formulation and forces generalization of training

to a real world situation. The stimuli in this task consist of a summary of three laboratory

tests (lung capacity, heart fluid, bone marrow count) and their orthogonal combination

with two measurement adjectives (low, high). These combinations will lead to the formu

lation of the rule that classifies the stimuli into either Diagnosis A or B for each of the

five conditions. 367

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Cognitive Disorders: Diagnosis and Treatment in the TBI Patient

Mark J. Ashley, Rose Leal, and Zenobia Mehta

CONTENTS

Introduction

Cognitive rehabilitation for people with acquired brain injury first became a clinical focus

in the late 1970s. The sequelae of acquired brain injury were increasingly recognized as

medical science became proficient at life-preserving

practices following severe injury to

the brain. Larger numbers of people survived traumatic and nontraumatic events alike

which resulted in injury to the brain. Rehabilitation services were largely restricted to

those rendered in an acute hospital setting while available discharge settings consisted of

the home, psychiatric hospitals, or skilled nursing facilities. The level of restitution of

physical and communicative deficits achieved was not sufficient to allow for a return of

many of these individuals to independent and productive lifestyles.

The significant limitations of available settings were soon recognized by the private

funding sector which had a long-term financial responsibility for some of these people

owing to the events surrounding their injury. That is, workers' compensation and liability

insurance carriers came to question whether further rehabilitative interventions might be

developed to reduce the level of disability following discharge from acute rehabilitation

hospitalization, thereby reducing the level of assistance for physical and cognitive deficits

that might be required and the costs ascribed thereto.

The field of postacute rehabilitation was born of this time, and with it, investigation

into existing treatment interventions that had been developed for other neurologically

impaired populations which might have applicability to persons with acquired brain

injury. Physical disabilities were identified to be less

disabling than cognitive disabilities

and this remains the case today. Cognitive disabilities continue to impose severe limita

tions on a person's ability to interact meaningfully and independently, as well as in an

age-appropriate fashion within most aspects of society. This is not to diminish the tremen

dous obstacles faced by people with physical disability but rather to point out that societal

accommodation to physical disabilities has been greater to date, while accommodation to

cognitive disabilities is both less prevalent and far more difficult to accomplish.

This chapter addresses cognition from a particular vantage point. Neuroscience has a

very broad concept of cognition. Cognition, as addressed in this chapter, will be more

circumscribed, excluding some areas of cognition which might be encompassed in the

view of the neuroscientist interested in computational modeling and the like. The chapter

reviews some neuroanatomical structures which subserve information processing. The

term information processing is used in a relatively narrow sense in this chapter, referring

predominantly to that information processing which supports so-called "executive func

tion." Cognitive skills and processes are discussed and rehabilitative avenues reviewed

insofar as they are the focus of concern for persons with acquired brain injury.

Cognition

Cognition, in simple terms, refers to conscious mental

activity such as thinking, remem

bering, learning, or using language. Cognition includes “awareness with perception, rea

soning, judgement, intuition, and memory; the mental process by which knowledge is

acquired.” 1 Coelho et al. 2 defined cognition to include such processes as attention, memory,

reasoning, problem solving, and executive functioning (i.e., self-awareness and goal set

ting, planning, self-directing/initiating, self-inhibiting, self-monitoring, self-evaluation,

flexible thinking). Reed and Seale 3 include attention, memory, visual-spatial skills, judg

ment, problem solving, awareness, comprehension, and psychomotor speed.

Cognition can be thought to include an individual’s ability to mentally represent, orga

nize, and manipulate the environment. Cognition is comprised of a group of “processes by

which sensory input is transformed, reduced, elaborated, stored, recovered, and used.” 4

“Among these processes are: attending (alertness, awareness, attention span, selective

attention), recognizing, discriminating among stimuli and identifying similarities and

differences, maintaining the temporal order of stimuli and responses to them, learning

and remembering (including retention span and immediate, recent, and remote memory),

organizing (including categorizing, associating, and/or synthesizing stimuli), compre

hending, thinking, reasoning, and problem solving and … . Essential to the most efficient

use of these processes is an adequately developed knowledge base (including general infor

mation, linguistic knowledge, academic skills, knowledge of social rules and roles, and

much more …). Cognition also includes the use of these processes to (1) make decisions

as to the most appropriate and functional ways of interacting with the environment, (2)

execute those decisions, (3) monitor responses to determine the appropriateness and

accuracy of those decisions, and (4) adjust behavior if it is determined to be inappropriate

and/or inaccurate." 5 A dimension of self-regulation of functional behavior is emphasized

in the definition of cognition in order to promote a treatment focus on functional goals

during cognitive interventions. 5

Cognition entails specific skill sets (e.g., the ability to maintain a focus of attention)

which, combined, form processes (learning, remembering, planning, problem solving).

Interventions designed to improve overall cognitive function must, therefore, address

both specific skill sets and processes. Since many cognitive skills combine to form pro

cesses of cognition, a review of the definitions above provides insight into the breadth

and complexity of cognitive skills and processes. The American Congress of Rehabilita

tion Medicine 6 and the American Speech-Language-Hearing Association 5 guidelines com

bined provide the most comprehensive analysis of cognitive skills and processes. These

include “attention,” “alertness,” “awareness,” “attention span,” “selective attention,”

“stimuli recognition,” “stimuli discrimination,” “maintenance of the temporal order of

stimuli,” “learning,” “retention,” “memory,” “organizing,” “categorizing,” “association,”

“synthesis of information,” “comprehension,” “thinking,” “problem solving,” “decision

making,” “planning,” “insight,” “reasoning,” “learning ability,” “maintenance of sequen

tial goal-directed behavior with self-correction of responses,” and “emotionality.”

Tulving pointed to the componential and hierarchical nature of memory. 7 Neuroscience

tends to support the view of a highly interrelated and integrated system of cognitive

function being subserved by the basic physiology. Amaral states: “A general principle of

brain information processing is that it is carried out in a hierarchical fashion. Stimulus

information is conveyed through a succession of subcortical and then cortical regions.” 8

Tulving’s concept of a hierarchical structure to memory systems included the idea that

interventions that impacted a system at any particular level would necessarily impact the

system as a whole. The hierarchical and interrelated nature of proposed memory systems,

together with the underlying neuroanatomical and neurophysiological substrates, become

important in determining an approach to designing interventions for memory system

problems following traumatic brain injury (TBI).

Restoration of physical function following TBI is, arguably, the most obvious form of

recovery of function. Observation of progression from one level of physical function to a

developmentally higher and more complex level is easily accomplished. Physical thera

pists have come to rely upon the integration of developmental principles in therapeutic

approaches such as neurodevelopmental therapy (NDT). 9–11 These techniques are predi

cated upon the premise that developmental order should be respected in the design and

implementation of therapeutic activities for recovery of physical function. Some physical

manifestations of TBI include a regression to more primitive movement patterns. NDT

techniques seek to apply training to facilitate progression to more advanced or higher

order levels of physical function. The normal postnatal acquisitional sequence of physical

skills is used as a template for the undertaking of physical restoration activities.

At the earliest, phylogenetic and ontogenetic development, then, may help to identify

both the structural and functional organization of central nervous system (CNS) structures.

Tulving argues that the evolutionary emergence of different systems is perhaps evidenced

at different stages of postnatal development of the organism. 7 The relationship of structure

and function is such that earlier developing structures and functions become incorporated

into later developing structures and their respective functions. Some of the oldest struc

tures of the CNS are the brainstem, the cerebellum, and the structures which comprise

the limbic system, including the thalamic matrix. In comparative terms, the telencephalon

represents the youngest of structures in the CNS. The telencephalon is among the last of

the neural structures to develop. It is a rostral continuation of the ventral thalamus and

subthalamic matrix. 12 In fact, the majority of thalamic efferent projections are to the fore

brain throughout phylogeny. 13

To further these points, myelination of neural structures follows a pattern which is

similar to the order of embryological emergence of those structures. 14 Maturation of func

tion is myelin-dependent. The myelogenetic fields of Flechsig 14 (Figure 13.1) and the orga

nization of cortical structures put forth by Luria 15 (Figure 13.2) bear considerable similarity

between the primary and intermediate myelin fields and the primary and secondary

Lurian areas, respectively. The primary myelin fields and the primary Lurian areas corre

spond to the primary cortices responsible for vision, audition, tactile sensation, and motor

function.

Information flow throughout the CNS is a primary concern for cognitive function. Tactile

sensory pathways include those responsible for pain and temperature (lateral spinotha

lamic tract), those responsible for conscious

proprioception and discriminative touch

FIGURE 13.1

The myelogenetic fields of Flechsig, modified from Yakovlev (1962) to demonstrate “primordial,” “intermediate,”

and “terminal fields.” Primordial fields show stainable myelin before or at term. Intermediate fields myelinate

at 6 to 12 weeks. Terminal fields myelinate after the fourth postnatal month. (a) Lateral surface, (b) medial

surface. (From An Introduction to the Neurosciences, Curtis, B. A., Jacobson, S., and Marcus, E. M., Eds., W. B.

Saunders, 1972, p. 461. With permission.)

(dorsal column–medial lemniscal pathway), and those responsible for unconscious prop

rioception (ventral and dorsal spinocerebellar tracts). The lateral spinothalamic tract syn

apses in the ventral posterior thalamic nucleus and projects via thalamocortical fibers of

the posterior limb of the internal capsule to sensory cortex in the postcentral gyrus of the

frontal lobe. Collateral projections form the spinothalamic tract synapse in the brainstem

within the reticular formation. The dorsal column–medial lemniscal pathway follows the

same course as the lateral spinothalamic tract via the ventral posterior nucleus of the

thalamus and posterior limb of the internal capsule on its way to the postcentral gyrus.

The anterior spinothalamic tract, which is responsible for perceptions of simple touch,

comprises a portion of the dorsal column. The ventral and dorsal spinocerebellar tracts

terminate at the level of the cerebellum.

Visual stimuli enter the system at a supratentorial level, coursing from the retina via

the optic nerve to the lateral geniculate nucleus of the thalamus. The stimulus progresses

from the lateral geniculate nuclei via Meyer’s loop and the geniculocalcarine tract before

terminating in the calcarine fissure and lingual gyrus of the occipital lobe, respectively.

Visual stimuli travels to the occipital primary sensory regions via both temporal and

parietal lobe structures, depending upon the quadrant of the visual field represented.

Auditory stimuli first registers at the dorsal and ventral cochlear nuclei located in the

pons. Auditory stimuli travel from these nuclei to the medial geniculate bodies of the

thalamus before continuing to the auditory cortex of the temporal lobes. Vestibular stimuli

FIGURE 13.2

(a) The first functional unit of the cortex — the sensory unit. (Dark-shaded areas are primary zones; medium

shaded, secondary zones; light shaded, tertiary zones.) Sensory input travels from primary to secondary to

tertiary and is thereby elaborated from sensation into processes. (b) The second functional unit of the cortex —

the motor unit. Symbolic processes from the sensory unit are translated into intentions in the tertiary motor

zones and then into patterns of action in the secondary and primary motor zones. (From Luria, A. R., The Working

Brain, Penguin Publishers, Harmondsworth, U.K., 1973. With permission.) (a) The sensory unit (b) The motor unit

also course through cranial nerve VIII and synapses in the brainstem on the superior,

medial, lateral, and inferior vestibular nuclei located in the upper medulla and lower pons.

Stimuli project from these nuclei to the spinal cord, cerebellum, reticular formation, and

to the nuclei of the oculomotor (III), trochlear (IV), and abducens (VI) cranial nerves via

the medial longitudinal fasciculus.

Olfactory stimuli travel from the olfactory bulb to the rhinencephalon and projects to

the piriform area of the medial temporal lobe, the anterior perforated substance and the

terminal gyri of the medial basal frontal lobe, and the anterior uncus located in the medial

surface of the temporal lobe. Olfactory stimuli also project to the amygdala and hippoc

ampal gyrus. Like visual stimuli, olfactory stimuli enter the CNS at a supratentorial level.

Olfactory stimuli reach the thalamus via projections from the piriform cortex and the

amygdala. Odorant stimuli can reach the neocortex directly or indirectly via the thala

mus. 16 The influence of olfactory stimuli on emotive state is supported by projections to

the amygdala and hypothalamus. Pheromones signal via these same pathways. The orbito

frontal and frontal cortices are involved in conscious odor discrimination.

Reticular Formation

The pathways reviewed, thus far, are systems which relay to specific thalamic nuclei and

act more directly upon the primary sensory cortices via various thalamic nuclei. The

reticular formation acts indirectly to provide sensory

input to the cortex, however, via the

nonspecific thalamic nuclei. Afferent input to the reticular formation is provided from

collateral branches of the spinothalamic and lemniscal pathways and information descend

ing from the cortex through the corticoreticular pathways. The corticoreticular fibers

include collateral branches of the corticospinal and corticobulbar tracts deriving from

cortical areas which are widespread. The cerebellum, basal ganglia, hypothalamus, cranial

nerve nuclei, and colliculi also provide afferent input to the reticular formation. The

superior colliculus is implicated in the covert orientation of attention to visual space, 17

and the midbrain has been implicated in the orientation of attention and maintenance of

arousal level. 18,19

Reticular efferents deliver information from the reticular formation to the hypothala

mus, the nonspecific nuclei of the thalamus, 20 and the descending reticulospinal path

way. 21 Pathways projecting from the reticular formation are part of the ascending

projectional system. The reticular formation acts indirectly on the cortex via the nonspe

cific thalamic nuclei. Projections from the nonspecific thalamic nuclei connect to all areas

of the cortex.

Hypothalamus, Thalamus, and Basal Ganglia

A primary function of the hypothalamus is regulation of the autonomic nervous system.

The hypothalamus integrates autonomic response and endocrine function with behavior

to maintain homeostasis of certain systems. Blood pressure and electrolyte composition

are maintained by control of drinking and salt appetite. Body temperature is regulated

by control of metabolic thermogenesis and behaviors that seek to warm or cool the

individual. Energy metabolism is regulated by feeding, digestion, and metabolic rate.

Reproduction is regulated through hormonal control. Finally, emergency responses to

stress are controlled by regulating blood flow to muscle and other tissues and release of

adrenal stress hormones. The hypothalamus receives inputs of sensory information from

all over the body, compares this information to biological set points and, upon detection

of deviation from the set points, adjusts autonomic, endocrine, and behavioral responses

to return to homeostasis. 22

The thalamus is comprised of four groups of nuclei — the anterior, medial, ventral, and

posterior. 8 The anterior nucleus is a single nucleus which receives its major input from the

mammillary nuclei of the hypothalamus and the presubiculum of the hippocampal for

mation. It is interconnected with the cingulate and frontal cortices and may be involved

in memory. The medial nucleus is comprised of the mediodorsal nucleus which has three

subdivisions. Each of these projects to a particular region of frontal cortex and input is

received from the basal ganglia, amygdala, and midbrain. The medial nucleus is also

implicated in memory. The ventral nucleus is comprised of the ventral anterior and ventral

lateral nuclei. These are involved in motor control. Input to these nuclei comes from the

cerebellum and basal ganglia, and output is to the motor cortex. The ventral posterior

nucleus, also part of the ventral nucleus, sends somatosensory information to the neocor

tex. Lastly, the posterior nucleus is made up of the medial geniculate, lateral geniculate,

and lateral posterior nuclei and the pulvinar. The medial geniculate nucleus receives

tonotopic auditory stimulus and projects it to the superior temporal gyrus. The lateral

geniculate receives information from the retina and projects it to the primary visual cortex. 8

The nuclei discussed thus far are referred to as specific thalamic nuclei. They project to

specific primary sensory areas of the cortex. Nonspecific nuclei, on the other hand, project

diffusely to several cortical and subcortical regions. The thalamus receives a great deal of

input from the cortex. In fact, cortical input to the lateral geniculate nucleus, for example,

is greater in number of synapses than input from the retina. Most thalamic nuclei are

similar. A single thalamic nucleus sends information to multiple cortical areas, which

return information back to the thalamus but to different thalamic nuclei. Irrelevant infor

mation is suppressed while so-called “correct input” is facilitated by positive feedback

via corticofugal projections. 23

The thalamus is surrounded by the reticular thalamic nucleus which forms an outer layer

to the thalamus. The reticular nucleus uses the inhibitory neurotransmitter GABA, while

most other thalamic nuclei utilize glutamate, the excitatory neurotransmitter. Neurons of

the reticular nucleus do not interconnect with cortical neurons, but terminate, instead, on

other thalamic nuclei as they exit the thalamus. The reticular nucleus exerts a modulatory

effect on the actions of other thalamic nuclei in this manner. As a result, a degree of

information processing occurs at the thalamus due to the monitoring of the thalamocortical

stream of information made possible by the collaterals of other thalamic nuclei synapsing

on reticular neurons as they pass through the reticular nucleus' outer layer. 8

The basal ganglia are comprised of four major nuclei: the striatum, the globus pallidus,

the substantia nigra, and the subthalamic nucleus. The striatum receives input from the

cerebral cortex, thalamus, and brainstem and projects to the globus pallidus and the

substantia nigra. The globus pallidus and substantia nigra, in turn, form the major output

projections from the basal ganglia. The basal ganglia are involved in a variety of behaviors

including voluntary movement, skeletomotor, oculomotor, cognitive, and emotional func

tions. 24,25 Basal ganglia output is back to the cortex, via the thalamus, or to the brainstem.

The basal ganglia serve as an important system linking the thalamus and cerebral cortex.

Information which originates from a specific cortical area may be returned from the

thalamus to other cortical areas.

Hippocampus

The hippocampus has been widely studied due to its role in memory. The hippocampal

gyri are located in the inferior medial temporal lobe. Damage to the hippocampus, or any

of the association areas in the temporal lobe with which it connects, will result in deficits

in explicit memory. 26–28 Explicit memory is sometimes referred to as declarative memory and

includes episodic and semantic memory. Episodic memory is memory for events and

experiences while semantic memory is memory for factual information. 28,29

Information appears to be first processed in the association areas of the prefrontal, limbic,

and parieto-occipital-temporal cortices. 28,30 Information is then passed to the parahippo

campal and perirhinal cortices and, from these, on to the entorhinal cortex. From the

entorhinal cortex, information passes to the dentate gyrus, the subiculum, and the CA1

and CA3 regions of the hippocampus. The dentate gyrus passes information to the CA3

hippocampal region, which then passes information to the CA1 region and on to the

subiculum. From there, information is sent back to the entorhinal cortex, 31 on to the

parahippocampal and perirhinal cortices, and back to the cortices. Hippocampal projec

tions to cortical areas are widely distributed. 31 The circuitous nature of these connections

provides support for a role in detection of novel stimuli, 32,33 associative memory, 34,35 encod

ing of explicit memory, 33 retrieval of explicit memory, 36 attentional control of behavior, 37

spatial memory, 38,39 and, possibly, a role in the development of long-term memory. 28

Processing of spatial scenes appears to involve the parahippocampus while spatial

memory involves the right hippocampus. Context-dependent explicit memory is more

dependent upon the left hippocampus. 39 Episodic memory encoding appears to involve

primarily the rostral portions of the hippocampal region, whereas retrieval involved

primarily the caudal portion. 40

The connection of the association cortices and hippocampal structures is quite important

for overall cognitive function. Information from several, widely distributed cortical regions

must be integrated to perform complex mental functions. The association areas receive

information from higher-order sensory areas and, ultimately, convey the consolidated

information to higher-order motor areas. 41 The motor areas organize planned actions. The

hippocampal role, together with associated involvement of other medial temporal and

limbic lobe structures, is found in the manner in which hippocampal input is received

from and output is projected to the associative cortices. These circuits may be active in

processes whereby previously stored information is modified by new experience. 28

The relationship between emotion and memory encoding is significant. Hippocampal

efferents project to the amygdala, the septum, the fornix, the thalamus, the mammillary

bodies, the medial preoptic area, and the periformical nucleus of the hypothalamus. 42 The

anterior hippocampus appears to exert an excitatory modulatory effect on the amygdala. 43

It exerts inhibitory effects on the fornix and both excitatory and inhibitory effects on the

ventromedial nucleus of the hypothalamus. The amygdala is implicated in self-preserva

tion activities such as the search for food, feeding, fighting, and self-protection 44 and the

association of sensory information with emotional states. McGaugh 45 cites evidence that

the basolateral region of the amygdala is crucial in memory consolidation arising from

emotionally impactful experience. Stress hormone production and other neuromodulatory

systems activated by such experiences are made possible via the anterior hippocampal

projections to the amygdala, which progress to the hypothalamus and the basal forebrain.

The posterior hippocampus also sends projections to the hypothalamus via the fornix.

Motivational significance of incoming stimuli is determined by the amygdala with sub

sequent coordination of multiple systems to enable an appropriate response.

Commissural and Association Tract Fibers

Information must be moved from one cerebral area to another. Transport between sub

cortical and cortical areas is accomplished by projectional fibers which comprise the

internal capsule. Fibers of the internal capsule carry information both toward and away

from the cortex. Axons of the internal capsule spreading out to all areas of the cortex are

known as the corona radiata. Fibers from the thalamus projecting to the cortex travel in the

internal capsule. Projections from the anterior and medial thalamic nuclei carry visceral

and other information and project to the frontal lobe via the anterior limb of the internal

capsule. Projections from the ventral anterior and ventral lateral nuclei of the thalamus

travel in the genu and posterior limb of the internal capsule and reach the motor and

premotor areas of the frontal lobes. The ventral posterior and medial thalamic nuclei

project to the sensory cortex of the parietal lobe via the fibers of the posterior limb of the

internal capsule. The posterior limb of the internal capsule also contains optic and auditory

fibers. Corticobulbar (head and face muscles) and corticospinal (neck and trunk muscles)

motor pathways travel via the posterior limb of the internal capsule to the brainstem

(corticobulbar) and spinal cord (coritcospinal).

Interhemispheric connections are accomplished by the corpus callosum and two smaller

commissural bundles. The anterior commissure interconnects the anterior temporal areas.

The hippocampal gyri are connected to each other via the hippocampal commissure.

Intrahemispheric interconnection is accomplished by association fibers. The temporal

and frontal lobes are joined by the uncinate fasciculus. The medial surfaces of the frontal,

temporal, and parietal lobes are connected by the cingulum, which also connects the

cingulate gyrus to the orbitofrontal cortex and the hippocampal cortex. Projectional fibers

from the thalamus to these regions are contained in the cingulum. The anterior cingulate

gyrus is implicated in executive attention 46 through the detection of conflicts occurring

during information processing that signal the need to engage top-down attentional pro

cesses. 47 The anterior cingulate cortex is active in conscious attention during auditory

processing. 48 It may provide an important connection between widely disparate aspects

of attention such as the mental operations of visual target detection and semantic content

by integration of information arising from the various multimodal association cortices.

The anterior cingulate gyrus has been implicated in episodic memory retrieval as well. 49

Finally, arcuate fibers connect adjacent gyri in neocortical areas.

Principles of Neurophysiology and Cognition

The study of cognition has long been the realm of experimental psychology. Carefully

designed research and detailed behavioral observation allowed insight into phenomena

such as sensitization and habituation. The limitations of psychological investigation, how

ever, rarely allowed for much beyond conjecture as to the nature of the physiological

underpinnings of such behaviors. Cognitive processes such as memory have long been

investigated, and early information regarding neurophysiological issues arose from obser

vation of persons with known injuries who may have been later studied at autopsy to

attempt to correlate, in gross anatomical terms, sites of lesion and observed premorbid

behavioral changes.

Advances in neuroscience continue to expand the information available regarding neu

rophysiological function and the cognitive processes which are subserved by that function.

It is now possible to discuss neuronal function and neurotransmission at the level of the

cell, ion, and neurotransmitter. Neuroanatomical organization has advanced considerably

from the early days when primary debate consisted of whether nerve cells interconnected

via a protoplasmic continuity or whether nerve cells existed individually and were con

tiguous rather than continuous. 31

As neuroscience continues to expand available information, conceptions about neurocog

nitive function will likewise be necessarily advanced and refined. It is important to utilize

available information, however incomplete it may still be,

to develop rational theoretical

constructs from which diagnosis and treatment of cognitive function is approached.

Information Processing, Neurotransmission, and Learning

Information processing is dependent upon the existence of three levels of storage: sensory

stores, short-term memory, and long-term memory. Baddeley's 50 early conceptualization

of these mechanisms led to the question of how information was transferred from short

term storage (STS) to long-term storage (LTS). Others have recently suggested a need to

revisit these concepts to consider frontal lobe structure which may enable (1) the updating

and maintenance of information, (2) the selection, manipulation, or monitoring of infor

mation, and (3) the selection of processes, subgoals, or planning. 51

Craik and Lockhart 52 proposed a level of processing framework designed to account for

how information progressed from STS to LTS. The level of processing framework theorizes

that information transfer from STS to LTS is impacted by the degree to which the stimulus

is processed. Superficial processing results in lesser likelihood of transfer of information

to LTS, while more in-depth processing more likely results in such a transfer.

Craik and Lockhart 52 proposed that attributes of encountered perceptual stimuli com

bine with the needs of the individual to determine both what information is recognized

and to what degree it is stored. Much of the totality of

sensory experience is lost in the

earliest stages of information processing as it is either not deemed to be immediately

relevant or it is “washed out” or overwritten in the early sensory store mechanism. 4

Information which is more familiar is processed more quickly and at a deeper level. Due

to the individual’s previous experiential encoding, a great deal more information becomes

available compared to that available for relatively novel stimuli.

The central nervous system responds to the demands of the organism. While some

systems are designed to maintain an overall equilibrium and have specific physiological

processes which serve that function, such as maintenance of the blood-brain barrier, other

systems can be seen to respond to demand. Regional cerebral blood flow and oxygen and

glucose metabolism can be seen to increase relative to activation of specific anatomical

structures during electrophysiological studies of cognitive function. Learning, as well as

neuronal activation, results in increases in regional cerebral blood flow and oxygen and

glucose metabolism.

At a cellular level, it has been demonstrated that different types of memory formation

place different demands on the cellular mechanisms for protein synthesis. Protein synthe

sis occurs within the nucleus of the neuron in direct response to learning. Protein synthesis

does not occur, though, for all types of memory. STS does

not require protein synthesis.

“All of the proteins, including receptors, ion channels, enzymes, and transporters, required

for short-term memory formation and temporary storage are already present in sufficient

abundance. In sharp contrast, however, long-term memory absolutely depends on the

synthesis of new proteins or the increased synthesis of already existing proteins.” 53

Synaptic activation and transmission lead to changes throughout the neuron. The

nucleus, axon, dendrite, and synapse undergo structural changes which support informa

tion processing, learning, and memory. Changes at the synapse are such that they support

the immediate, short-term, or long-term demands of the information processing process

and either encourage or discourage further synaptic transmission. When transmission

occurs across a synapse, the synapse becomes “potentiated,” thereby making the synapse

more responsive to the next transmission. 54 Potentiation of the synapse can be of varying

durations, lasting seconds to years. Posttetanic potentiation (PTP) lasts for a minute or

less, while short-term potentiation (STP) lasts somewhat longer. PTP and STP result from

increases in the number of quanta released and/or the strength of their postsynaptic

effects. 55 Long-term potentiation (LTP) lasts weeks to years. LTP requires several simulta

neous signals to be received by the neuron and effectively “strengthens” the synapse.

LTP has an inhibitory counterpart known as long-term depression (LTD). LTD, a decrease

in synaptic responsivity which is activity dependent, has been recently demonstrated to

be induced postsynaptically, and it is possible that LTD may also require the production

of a retrograde messenger. 56 Both LTP and LTD are viewed as cellular mechanisms

involved in learning and memory. Habituation and sensitization are nonassociative types

of learning and can be both short- and long-term in nature. Habituation and sensitization

may be subserved by short- and long-term potentiation and depression. 57

In studies with Aplysia, Frost et al. 57 demonstrated that short- and long-term potentiation

were dependent upon the presentation of serotonin (5-HT). A single presentation of 5-HT

resulted in an increase in the excitatory postsynaptic potential between the sensory and

motor neuron that lasted minutes. Presentation of five applications of 5-HT resulted in an

increase in the excitatory postsynaptic potential that lasted 24 hours, required new RNA

and protein synthesis, and involved the growth of new synaptic connections between the

sensory and motor neuron. It is important to note that 5-HT is the modulatory neurotrans

mitter for the studied sensory-motor synapse in Aplysia. A number of studies have dem

onstrated, with differing species, similar mechanisms underlying learning and the

development of nondeclarative motor skills and explicit (hippocampus-based) memory. 58–60

In instances where LTP occurs, changes occur within the cell body as well as in the form

of changes of gene expression. These changes may impact the function of all synapses or

may be restricted to specific synapses. In instances where only select synapses undergo

LTP, other synapses of the same neuron are more readily able to undergo LTP due to

changes in the genetic expression at the cell body. Castelluci et al. 61 noted that both genetic

expression and protein synthesis, not necessary for formation of short-term memory, likely

were required for acquisition of long-term memory. Additionally, it has been determined

that neurotransmitters not only serve transmission of a signal across a synapse but also

function in the regulation of local protein synthesis, independent of the cell body used to

establish synapse-specific changes in synaptic strength. 62 Frost et al. 63 found underlying

circuit modification could be accomplished by at least four neuronal sites for short-term

memory formation in aplysia. Martin et al. 62 later demonstrated that local protein synthesis

occurred at the synapse independent of the soma and its nucleus, thereby allowing for

long-term branch-specific facilitation.

While these studies are exciting in their implications, LTP is not the only substrate of

memory. 64 LTP, by itself, cannot account for all aspects of potentiation. The role of adhesion

chemistry has been proposed by Lynch 64 as responsible for explanation of the time con

straints observed for LTP and memory function. Three transmembrane cell adhesion

receptors have been identified: integrin, cell adhesion molecules (CAMs), and cadherins.

“Integrin activation/engagement thus emerges as that process whose temporal

requirements dictate the particular time courses recently discovered for LTP and repeat

edly described for memory.” 64

Other morphological changes are known which may subserve LTP. Schubert 65 found

that synaptic cleft modifications occur following synaptic transmission. Following

repeated transmission across a synapse, the size of the synaptic cleft is reduced, and

glycoproteins released into the cleft act to bind the synaptic endplates closer together.

Additionally, the synaptic endplates themselves broaden, resulting in greater exposure of

neurotransmitter vesicles. The result is more rapid release of neurotransmitter into the

synapse and less distance for the neurotransmitter to travel. More rapid release and uptake

of neurotransmitter and, consequently, more rapid transmission occurs.

Neurons are organized in adjacent columns of cells within the central nervous system.

Cells within columns serve separate but similar functions, and greater numbers of com

putational columns are correlated with area size of the cortex dedicated to specific func

tion. 8 Activation of a single neuron can cause increased electrical activity in adjacent cells

and may cause a focal neuronal LTP response. 66 Aggregate groups of neurons are thought

to function most probably together. 67 Activation of adjacent cells within columns may

facilitate a desired level of processing or compound information processing. Both nitric

oxide and carbon dioxide have been identified as retrograde messengers in neurotrans

mission and may play a role in the widespread LTP. 68 Nitric oxide is a relatively short

acting neurotransmitter. Its release has been demonstrated to be experienced by closely

adjacent synapses. 66 Nitric oxide has been implicated in reference memory in studies of

working vs. reference memory in rats. 69,70

Simple neural activation is not sufficient to bring about certain morphological changes.

Reactive synaptogenesis has been demonstrated to occur only when the neural activation is

associated with learning. 71,72 During this process, new dendritic spine formation occurs at

the synaptic level following repeated neurotransmission. This process is fairly rapid, with

studies showing it to occur within 10 to 15 minutes. 73 Synaptogenesis must be supported

by both glial cells (specifically, astrocytes) 74 and adequate blood supply. 71 The time frame

required for synaptogenesis to occur may be more than coincidental to the time required

to allow for the transport of requisite proteins, which must transpire in order to allow for

information to be transferred to LTS.

Modulatory neurotransmitters play a major role in information processing. The six

primary modulatory neurotransmitter systems consist of the noradrenergic (norepineph

rine), adrenergic (epinephrine), dopaminergic, serotonergic, cholinergic, and histaminergic cell

groups. These cell groups constitute the long projection system of the reticular formation. 75

In addition, there are over 50 neuroactive peptides that act as neurotransmitters, though

not all are active, of course, within the brain.

A nucleus of interest in the noradrenergic system is the locus ceruleus located dorsally

and lateral of midline in the periaqueductal and periventricular gray matter of the pons.

The locus ceruleus is implicated in maintenance of vigilance and responsiveness to unex

pected stimuli. Noradrenergic neurons of the medulla project to the hypothalamus, con

trolling endocrine and cardiovascular function.

Dopaminergic projections from the nuclei of the brain stem traverse many systems.

Dopaminergic neurons project to the telencephalon and are involved in motor movement.

Neurons project to the frontal and temporal cortices as well as to limbic system structures

of the forebrain via the mesocortical and mesolimbic dopaminergic pathways. These

structures are involved in emotion, memory storage, and thought.

Most of the serotonergic neurons of the brain stem are located in the raphe nuclei. These

neurons project to essentially the whole of the

telencephalon. Some pathways project to

the hypothalamus and are involved in cardiovascular function, while those projecting to

the forebrain act to modulate the responsiveness of cortical neurons. Serotonergic neurons

are involved in regulating attention and complex cognitive function. 76

Cholinergic neurons project from the mesopontine tegmentum and the basal forebrain.

The neurons of the pontine region provide a descending projectional pathway to the nuclei

of the pontine and medullary reticular formation. They also project in a major ascending

pathway to the thalamus. The cholinergic neurons are thought to impact the sleep/wake

cycle via these projections.

Histaminergic neurons are located in the posterior lateral hypothalamus and the tuber

omammillary nucleus. 75 These neurons project to the spinal cord and to the entire cortex.

These projections are thought to contribute to cortical arousal and to an arousal response

at the level of the brainstem.

Once neurotransmitters are released into a synapse, they must be removed from the cleft

via one of three mechanisms in order to preserve responsivity of the synapse. Neurotrans

mitters can be removed by diffusion, enzymatic degradation, and reuptake. Reuptake is

the most common mechanism used for inactivation. Enzymatic degradation and reuptake

offer two important means of pharmacological intervention in neurotransmission.

Sensory information entering the CNS makes its way to the brainstem with the exception

of visual and olfactory stimuli. Visual and olfactory stimuli remain above the tentorium

and only oculomotor responses involve the brainstem. The reticular activating formation

receives cortical, auditory, tactile, proprioceptive, and vestibular input. In addition, the

reticular formation receives input from the cerebellum, basal ganglia, hypothalamus, and

colliculi. The ascending projectional system sends information from the brainstem reticular

formation to the nonspecific thalamic nuclei, 20 the hypothalamus, and the reticulospinal

pathway. The ascending projectional system reaches the cortex via the widely distributed

thalamic projections arising from the nonspecific nuclei. A broad spectrum of structures

in the neuraxis is involved in arousal and attention.

At the brainstem level, the mesencephalic reticular formation and its thalamic projec

tions have been implicated in maintenance of arousal 19 and the orientation of attention. 17,77

In fact, substantial changes occur via the autonomic nervous system in relation to con

scious direction of attention. These include changes in heart rate, vascular dilation, pupil

size, and galvanic skin response. 78

The basal ganglia project to the cortex indirectly via the thalamus. Bares and Rektor 79

studied the role of the basal ganglia in cognitive

processing of sensory information and

found the basal ganglia to be active in a contingent negative paradigm linked to a motor

task. Experience in Parkinson’s disease has resulted in the suggestion that dopamine might

play a role in regulating attention. 80 The striatum receive inputs from all cortical areas and

project principally to the prefrontal, premotor, and supplementary motor areas via the

thalamus. These areas are involved in motor planning, shifting attentional sets, and in

spatial working memory. 23 Nauta 24 notes the circuitous connections between the cerebral

cortex, limbic system, and corpus striatum in the overall fluidity of attentional processes.

The thalamo-frontal gating system is implicated in selective or controlled attentional

processes. 81 Distractibility may occur following disturbance of the diffuse thalamic pro

jection system. Difficulties with interference and integrational behaviors of judgement,

planning, and socially appropriate behavior are found with damage to the thalamo-frontal

gating system. A fair amount of information processing occurs at the level of the thalamus.

The purpose of the thalamo-frontal gating system is to direct selected information up to

cortical structures. Incoming stimuli are enhanced or attenuated by the facilitation or

inhibition of transmission of neural impulses. Attention can thus be directed to specific

stimuli while other stimuli are suppressed. Perception of stimuli at the cortical level only

occurs when the diffuse projection system is also active. 21

At the cortical level, frontal, posterior parietal, and cingulate cortices are involved in

attentional processing. 82–85 The neocortex is involved in response selection based upon

cognitive or semantic dimensions. 86 The associative cortices appear most active in atten

tional processes. 87 One hypothesis suggests that a competition for neural resource is

created when cells in associative cortex respond to a novel stimulus. 88 The number of cells

available to respond to another stimulus is decreased proportionately to the number

responding to the first stimulus. Experimental evidence supports this hypothesis in the

finding that some pathways were facilitated by attention to a signal, while others were

simultaneously inhibited. 89 Conscious processing of a stimulus causes a decrease in the

ability to detect new stimuli. 90

Information appears to be dealt with either reflexively or intentionally within the system.

Tasks which require conscious direction of attention take up attentional resource, slowing

information processing of other stimuli. Repeated task completion, however, may allow

for deliberate attentional resource to be decreased, changing over to automatic processing,

thereby freeing system resources.

It is easier to attend to different aspects of the same object than to attend to the same

attributes in different objects. Some of these limitations are due to similarity of perceptual

information of the attended information. Information presented in the same modality is

harder to attend to than information coming from different modalities. Duncan 91 demon

strated that ongoing cognitive processes, too, can interfere with the detection of new

signals. These include storage of recently presented information, generation of ideas from

LTS, and development of schema.

“Perhaps because of these limitations, much of perceptual input goes unattended while

some aspects become the focus of attention. Attending, in this sense, is jointly determined

by environmental events and current goals and concerns. When appropriately balanced,

these two kinds of input will lead to the selection of information relevant to the achieve

ment of goals and lends coherence to behavior. The system must, however, remain suffi

ciently flexible to allow goals and concerns to be re-prioritized on the basis of changing

environmental events. This balance appears to be adversely affected by major damage to

the frontal lobes … .” 92

Large amounts of information can be screened in the face of competing stimuli, such as

in dichotic listening studies. Information retention appears to be based on specific features

which are determined by the listener. 93 Evidence suggests that selective attention occurs

in the early levels of processing for both visual and auditory attention. 94

Attentional processing can be deliberate or automatic. 95 Deliberate attentional processes

require greater system resource than automatic processes. Anderson 95 found that atten

tional processes seem to progress from deliberate to automatic with practice. The existence

of a brief visual sensory register was demonstrated by Spurling. 96 Visual stimulus was

first referred to as an icon 4 and the auditory equivalent of iconic memory is referred to as

echoic memory. 4,97,98

Sensory registers such as iconic and echoic store allow for information to be entered

without the subject paying attention to the source. 4 These sensory registers store informa

tion in a literal way, can be overwritten by further input in the same modality, are

vulnerable to “wash-out,” are modality specific, and have a moderately large capacity.

While sensory registers can store a great deal of information, information is initially

stored for very brief periods of time (less than 60 seconds) in iconic and echoic store

mechanisms. Information which is retained beyond this time period is thought to have

been processed and integrated into other memory structures or other cognitive processes.

Note the similarity between these concepts and those of PTP, STP, and LTP. Rate of

forgetting has been shown to be 1 / 4 to 2 seconds for sensory stores and under 30 seconds

for STS. Rate of forgetting is very slow or does not occur in LTS. 99

Sensory store mechanisms also have some limitations in capacity. 78,96 The size of sensory

stores has been found to be dependent upon the nature of the information presented. Two

different studies found that recall for words was between two and four words. 50,100 Crannell

and Parrish found sensory store memory span to be between five and nine items, depend

ing upon whether the items were digits, letters, or words. 101 In experiments where words

were strung together to form sentences, recall of up to 20 words was found. 102

Perceptual Features

The human perceptual system is inherently designed to give priority to certain types of

perceptual cues. 103 Perception of certain cues is facilitated by basic physiological mecha

nisms. Others, however, are guided by experience. The visual system, for example, is

physiologically predisposed to enable an individual to register the visual stimuli associ

ated with a falling snowflake. However, only through experience could an individual gain

an appreciation for different types of snow. Sensory stimuli from different sensory systems

will, likewise, have both physiological and experiential features. These features have been

referred to as perceptual attributes or features. Some perceptual cues, particularly those

arising from a physiological predisposition, have been demonstrated to be represented in

different languages and cultures in so-called “natural categories.” 104

Perceptual features can be those which are descriptive of a physical characteristic (iconic)

or those which are descriptive of functional characteristics (symbolic). The iconic features

of the table include that the table is made of wood, is 4 feet tall, is rectangular, weighs

200 pounds, is brown in color, and has a smooth surface. The symbolic features of the

table would include that it is used as someplace to work or to eat. Perceptual features can

also include “characteristics.” For example, the characteristics of “pretty” or “fast” might

be considered perceptual features of a car. Essentially every noun, verb, preposition,

adjective, and adverb can be a potential feature. Of course, perceptual features are not

just limited to objects. Events also have perceptual features. A lecture, for example, might

have the perceptual feature of “boring” or “interesting.” Essentially, the object or event is

comprised of its perceptual features. 104,105

The encoding of memory has been described as a process of utilization of perceptual

features in the establishment of an internal representation of an event. 106 Perceptual fea

tures of an event, which can include the context of the events (external context), are

combined with perceptual features that may arise from the individual’s previous experi

ence (internal context) to encode the event in memory. Each perceptual feature can also

be used for recall of an event. Only those perceptual features that were utilized during

encoding can be used for recall. “… The effectiveness of a retrieval cue depends on its

compatibility with the item’s initial encoding or, more generally, the extent to which the

retrieval situation reinstates the learning context.” 52 The memory trace, its coding charac

teristics, and persistence are by-products of perceptual processing. 107 Craik and Lockhart 52

suggest that trace persistence is a function of the depth of analysis and that deeper levels

of analysis lead to stronger, longer lasting, and more elaborate memory trace persistence.

As sensory stimuli are converted to mental representation in the form of memory, the

actual input attributes may be purged.

The perceptual features which are encoded at the time of stimulus presentation will

impact both long-term retention and recall. Additionally, the integrity and nature of the

organizational structure used or developed at the time of acquisition will impact long

term retention. 108,109 Long-term retention of information may be directly related to the

depth of information processing of the sensory experience. “Highly familiar, meaningful

stimuli are compatible, by definition, with existing cognitive structures. Such stimuli (for

example, pictures and sentences) will be processed to a deep level more rapidly than less

meaningful stimuli and will be well-retained. … Retention is a function of depth, and

various factors, such as the amount of attention devoted to a stimulus, its compatibility

with the analyzing structures, and the processing time available, will determine the depth

to which it is processed." 52

A perceptual assay is conducted beginning with the sensory registers. An overwhelming

amount of information is available at any point in time to the system because both relevant

and irrelevant information is being experienced. Stimuli with which the individual has

experience will be recognized and processed more completely then novel stimuli unless

the situation demands greater attention to the novel stimuli. The ability to discern per

ceptual features is physiologically quite keen. In studies where a novel stimulus is pre

sented and habituation is allowed, a slight change in the perceptual characteristics of the

stimulus following habituation results in changes in the autonomic nervous system and

EEG recordings. 110

Perceptual salience has been described by many authors. 111–115 Perceptual salience results

when a particular perceptual feature becomes the focus of inordinate attention, sometimes

to the exclusion of recognition of other features. Perceptual salience can be so strong that

it interferes with other cognitive processing. Developmentally, perceptual salience appears

to assist in the acquisition of certain concepts. Preschool-age children are more perceptu

ally salient for variability than older children. Older children show no differential sensi

tivity between variability and constancy. 113 In fact,

perceptual salience for variability lead

6-year-olds to make more overdiscrimination errors due to attention paid to feature dif

ferences which were irrelevant. 116 Reflectivity has been noted to increase and impulsivity

decrease with age. 117,118

The degree to which an individual can move freely amongst perceptual attributes

will impact that individual's creativity and problem solving. Frequently, problem

solving requires a novel use of perceptual features. The chair's iconic features of

construction and height can allow the chair to be used as a ladder. However, perhaps

the most salient feature of a chair is the symbolic attribute (function) of "to sit on." In

order to problem solve the use of a chair in place of a ladder, the individual must be

able to survey the chair's iconic features, ignoring its typical symbolic feature (func

tion), and determine if the chair can safely be used to stand on. A chair on rollers

might be deemed too unstable. Once this is accomplished, the novel functional appli

cation as a ladder may become stored as simply another acceptable functional appli

cation of the chair.

Perseveration following traumatic brain injury may, in fact, be a manifestation of

perceptual salience. Deficits in processing featural information have been noted in

people with TBI. 119 Observed patterns of response showed a tendency to base decisions

upon a single salient feature and lesser likelihood of responding to complex multidi

mensional stimuli.

Categorization

The ability to perceive, assay, and utilize perceptual features is crucial to categorization. 120

Perceptual features become categorical descriptors and, as has already been discussed,

are critical for memory encoding and retrieval. In early developmental stages, perceptual

salience for variability may support the individual's ability to encounter a broad spectrum

of perceptual features. As experience with the environment increases and age advances,

a tendency toward constancy emerges. 113 Experience with the environment allows effi

ciency in perception. That is to say, a novel experience with a chair requires maximal

attentional and perceptual resources. As experience with the chair increases, the features

of "chairness" have been encoded and future encounters with a chair place less demand

on perceptual and attentional systems. Just as the specific perceptual features of a chair

are grouped both to define the chair and to encode it, large amounts of information from

the environment must be dealt with similarly. Classification or categorization therefore

allows for large amounts of information to be managed. 121 Categorization is thought to

be crucial to nearly all cognitive ability. 122 "In dealing with the world, people have a system

for classifying objects into categories. The system makes these classifications on the basis

of salient attributes like shape, size, function, and activity. … The systems for classifying

and for naming are not really distinct.” 123 Of course, categorical organization need not be

restricted to objects but can include experiences. “Categorization may be what makes

possible human perception, memory, communication, and thought as we know it.” 124

Three styles of categorization have been identified as involved in information process

ing: rule application, exemplar similarity, and prototype similarity. Each categorical process

involves distinct regions of the brain. Exemplar similarity categorization involves the

medial temporal and diencephalic structures and requires explicit memory. Exemplar

based categorization probably involves reference to memory storage areas of the cortex

which correspond to the nature of the information being referenced, i.e., picture recogni

tion to the occipital regions, verbal recognition to the temporal regions, and so on. Addi

tionally, experiments where category naming is involved show routine activation of the

angular gyrus in the left hemisphere. 125 Finally, when the stimulus used is presented

pictorially, activation is seen in the occipital cortex, not the angular gyrus. 126

Frontal lobe damage has been noted to impact rule application but not exemplar simi

larity. Specifically, the dorsolateral prefrontal cortex has been implicated in rule-following

as seen via the Wisconsin Card Sort 127 which requires discerning rules from observation

and context relation. D'Esposito et al. 128 showed the dorsolateral prefrontal cortex to be

involved in rule-based categorization when the task required switching attention between

mental processes. For rule application, the individual must (1) "selectively attend to each

critical attribute …," (2) "for each attended attribute, determine whether the perceptual

information instantiates the value specified in the rule," and (3) "amalgamate the outcomes

of Stage 2 so as to determine final categorization." "The first stage involves elective

attention, the second involves the perceptual instantiation of abstract conditions, and the

thiard requires the working-memory operations of storing and combining information." 129

Prototype similarity categorization appears to call upon implicit representation. As such,

use of prototype similarity categorization may be dependent upon the level of processing

required to make categorical judgements based on available perceptual information or the

lack of success in application of exemplar similarity based strategies.

Utilization of perceptual features in categorization is referred to as the featural

approach. 104,105,130–134 As a category is defined or created, category members vary in the degree

to which they represent the category. In the category "birds," a robin is a fairly typical

member of the category. Conversely, an emu would still be a

member; however, it would

not be a typical member. “Typicality” is quite important in categorization. Members of a

category share many, though not all, perceptual features. A core group of perceptual features

is required of all category members; however, other frequently shared perceptual features

may only be “characteristic” of the category and not required for category inclusion.

Typicality bears on processing speed. 104,135 Defining features are those features which

are necessary of an item to be included in a category. Characteristic features are those

features that are commonly seen but need not be present for category inclusion. 136 The

combination of defining and characteristic features, or lack thereof, impacts verification

time for category inclusion/exclusion. 136

Processing speed, as measured through reaction time studies, is also dependent upon

access to categorical information and differences in categorical complexity. 134 It has been

suggested that naming is actually an act of categorization and that word-finding problems

in aphasic patients might be viewed as concept formation disturbances. 137 Speed of prob

lem solving appears to be assisted by object labeling. 138

The development of categorization skills follows an acquisition sequence: (1) piling,

(2) keychaining, (3) iconic categorization, and (4) symbolic categorization. 139 Piling occurs

when the individual places all items in a single group without regard for shared attributes.

Keychaining (or edge matching 139) involves a serial ordering of members of the category

where only a single feature is shared between adjacent members. Item 1 and Item 2 might

share color while Item 2 and Item 3 share shape. Item 1 and Item 3 may not share any

attributes. Difficulties with keychaining are often manifest in the communication patterns

of people with TBI. Discourse analysis shows people with TBI have impairment of

productivity, content, and cohesion. 140 A conversational topic is, in fact, a category. Lan

guage, on the other hand, is quite abstract and, consequently, tangential speech or diffi

culties in maintaining topic cohesion is most likely a manifestation of difficulty

maintaining categorical boundaries.

In iconic categorization, iconic features or physical attributes are utilized for defining

category members. Items are grouped on the basis of a shared iconic feature or features.

Symbolic categorization requires that members of the category share a common symbolic

feature or function.

Categories can be simple or rather complex, but categorization remains a binary process.

The category “car” is fairly simple in that an item is either a car or not. The category can

be complicated by adding adjectives and adverbs such as “foreign” car or “fast foreign”

car; however, the process remains a binary one.

Individuals with left hemisphere lesions experience

problems in categorizing fruit and

vegetable items, but are able to categorize on the basis of perceptual features alone. Right

hemisphere lesions, however, produce a reverse effect. Lesions in the left posterior hemi

sphere cause individuals to have difficulty with weak categorical boundaries that can lead

to reclassification, while those with left anterior hemisphere lesions evidence highly cat

egorical responses and categorical boundary rigidity. 141 Individuals with left posterior

disease experience difficulty sorting words or pictures of objects into categories. 142,143

Fluent aphasics have been found to have difficulty in the use of perceptual or contextual

information and recognition naming. 144 People with Broca's aphasia and normals had no

difficulty. In general, Broca's aphasics and individuals with right hemisphere lesions are

more competent in categorization than fluent aphasics, though categorization ability may

not be normal. 145–147 Several studies have demonstrated that fluent aphasics have more or

less difficulty with determination of category membership depending upon the "repre

sentativeness" or typicality of the stimulus. 145,148,149 A study evaluating the ability to verify

category membership and generate exemplars involving both fluent and nonfluent apha

sics found that both groups required extended verification time and had difficulty in

generating atypical categorical exemplars. 150 Ability to generate typical category exemplars

was better for both groups. The study concluded that subjects experienced diminished

representations of boundaries around the category's referential field.

Verbal recall of categorized and noncategorized word lists was evaluated in epileptic

patients with left or right temporal lobectomies and normals. The left temporal group had

poorer performance in recognition and recall compared to normals. There was no differ

ence between normals and the right temporal group for recognition or recall. Performance

was enhanced for both groups with word lists that were categorized. 151 Verbal learning

in amnesiacs and frontal lobe patients was studied using "categorizable" word lists.

Frontal lobe patients did not spontaneously categorize the word lists whereas amnesiacs

did. When categorization was forced, frontal lobe patients' performance improved. 152

Categorization and its many manifestations cannot be ascribed to a single area of the

brain. In fact, some of the most exciting work has been done utilizing PET scans, functional

magnetic resonance imaging (fMRI), and EEG. Naming actions and spatial relations have

been shown to activate the left frontal operculum, the left parietal lobe, and sectors of the

left inferiotemporal cortices. 153 Processing of familiar words involves the right prefrontal

cortex, posterior left parahippocampal gyrus, left medial parietal cortex, and the right

superior temporal gyrus while novel words activated the left hippocampal region. 154 There

appears to be an anterior-posterior functional differentiation involving the medial tem

poral lobe (MTL). The anterior MTL is crucial for processing of novel episodic information

while the posterior MTL is involved in processing for familiar verbal information. 154 Visual

confrontation naming shows activation of the left frontal, bilateral temporo-occipital junc

tions, and inferior temporal regions, with differential activation of the right inferior tem

poral cortex seen for living vs. nonliving category items. 155 Just these few studies show

how highly differentiated cortical structures are for categorical processes.

Cognitive Distance

Piaget noted that, as an individual became better able to represent experience cognitively,

he was better able to do so while being physically removed from the experience itself. 156

Availability and accuracy of information about an object or experience varies with prox

imity to the object or experience. For example, available information about a “table” is

greatest when the table is present. Information availability decreases as proximity to the

object decreases. A color photograph of the same object provides less opportunity for

direct sensory appreciation of attributes than does the actual object. Likewise, lesser

information is available in a black and white photograph, progressing to a line drawing,

to the written word “table,” to the spoken word “table,” and, finally to concept of “table.”

As feature availability decreases to sensory mechanisms, reliance upon previously stored

information increases. Such reliance is logically dependent upon the extent of previously

stored information as well as the structural integrity of the underlying neural network

allowing either direct or indirect access to stored information. The neural network must

allow access to distributed information stored in various cortical regions (e.g., category

naming in the left angular gyrus; pictorial information in the occipital cortices).

Information is input to as many sensory stores as the individual needs to recruit to

“experience” the table. Visual sensory stores take in lines, angles, color, and may allow

for estimation of dimensions of the table and recognition of the material from which it is

constructed. If visual sensory input is inadequate to determine information of interest,

other sensory mechanisms such as touch and audition can be recruited to identify addi

tional attributes, or the individual may call upon experience-based, stored knowledge to

fill in missing attributes.

Since sensory information is first processed at primary sensory cortices, any amalgam

ation of multisensory information requires that information processing continue from

primary sensory cortices to unimodal sensory cortices and on to higher-order sensory

(associational) cortices. Of course, in instances where the individual can rely upon exem

plar or prototypic knowledge derived from previous experience with the object or event,

information processing is impacted, usually more efficiently, though not necessarily. “The

semantic representation of an object is composed of stored information about the features

and attributes defining that object, including its typical form, color, and motion, and the

motor movements associated with its use. Evidence from functional brain imaging studies

of normal individuals indicates that this information is represented in the brain as a

distributed network of discrete cortical regions. Within this network, the features that

define an object are stored close to the primary sensory and motor areas that were active

when information about that object was acquired.” 157

Diffuse axonal injury (DAI) is a common characteristic of nearly all traumatically

induced brain injury. DAI impacts cortical and subcortical pathways which serve the

distributed network of discrete cortical regions where features that define an object or

experience are stored. Both storage and recall of information are necessarily impacted by

DAI and made less efficient. DAI is most frequently seen in the long tracts of the midline

structures of the brain. 158 The cingulum is thought to be an important structure in the

transfer of information from distributed regions of the brain to association cortices for

integration. As such, the prevalence of DAI in the regions of the brain surrounding the

cingulum will necessarily impact information transfer.

Cognitive distance should be viewed as an important clinical entity for reestablishing

the individual’s ability to not only take in sensory information when it is readily available,

but also to call upon information when available sensory information is reduced or,

perhaps, absent. Burger and Muma 159 showed that cognitive distance was a factor in

aphasic and elderly nonaphasic individuals where performance was enhanced with objects

contrasted to performance with pictorials of the same objects. Muma 160 noted similar

discrepancies in performance with learning-disabled, mentally retarded, and autistic chil

dren. Muma reported improved performance by an autistic child when play with items

in a real house with a real kitchen was compared to play with items in a toy house. The

ability to abstractly identify features of objects or experiences that may be relevant to a

situation depends upon both the ability to call upon stored featural information and the

ability to use that information in both conventional and novel ways.

Intervention Techniques and Strategies

Individuals who have sustained traumatic brain injury exhibit cognitive disorders in the

areas of memory (long- and short-term), attention, processing speed, fluid reasoning,

categorization, and shifting. A variety of formal measures have been utilized to determine

the presence and extent of cognitive dysfunction such as the Woodcock Johnson-III (Tests

of Cognitive Abilities), 161 portions of the Scales for Cognitive Abilities for Traumatic Brain

Injury, 162 Muma Assessment Program, 163 and the Ross Information Processing Assess

ment. 164 Due to the nature of the brain injury, modifications to formal measures may be

required if the assessment is to be a true measurement of the individual's cognitive skills.

For example, time limits are often a part of the diagnostic tool. However, if the individual

is processing information at a much slower rate, then it would be appropriate to allow

for more processing time to complete tasks. Additionally, test items may be enlarged or

simplified to accommodate for visual or motor deficits. All modifications must be reported

in the initial evaluation report.

Conditions for Cognitive Rehabilitation

A number of factors should be considered in determining whether the individual is able

to benefit from cognitive rehabilitation. First, the system must be metabolically optimized

in order to properly support rehabilitation efforts and learning. At the earliest stages

after brain injury, metabolic function can be compromised by medications, cerebral

swelling, and neuroendocrine and biochemical imbalances. These factors, combined with

other system involvement commonly seen following TBI, 165 raise questions about the

influence of these systems on a recovering CNS. Pulmonary,

infectious, renal, hepatic,

or endocrine dysfunctions can all compromise cerebral function. General anesthesia can

delay recovery following TBI. Consequently, the overall medical stability of the individ

ual should be considered.

At the metabolic level, neuronal death within the CNS can be accompanied by the death

of surrounding cells in the form of anterograde and retrograde axonal degeneration.

Clearly, metabolic status impacts the extent of degenerative processes. 166 In some instances,

cells in the vicinity of those that have died will enter a state of metabolic paralysis. These

cells are only able to generate an action potential that is approximately one-seventh the

strength of a normal action potential. If metabolic compromise occurs while a cell is in a

state of metabolic paralysis, these cells will likely succumb even to metabolic events that

will not harm normally functioning cells.

Diffuse axonal injury (DAI) is a component to nearly all TBI 158 and DAI impacts not only

neurons, but axons, dendrites, glial structures, and vascular supply. Cellular death is, in

part, dependent upon the proximity of a sheared axon or dendrite to the cell body. Recovery

from axonal shearing occurs via axonal sprouting and collateral sprouting, the latter being

not dependent upon neuronal damage for elicitation. 167 Environmental enrichment bears

positively on the density of dendritic, glial, and vascular structures. 74,168 Rehabilitative

therapy should represent such enrichment. Cortical representation is continuously modu

lated in response to activity, behavior, and skill acquisition in normal function. Evidence

suggests that similar processes occur following injury, with adjacent areas taking over

function or via use of alternative pathways. 169 Changes which take place over long periods

of time probably are subserved by LTP, axonal regeneration, and sprouting.

Neuroendocrine dysfunction following TBI has been found in up to 40% of persons

tested. 170,171 Thyroid, pituitary, and adrenal function must be evaluated and treated prior

to undertaking cognitive rehabilitation. Thyroid and steroid hormone impact on neural

structures should be considered. Thyroid hormone regulates availability of cytoskeletal

proteins necessary for neuronal growth. 172 Concentrations of thyroid hormone receptors

have been found to be highest in the hippocampus, amygdala, and cerebral cortex of

rats. 173 Depletion of thyroid in adult rats results in a significant reduction in dendritic

density in the cerebral cortex. 174–176

Glucocorticoid receptors are prominent in the limbic system. 177 As a significant portion

of the information processing circuitry, in particular as it relates to the medial temporal

lobe complex, limbic function should be optimized. Estrogen has also been demonstrated

to impact dendritic density as well as acetylcholine synthesis. 178,179 In fact, estrogen therapy

has been shown to be effective in Alzheimer's disease. 180

Timing of rehabilitation intervention may impact efficacy of treatment as some inter

ventions do not appear to be effective if undertaken too early after injury. 181

Therapeutic Intervention

The interventions that follow have been designed to be approached in a hierarchical order

that is fashioned after the normal developmental sequences observed in linguistic and

cognitive development. The approaches attempt to respect the underlying physiology. The

techniques are remediative rather than compensatory in nature. There is relatively little

evidence to support the undertaking of certain compensatory approaches such as memory

notebooks, and there is little clear physiological rationale for such an approach if one

desires to build skill sets.

Attention is presumed to be the most basic of skills, though clearly, attentional function

cuts across all levels of cognitive function. Ability to identify and deal effectively with

perceptual features follows with progression to building categorizational skills. Cognitive

distance skills are addressed throughout the process. The assumption is that these skills

subserve most, if not all, other cognitive processes. Given the interrelated nature of cog

nitive processing, it is important to conduct treatment in an organized and hierarchical

fashion. It is important to complete all aspects of the

treatment protocol to be outlined, in

order and completely. Individuals who possess competencies in certain areas will progress

through those modules very quickly, though they will benefit from the developmentally

oriented approach. Pre- and posttreatment testing using broad measures of neuropsycho

logical function should be undertaken in order to document changes. Care should be taken

in choice of test instruments to ensure that tests which measure specific skill sets being

trained are not utilized; instead, broader, more generalized measures should be used.

Attention

One of the major cognitive deficits following traumatic brain injury is attention. This can

include complaints of inability to concentrate, being overly sensitive to noise, having

difficulty with task completion and multitasking. While therapists often recognize the

manifestation of attentional deficits, the underlying cause may be increasingly difficult to

conceptualize. For example, when an individual presents with “distractibility,” the ther

apist acknowledges the need to simplify the environment; however, this does not ade

quately address the holistic nature of the attentional disorder. Therefore, intervention

techniques targeting only one aspect of the disorder will not result in true consistent

improvements of the disorder as a whole. Additionally, the same is true for individuals

who display perseverative behaviors. The term perseveration

does not adequately commu

nicate the complex essence of the disorder.

A holistic approach to outlining the deficit is beneficial in the assessment and treatment

process. A distractible individual finds directing and/or maintaining a focus of attention

challenging. Therefore, the therapist must introduce activities designed to improve the

individual's ability to direct and/or maintain a focus of attention. Concepts and techniques

used to build attention skills include, but are not limited to, modification of environmental

stimuli (auditory and visual), increasing complexity of tasks, and cognitive distance.

Whereas there are several manners in which to address attention, designing a bot

tom-top therapeutic program allows for a developmental approach to building attention

skills. Taking this approach with all individuals exhibiting attentional deficits ensures that

all skills have been acquired in a developmental and sequential fashion, setting the foun

dation for higher level cognitive processes. At the base of the hierarchy lies focused

attention, the ability to direct one's attention to a specific stimulus. Once the individual

is capable of directing his/her attention, the person must be able to sustain that attention.

The higher levels include being able to selectively attend to a specific stimulus in the

presence of numerous auditory and visual distractors, alternating attention between two

or more tasks and, finally, simultaneously attending to two

or more tasks.

Keeping with the framework of attention, the environment must be initially modified.

Therapy should be performed in a controlled and enclosed environment where auditory

and visual stimuli are minimal. The treatment area should be designed such that fur

nishings/paraphernalia, lighting, and temperature can be managed. For example, an

individual exhibiting a severe attentional deficit may require an environment with little

visual and auditory stimuli present, such as a room without furniture, with low lighting,

and temperature adjusted to their liking. It may be necessary for the therapist to adjust

his/her clothing by wearing a smock to decrease color stimuli from clothing, remove

jewelry, etc.

Once the individual can perform simple therapeutic tasks in the controlled environment,

auditory and/or visual stimuli may be gradually introduced, moving from least to most

salient and advancing in one sensory modality at a time. For example, therapy for an

individual who enjoys rap/soul music may start with soft, relaxing music and then

progress to more energetic music at louder levels, ending with the type of music the

individual enjoys most and knows well. Similarly, initiating tasks in a sterile environment,

one without furniture and other visual distractions, may be necessary. Again, when the

individual is able to perform tasks in these settings,

visual stimuli can gradually be

introduced. It may be necessary for all disciplines to conduct therapy in a sensory-con

trolled environment.

An important part of the therapeutic process involves task complexing. Following the

framework of a bottom-top approach, tasks should start with physical activities and

gradually progress to mental activities. Physical activities can include sorting/categorizing

by iconic features such as color or size, whereas abstract activities can include symbolic

categorization.

The principles of cognitive distance, previously mentioned in this chapter, should also

be taken into account. Treatment should begin with the utilization of objects since objects

are most concrete. With an object, individuals have the ability to physically determine its

size, weight, and texture. As cognitive distance increases, use of pictorials (color, black

and white, and line drawing photographs) is introduced.

Keeping the preceding principles in mind, when working with a severely impaired

client, tasks should initially target physical activities with the use of objects. Complexity

is increased by adding more objects or lengthening the time required for engaging in tasks.

For example, the individual may be required to attend to tasks for 10 seconds. Once this

is achieved, the individual should be required to perform this task consistently with 80%

accuracy. The next level would involve increasing the length of time engaged in the activity.

Oftentimes, when working with severely impaired individuals, it is necessary to perform

a single therapeutic activity repeatedly for lengthy periods of time in order to build basic

attention skills. It is important to monitor accuracy and response time to determine when

it is appropriate to progress the individual to the next level of difficulty.

In spite of the degree of impairment, treatment should always be initiated in a stimulus

controlled environment and with a physical task. In this way, concentration is improved,

adequately preparing the individual for increasingly cognitively distant tasks. Once appro

priate performance accuracy and response times are achieved in a stimulus-controlled

environment, visual and auditory distractors can be gradually added, one modality at a

time, to increase environmental complexity. The therapeutic environment should contin

ually challenge the individual to the point where activities are performed in a stimulus

rich environment. It is imperative to ensure that data is collected throughout the thera

peutic process, including changes in environmental complexity. A general criterion for

increasing task and environmental complexities for physical activities is 90 to 100% accu

racy, whereas 80% accuracy is appropriate for mental activities. Time limits to perform

tasks can be modified depending on the individual’s physical limitations. For example,

when analyzing the task completion time, the therapist should note whether processing

speed was impacted by the existence of a physical impairment such as the use of a

nondominant hand.

There are various ways to systematically alter activities while regarding the three pri

mary variables of environmental stimulus, task complexity, and cognitive distance. Table

13.1 shows the order of therapeutic task presentation, including variables such as level of

task and environmental complexities. Treatment should begin with performing physical

tasks in a controlled and enclosed environment and ultimately progress to mental tasks

in a stimulus-rich environment.

A hierarchy of varying levels of attention should be utilized to strengthen concentration

skills. At the base of the hierarchy lies sustained attention. This is the individual's ability

to direct and maintain focus to a task across a period of time in a quiet environment.

Therapeutic activities addressing categorization, memory, visual and auditory processing,

direction following, shifting, and problem solving can be performed to address the devel

opment of attentional skills. Physical or concrete tasks, such as sorting, scanning, and

direction following, should be initiated first. Individuals with very poor attention may

start with simple auditory sustained attention or vigilance tasks. Such tasks require the

individual to listen to a string of stimuli targeting a specific number, letter, or word for

short periods of time. Once attention and accuracy improve, the length of time may be

extended. The same hierarchy can be utilized for visual sustained attention tasks. For

example, the individual can sort picture cards or hardware pieces into different categories.

Visual scanning or vigilance tasks can involve searching magazine articles for a target

word. Again, once this task has been mastered, the addition of multiple targets further

challenges attentional skills. Auditory scanning activities involve listening to stories or

passages and indicating a targeted response for a designated word and then increasing

the number of target words. Basic level strategies to improve accuracy on concrete tasks

include having the individual double-check his/her work.

Once individuals demonstrate the ability to maintain attention with good accuracy on

concrete tasks, more mental or abstract tasks can be implemented. Working memory tasks,

such as reordering a string of numbers from smallest to largest or in backward order, are

more cognitively challenging. Other working memory tasks include listening to sentences

and reorganizing the words within the sentences in alphabetical, reverse alphabetical, TABLE 13.1 Order of Distractor Presentation No Distractor Simple Auditory or Visual Distractor Multisensory Distractor Physical task Physical/Mental task Mental task 1 4 7 2 5 8 3 6 9

and/or progressive word length order. Mental math calculations can also be performed.

Higher level visual processing tasks, such as iconic store modules, can also be performed.

This task involves viewing a card with rows of letters for a brief period of time (2 seconds)

and then being able to recall a specified row. Several Attention Process Training 182 tasks

involving attention, processing, and categorization may be initiated. These tasks involve

listening to a string of words and identifying items which fit into a designated category

(e.g., round objects, pairs, related words, opposite words, etc.).

The next level in the attentional hierarchy is selective attention. It should be noted that

consistency must be established prior to progressing the individual to a higher distractor

level. Once the individual exhibits the ability to consistently perform tasks in a quiet and

controlled environment, a hierarchy of distractors should be introduced. Initially, noise

(e.g., a radio playing) should be presented in the controlled environment. Then, the

individual can be moved from the controlled environment to a familiar environment with

minimal distractions within the clinical setting. This would simulate a person in a living

or family room, providing the individual with the opportunity of a chance conversation

and/or just the presence of others nearby. To further challenge the attentional system, the

next level should require the individual to perform tasks in a highly distractible, familiar

setting (e.g., lobby, lounge, or gym areas). Finally, the individual should be placed in

unfamiliar and high traffic areas (e.g., mall, bowling alley, bus station, etc.).

The highest level of attention is divided attention, which requires the ability to attend

to two or more different tasks simultaneously. Individuals divide their attention while

driving, taking notes in class, performing household chores while watching television,

etc. Divided attention can be addressed in a variety of ways, such as performing previ

ously-mentioned concrete and abstract tasks while simultaneously answering a series of

questions differing in levels of complexity. For example, the individual may be required

to sort hardware pieces into categories while simultaneously responding to varying com

plexity of yes/no questions. The therapist can document response time to complete the

sorting task and the percentage of correct responses as well as delayed responses to yes/

no questions. In this way, processing speed can be monitored not only for task completion

but also for frequency of delayed responses.

Perseverative behaviors are another type of attentional deficit. A perseverative response

may be characterized as an inability to shift a focus of attention among perceptual features.

Therapeutic activities which decrease perceptual salience and establish the use of iconic

and symbolic feature identification skills usually result in a reduction of perseverative

responses. For example, the therapist may present an object to an individual and direct

his/her attention to various perceptual features of the object such as color, shape, con

struction, etc. Some perseverative behaviors, however, may be a result of perceptual

salience in other sensory domains, such as self-abuse as a result of sensory integration

deficits. Treatment for improving perceptual salience will be discussed later in this chapter.

Attentional deficits also include problems with vigilance, referring to the ability to sustain

a focus of attention and regulate incoming information for a particular set of features. For

an individual to be successful, he/she must first be able to quickly take in large amounts

of visual and/or auditory information, resisting distractions of extraneous stimuli, and

then be able to filter that information for the preferred feature(s). This process requires

quick processing speed and increased cognitive distant skills. Thus, therapy should address

sustaining attention in a multisensory environment and building cognitive distance skills.

Cognitive shift refers to the ability to alternate attention from one activity to another with

the least amount of interference to sensory stores, task sequencing, and task accuracy. This

cognitive skill is hierarchically more complex and often impaired in the individual with

traumatic brain injury. Basic level attention should be relatively intact prior to addressing

cognitive shift skills.

Cognitive shift activities should adhere to the concepts of task complexity and presen

tation of external sensory stimuli. Activities should begin with two simple physical tasks,

requiring the individual to shift from one activity to the other and back. Data collection

includes response time to shift between tasks and accuracy of task completion. Once the

individual demonstrates competency with physical tasks, task complexity should then

progress to physical and mental, then to mental only. Tasks can be further complicated

with the addition of external sensory stimuli. Table 13.1 can be referred to for the order

of distractor presentation.

Physical tasks include simple rote motor tasks such as linking chains together or sorting

objects by a designated iconic feature (e.g., color, shape, size, weight, etc.). Mental tasks

include sorting picture or word cards by categories, sorting objects by a designated sym

bolic feature (e.g., things that provide light, things that are used for scooping, things that

make noise, etc.), performing various math calculations, etc. Recalling a sequence of shifts

can be added for increased complexity. A telephone book scanning activity can be per

formed involving the individual in locating addresses and phone numbers of businesses

in a specified order. Other tasks addressing shifting can be located in the Attention Process

Training kit. 182 For example, one task may be to listen to a string of words and alternate

between identifying fruits and articles of clothing throughout the task. Higher level shift

ing tasks address memory, initiation, and time management by incorporating visual and

self-regulating tasks into the treatment program. 182 Now, the individual no longer has an

auditory cue from the therapist but rather is presented with a visual cue and/or a specified

time interval to shift. Two or three sets of instructions are told to the individual. Visual

tasks require the individual to shift when presented with a visual signal. For example,

when performing a visual scanning activity, visual marks should be placed randomly

throughout the page. When the individual arrives at a visual mark, he/she must first

recognize the mark to be a symbol, recall which set of instructions to perform, and then

initiate the task to be performed. Self-regulating tasks require the individual to self-initiate

alternating between two tasks at specified time intervals by monitoring time on a stop

watch. For example, when provided with math worksheets, addition tasks are performed

initially. The individual performs the math calculations while simultaneously monitoring

time. After the established time interval (e.g., every 30 seconds), the individual must then

recall and initiate the next set of instructions. These tasks can be performed with the

hierarchy of distractors presented in Table 13.1.

Feature Identification

A therapeutic tool known as the Cognition Module can be used to improve overall cognitive

functioning in a structured and developmental manner. At the first level of feature iden

tification, the individual is trained to attend to and identify different perceptual features

of real objects. Perceptual features can be broken down into seven iconic and one symbolic

feature. Iconic features consist of, but are not limited to, color, shape, construction, size,

weight, texture, and detail. The symbolic feature requires the individual to identify the

function of objects. The list of perceptual features reflects some of the “linguistic univer

sals” referred to by Rosch. 105

Cognitive distance is introduced at Level I. The individual describes the iconic and

symbolic features of real objects. Cognitive distance is built by progressing the individual

through a hierarchy of sublevels consisting of objects, color photographs of objects, black

and white photographs of objects, line drawings of objects, written words, and, ultimately,

spoken words. When objects are no longer physically represented, the individual is

required to rely on mental representation of objects.

Initially, a checklist of the eight features may be required. Once the individual begins

to learn the features in an organized manner, the checklist can be faded. Criterion for

successful completion at this level is individually based. While it is important to monitor

accuracy at each sublevel, the therapist should keep in mind the broader scope of perfor

mance. Therefore, a comparison of the overall performance

between sublevel objects and

spoken words should determine whether the individual is ready to progress to the next

level. For example, individuals may demonstrate difficulty at lower sublevels; however,

through repetition, accuracy may improve at the spoken word sublevel. Because the

individual has achieved greater task accuracy at a more cognitively distant task, it can be

inferred that the individual's level of cognitive functioning has improved. Response times

should be fairly quick; however, should not be a criterion for progression to the next level

as individuals with brain injury commonly present with slower processing speed.

Level II requires the individual to expand feature identification skills. The individual

must identify the eight features one by one and also provide an extended feature. For

example, when describing a stop sign, the individual must verbalize that the stop sign is

red and must identify another object which is also red, such as an apple. Responses

provided must be different for each of the eight extended features, thereby maximizing

categorization, word finding, and memory skills. Additionally, the extended feature

response should not be an object within the individual's visual field. The cognitive distance

hierarchy ranging from real objects to spoken words should again be followed.

Level III focuses on abstract negation. The purpose of this section is to further expand

feature identification skills through negative categorization. At this level, the individual

is required to identify the eight perceptual features of the object in terms of what the object

is not and then state another object which does not have the same characteristics. For

example, when describing a stop sign, the individual must verbalize that the stop sign is

not blue and must identify another object which is not blue, such as the sun. Again, the

cognitive distance hierarchy ranging from real objects to spoken words should be followed.

It is often difficult for individuals with traumatic brain injury to provide extended and

negative feature identification secondary to decreased visual imagery skills. Visual imag

ery is important in everyday life to assist with episodic memory, abstract thinking, and

problem solving. Often, individuals exhibit a limited repertoire of responses secondary to

decreased visual imagery, word finding, and categorization skills. Several strategies can

be used to assist with these skills. For example, visual imagery cues can assist with

visualizing familiar places, such as different rooms in a house, playground, garage, mall,

or office. If the individual is unable to verbalize an extended feature, further visual and/

or semantic cues may be utilized. For example, if the individual was unable to visualize

something in a kitchen which was also yellow, a cue to think of a fruit or something in a

refrigerator may help trigger a response. With an increase in cognitive distance, for exam

ple, at the spoken word level, the inability to recall a target item is often observed. Cuing

the individual to recall previous responses may be beneficial. However, providing struc

ture to the task, such as having the individual state the name of the object prior to

describing each feature, is usually more effective.

A higher level visualization task may be used to have the individual describe a given

experience. Initially, it may be necessary to target familiar experiences, such as a child's

birthday party, Christmas Eve, hobbies, etc. As the individual's visual imagery skills

improve, increasing the cognitive distance by having the individual describe situations or

experiences he/she is not familiar with can be used.

Mental flexibility is another skill which is addressed throughout the cognition module.

The ability to perform negative categorization is significantly impacted by the individuals'

mental flexibility, visual imagery, and cognitive distance skills. When provided with an

object (e.g., a banana), the individual with reduced mental flexibility will often say "The

color is not yellow" when, in fact, it is. With cues such as verbalizing colors other than

yellow, and repetition of the task, mental flexibility is noted to improve.

Categorization

The next level of the Cognition Module requires the individual to identify iconic and

symbolic features of objects grouped together. Each

sublevel is divided into two parts. As

suggested by the cognitive distance hierarchy, activities begin with real objects arranged

in three rows with three objects in each row. The first part requires the individual to identify

one perceptual feature in common across the three rows. For example, if rows of red, yellow,

and blue objects are set on a table, the individual must recognize the common perceptual

feature as being “color.” The next part of this level requires the individual to identify three

different perceptual features. Therefore, each row targets a different feature. For example,

the first row can consist of items of similar “color,” such as a fork, spoon, and knife. Another

row can consist of items of similar “shape,” such as a ball, plate, and tire. The last row can

consist of items of similar “function,” such as a flashlight, candle, and penlight. To further

address mental flexibility, the therapist can ask the individual to provide additional

responses. For example, in addition to color, a fork, spoon, and knife have the same shape,

construction, size, texture, detail, and function. At this level, the cognitive distance hierarchy

progresses to written words and does not include spoken words.

The next level of the Cognition Module requires symbolic categorization. For some

individuals, symbolic categorization may be less difficult than iconic categorization.

Research indicates that symbolic categorization may be more easily stored. 184 However,

this may not be reflective of an intact feature processing system. Therefore, while it may

appear that the individual has a basic understanding of symbolic features, this may only

be a cursory understanding of common functional attributes of objects and not a true

representation of proficiency in feature identification and categorization skills.

The purpose of this level is to develop the ability to categorize objects by function. This

level consists of three steps and three levels of cognitive distance (color photographs of

objects, black and white photographs of objects, and spoken word). If photographs are

too abstract for an individual to begin with, it may be necessary to first use real objects.

When shown a photograph of an object, the first two steps are to identify the traditional

function of the object and the category to which it belongs. The next step involves ver

balizing three alternate functions of the object. This includes functions the object can

perform but are not typically done with the object. For the last step, the individual must

shift his/her perspective and identify three functions the object cannot be used to perform.

At this level, the individual must integrate all iconic and symbolic features to think of

alternative and negative functions of objects. For example, alternative functions of a fork

may be to dig with, stir with, scratch with, use as a hair clip, use to poke holes with, or

used as a screwdriver. In order to visualize these functions, analysis and synthesis of iconic

and symbolic features must occur. Therefore, since the construction of the fork is strong

and hard and it has a long, flat handle and sharp tines, it should be able to carry out the

functions mentioned previously. For individuals who exhibit poor mental flexibility, it

may be necessary to bring their attention to the eight features of the target object. The

same cues may be used for identifying negative functions of objects. Additionally, having

the individual recall the traditional function of the object and then determining other

objects which do not serve the same purpose may assist with negative categorization.

Again, therapists should closely monitor individuals' responses so as not to allow for

repetitive responses and, instead, to facilitate a wide spectrum of responses.

Processing speed can be monitored by timing the individual's response times to the

different levels of the Cognition Module. When progressing to higher levels or increasing

the complexity of tasks, response times may become lengthier. However, it is expected

that response times improve with repetition. When comparing performance on a lower

sublevel to a higher sublevel (objects, spoken word), if response times maintain, it can be

inferred that processing speed actually improved secondary to the increased cognitive

demands of the higher sublevel. Other tasks to help improve processing speed include

performing word fluency activities such as naming as many

items within a concrete

category (animals, modes of transportation, occupations, etc.) or an abstract category

(naming words beginning with a specific letter of the alphabet).

The Cognition Module assists with the overall thought organization process in numerous

ways. The initial task is to learn the iconic and symbolic features in an organized manner.

Therefore, it is important to consistently cue the individual to a specific order allowing for

improved organization and efficiency of information processing. Cognitive skills such as

attention, feature identification, categorization, cognitive shift, and cognitive distance are

required simultaneously. Perceptual salience (an excessive amount of attention to a particular

perceptual feature) can be refrained from through the use of seven iconic and one symbolic

feature. Categorization skills are optimized throughout the Module by initially performing

feature identification tasks using iconic and symbolic features. Each level consists of sub

levels which address cognitive distance, requiring the individual to rely heavily on mental

representation of objects by diminishing the amount of physical information presented.

The therapeutic tools reviewed in this chapter are designed to reestablish basic level

cognitive abilities. Higher level thought processes and memory cannot be adequately

addressed if basic level cognitive skills are not first put into place. The Cognition Module

is not meant to be the only treatment activity; rather, it is an essential part of the overall

rehabilitation program. Different activities can be used to develop attentional and cogni

tive shift skills.

Summary

Cognitive rehabilitation for people with TBI is a crucial component of the rehabilitative

process. While compensatory practices possess some appeal due to the financial and length

of stay constraints imposed upon treatment, remediative practices should be undertaken

for cognitive deficits following TBI. Compensatory strategies should only be introduced

as tools to supplement cognitive function. Remediative practices must be based upon

sound theoretical constructs and be in harmony with known functional attributes of the

neurological system. Likewise, cognitive rehabilitation must be approached like any other

acquired skill set, that is, hierarchically or developmentally. The interrelational nature of

cognitive functions must be respected in undertaking therapeutic interventions. Finally,

broadly-based cognitive evaluation should be undertaken before and after treatment in

order to evaluate and document improved function across cognitive domains.

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14

The Use of Applied Behavior Analysis in Traumatic

Brain Injury Rehabilitation

Craig S. Persel and Chris H. Persel

CONTENTS

Introduction

The issue of maladaptive behavior, as an associated consequence of traumatic brain injury

(TBI), is one of the most important aspects in brain injury rehabilitation since behavior

disorders often represent a significant barrier to effective rehabilitation and functional

outcome. 1,2 Changes in personality and behavior are also familiar consequences of TBI. 3-7

In the acute stages of recovery from TBI, it is common for a person to exhibit a variety of

behavior disorders. 8 Such behavioral disturbances are considered by many to be a phase

of normal recovery of cognition. 9–10 When these behaviors continue beyond acute recovery,

however, and begin to form standard patterns of interaction with others, genuine concern

is warranted. Behavioral disorders are disturbing to families and staff, 11 disruptive to

therapy, 12 and can jeopardize client safety; 13 thus, effective behavior analysis can be a

powerful tool for teaching people more positive ways of interacting with their environment.

The purpose of this chapter is to clearly illustrate and simplify the concepts, techniques,

and uses of applied behavior analysis with those suffering from traumatic brain injury.

Although it is assumed that the reader has some basic understanding and/or experience

with applied behavior analysis, difficult technical terms have been avoided wherever

possible. When only technical jargon will suffice to effectively explain or label a particular

concept or method, the term is defined.

In keeping with the more practical nature of this chapter, a couple of areas related to

applied behavior analysis will not be covered. First, single-subject research design will

not be discussed. Although single-subject research is important to the scientific advance

ment of applied behavior analysis, we feel that it requires special attention that is beyond

the scope of this chapter. Second, there will be no instruction for measuring inter-rater

reliability. Although substantiating agreement between independent observers is impor

tant in determining reliability of data, like single-subject research design, it falls within

the boundaries of research and not necessarily the practical application of behavior tech

nology. Collecting inter-rater data is also a very time-consuming and expensive procedure

and not one to which most rehabilitation facilities are willing to devote resources.

Included in this chapter are the tools necessary to organize and carry out effective

behavior programming for people with traumatic brain injury. The person with traumatic

brain injury represents a special challenge to rehabilitation professionals and family mem

bers. Maladaptive behavior is only one facet of a complex neurobehavioral picture. Cog

nitive, physical, and emotional changes resulting from brain injury must be taken into

consideration in the overall behavioral treatment of the client with TBI. Behavioral treat

ment does not work alone. Behavioral programming is most effective when it is integrated

with a comprehensive rehabilitation program. For example, as a client's information

processing skills increase, so does the ability to deal with cognitively challenging situa

tions. As adjustment to disability improves, the client becomes better equipped to face the

loss of functional ability. As motor and perceptual skills develop, so does the opportunity

to live more independently. Behavior programs provide a

“meta-structure” within which

the various therapeutic disciplines are carried out.

The challenge is to rehabilitate people with traumatic brain injury in the least restrictive

setting possible. 14 Hopefully, this chapter will provide therapists, educators, family mem

bers, and other involved people with the materials and methods necessary to help clients

with traumatic brain injury regain their highest level of independence.

The Brain–Behavior Relationship

As many readers know, traumatic brain injury can have many serious consequences.

Physical, cognitive-communicative, functional, and psychological skills can be severely

affected. Common areas of physical deficit are ambulation, balance and coordination, fine

motor skills, strength, and endurance. 15 Cognitive deficits can encompass language and

communication, information processing, memory, and perceptual skills. 16 Functional skills

such as hygiene and grooming, dressing, and money management, to name but a few, are

usually affected. 17 A person’s psychological status is also stressed. Depression, anxiety,

adjustment to disability, and sexuality issues are frequently encountered by people with

TBI. 18–20 Any or all of these difficulties may bear directly on the behavior of a client. Recent

studies have even linked cognitive recovery with the degree of psychopathology. 21,22 Com

pound these with medical issues such as location of damage, severity of injury, seizure

disorders, preinjury characteristics of personality, 23-25 intelligence and learning style, and

a complex neurobehavioral picture is created.

Brain injury can occur in a number of ways. Traumatic brain injuries, as opposed to

stroke, Alzheimer's, Parkinson's, etc., typically result from accidents in which the head

strikes an object (e.g., windshield, ground). This is the most common type of traumatic

brain injury. However, other brain injuries, such as those caused by insufficient oxygen

(e.g., cardiac arrest, near drowning), poisoning (e.g., toxic fumes), or infection (e.g., enceph

alitis) can cause similar deficits. 26,27 Many of the most severely behaviorally-challenged

clients we have worked with over the years were injured in these "less common" ways.

Mild traumatic brain injury (MTBI), another important category of brain injury, is char

acterized by one or more of the following symptoms: a brief loss of consciousness, loss

of memory immediately before or after the injury, any alteration in mental state at the

time of the accident, or focal neurological deficits. 28 In many MTBI cases, the person is

only "dazed," yet continues to endure chronic functional difficulties. 29 Some people suffer

long-term effects known as postconcussion syndrome (PCS). 30 Persons suffering from PCS

can experience subtle, yet significant, changes in cognition and personality 31 and even

experience seizure-like symptoms. 32

All of these brain injuries will influence behavior. The relationship between the brain

and behavior is very complex and beyond the scope of this chapter to comprehensively

review; however, it is important for those involved in behavioral programming to have

at least a rudimentary understanding of this association because of its significant, under

lying effect on behavior. 33 Problems such as denial, apathy, emotional lability, impulsivity,

frustration, intolerance, lack of insight, inflexibility, perseveration, confabulation, lack of

initiation, poor judgment and reasoning, and decreased social skills can often be linked

to specific areas of brain damage. 34–36

To begin with, most TBIs result in widespread damage to the brain. This is because the

brain is “bounced” and “twisted” inside the skull during the impact of an accident. Nerve

cells are torn from one another in what is known as diffuse axonal injury. 37 Localized damage

also occurs when the brain is forced against the skull during the “acceleration-decelera

tion” phase of an accident. The brain stem, limbic system, frontal lobe, and temporal lobes

are particularly vulnerable in this type of injury.

The brain stem is located at the base of the brain near bony areas. Aside from regulating

basic arousal and vegetative functions, the brain stem is involved in attention and, thus,

short-term memory skills. Deficits to these areas can lead to disorientation, frustration, and

anger. The limbic system, higher up in the brain, is

associated with emotions and affect.

Disorders of the limbic system can result in explosive rage. 38,39 Connected to the limbic

system are the temporal lobes, which are involved in many cognitive skills such as memory,

language, and sequencing. Damage to the temporal lobes, or seizures in this region, have

been associated with a number of behavioral disorders. 40 The frontal lobe is almost always

injured due to its size (taking up 29% of total cortical space) and its location near the front

of the cranium. 41 The frontal lobe, like the temporal lobes, is involved in many cognitive

functions. It is also considered our emotional control center and home of the personality. 42

Damage to this area, resulting in what is sometimes called frontal lobe syndrome, can result

in decreased judgment and increased impulsivity, irritability, and aggression. 43

Medication

It is now widely recognized that pharmacological intervention for behavioral disorders

with the postacute client with TBI is not necessarily the treatment of choice. 44 It is much

more desirable to implement behavior programs that manipulate the environment and

help the client develop self-control. 45 Many medications used in the past with other

populations to combat behavior problems may elicit more agitation from the traumatically

brain-injured person or confuse them at a time when attention and arousal are often

already problematic. 46–48 Recent studies have indicated

that disorientation, which can be

compounded by medications, is closely related to both physical and verbal aggression

with the traumatically brain injured. 49 Although a number of medications, such as halo

peridol, amantadine, and propranolol, have proven useful in treating behavior problems

in the early stages of recovery from TBI, 50–61 the brain-injured person may experience

more cognitive confusion and react with increased agitation. The use of stimulants, such

as methylphenidate, to reduce behavior problems have shown mixed results. 62,63 This is

not to say that medications should never be used, but there should be careful monitoring

of the interactive effects of medication with behavior, as well as awareness of the potential

for over-sedation, increased seizure activity, 64 or chronic overuse resulting in permanent

side effects for the client, such as tardive dyskinesia, motor restlessness, and others. 65–67

The treatment setting may be such that pharmacological management is necessary. In

those unfortunate circumstances, medications should be closely monitored because they

can often lose effectiveness. The choice then may be between prescribing no medication,

trial periods of alternative medications, or medication dosages to the point of sedation.

Once a person has progressed beyond acute hospitalization, many behavior medications

can be tapered while closely observing the person’s behavior within the structure of a

behavior program. 68 This approach makes it much easier to reach an educated decision

regarding continuation of the medication.

Ethics

Applied behavior analysis (sometimes referred to as behavior modification) has always been

plagued by controversy. The mere mention of behavior modification is usually enough to

elicit a strong response from professionals and the public alike. For many, the use of

behavior modification principles and techniques is, in some way, “forcing” a person to

change against his or her will. Deep-rooted concepts regarding democracy, free will, and

humanism are threatened by the notion of applying scientific methods to change human

behavior.

What many of us fail to realize is that our behavior is continuously being modified.

Influences from politicians and parents to television and teachers help shape and pattern

our behavior. Applying behavior analysis is not meant to assume an authoritarian role

over a person but to analyze the relationship between events and behavior. The goal is to

increase, not decrease, personal freedom by expanding the behavioral options available

to the person, thereby enhancing opportunities for community, social, and family inter

action. Such opportunities are severely restricted for people with behavior problems.

Applied behavior analysis is a structured technique for reducing behaviors that limit

independence and increase actions that empower a person.

Of course, misuse of applied behavior analysis has occurred, and punishment techniques

have been overused. However, the notion that applied behavior analysis should not be

used, or more specifically, that punishment should be severely limited, is neither rational

nor practical. The alternatives to applied behavior analysis are typically medication, 69

physical restraint, 70,71 or life in a locked institution, all of which carry their own ethical

ramifications. 72 Applied behavior analysis, used within proper guidelines, is an effective

and humane method for reducing maladaptive behaviors and teaching new skills.

A number of authors and governmental agencies, such as the California Department of

Developmental Services, have published guidelines for positive behavioral services and

procedures. Alboreto and Troutman 73 outlined a number of basic concepts regarding the

ethical use of behavior analysis.

• Least restrictive setting — clients should be living in the least restrictive setting and be provided a therapeutic environment that is safe, fun, and offers access to a variety of activities. 74 Recreational activities and social/community involvement are essential elements of an effective rehabilitation environment.

• Benefits the client — the goal of any behavior procedure should be to benefit the client and protect their welfare, not to improve staff convenience. For example, pharmacological management of behavior is very often used with the latter objective in mind.

• Competent and trained staff — clients should be treated by competent staff members, trained and supervised by

experienced professionals. Behavior programs are only as sound as the staff that implements them.

• Teach functional skills — clients should be taught functional skills to replace maladaptive behaviors. 75 Behavior problems may be a result of the client's reduced ability to perform independently in his/her environment or of a decreased behavioral repertoire.

• Systematic program evaluation — behavior programs should be methodically evaluated for effectiveness. Data analysis is a crucial component of this process.

• Reinforcement program priority — behavior programs that include punishers should be used only after other reinforcement programs have been exhausted. Long-term maintenance and generalization are only two of many reasons why reinforcement programs are the procedure of first choice.

We have added some additional guidelines to consider:

• Least aversive procedure — when two programs are deemed effective, the least aversive procedure should be used. Aversive procedures typically produce more negative side effects.

• Appropriate target behaviors — make certain that behaviors determined as "maladaptive" are not based on personal values of staff. The inappropriateness of many behaviors is subjective.

• Monitor side effects — while reducing target behaviors, closely observe for an increase in other inappropriate behaviors. This is particularly important when implementing an aversive procedure.

• Reasonable intervention procedure — all maladaptive behaviors exhibit a "degree" of inappropriateness that have implications for the type of procedure recommended. For example, verbal aggression would generally not require a physical restraint.

As the number of people with traumatic brain injury increases, rehabilitation programs

will face difficult ethical questions. 76 Accountability is the key. All facilities carrying out

behavior programs should have clear goals, comprehensive

data collection, and the ability

to provide rationale for starting, continuing, and ending a behavior program. This includes

a means of closely monitoring all the previously discussed guidelines to operate ethically

sound behavior programs. Applied behavior analysis is a powerful tool for changing

behavior. If used correctly, clients are given the opportunity to relearn many lost skills

and to become as independent as possible in the shortest amount of time.

General Management Guidelines

The environmental conditions posed by treatment and care settings for people with

traumatic brain injury can have significant impact on behavior. Organizing the therapeu

tic setting and carefully planning an approach to the client can increase opportunities

for successful learning and decrease the chances of a behavioral episode. The following

are ten recommendations for structuring a positive learning environment for the person

with TBI:

• Allow for rest time — people with TBI, especially in the initial stages of recovery, can be extremely fatigued. 77 Monitor the person's behavior and schedule rest periods during those times related to an increased probability of problem behavior. A word of warning though — do not forget to reduce these rest periods as the person recovers and gains endurance.

• Keep the environment simple — people with TBI are easily overstimulated by their surroundings. The inability to filter out external stimuli can lead to confusion and increase the chances of a behavioral episode. Interruptions and distractions should be kept to a minimum and the therapy session format kept consistent.

• Keep instructions simple — instructions, prompts, and cues should be kept as concrete and simple as possible. This may mean writing down instructions as well as stating them. It may also mean keeping verbal prompts to a minimum. Many people with TBI have difficulty processing auditory information. Instead, try using nonverbal instruction techniques such as modeling (demonstrating) or gesturing.

• Give feedback and set goals — self-monitoring skills can be diminished with the traumatically brain injured. 78 They must rely on others to provide feedback until the ability is relearned. 79,80 Provide frequent and consistent positive feedback of success. Most people respond well to supportive encouragement. Setting goals helps the client predict where he/she is "going" with therapy and provides him/ her with some incentive for completing therapeutic tasks. 81,82

• Be calm and redirect to task — people who cannot control their own behavior need others to demonstrate and produce a stable, nonthreatening environment. Remaining calm while the client is escalated can help reduce agitation and decrease the chances of inadvertently reinforcing the client with attention for acting out. A related method gaining widespread attention, "gentle teaching" uses a variation of this approach as a central technique. 83,84 It involves ignoring the exhibited behavior, redirecting the client to the task, 85 and rewarding successful performance. However, "gentle teaching's" rather unstructured approach, lack of scientific support, and philosophical assumptions contrast sharply with traditional behavior analysis. 86

• Provide choices — research indicates that providing clients with choices can reduce serious behavior problems. 87 Giving them opportunities to choose tasks can be an effective technique when working with the traumatically brain injured. It allows clients an element of freedom and a measure of control over their environment. Some clients, however, require "limited" choices that decrease the range of decisions so that they are not overwhelmed or left with an open-ended opportunity to say "no."

• Decrease chance of failure — do not work above the client's level of ability. This will only lead to frustration and increase the chance of a behavioral episode. Try to keep the success rate above 80%. This ensures that the client is challenged, while at the same time feeling successful. A variation of this technique is

known as behavioral momentum. This procedure involves presenting tasks with which the client is likely to comply immediately before presenting tasks that are likely to be more problematic. 88 This establishes a high rate of performance (and, hopefully, reinforcement) just prior to more difficult tasks, with the idea that compliance will be more likely to continue.

• Vary activities — although there is a need for consistency and repetition when working with the person who is traumatically brain injured, there is also a need to keep the session interesting. Therapy can become boring and frustrating if the same tasks are endlessly repeated. Vary the activities to maintain interest and increase success. Also, try interspersing easy tasks (those likely to be done correctly) among more difficult tasks. Studies have shown this procedure to be effective in reducing the likelihood of aggression. 89

• Overplan — do not approach a session with only a few ideas or activities to complete. There will be days when the client finishes everything quickly and you are left with nothing else to do, or the client may be having a difficult time (e.g., more confused) and you need some alternate activities more suited to the functioning of the client that day. Be prepared for anything, and confronting a behavior problem will be less likely.

• Task-analyze — try dividing a task into smaller steps. Each step can then be treated as a complete task. Functional skills, such as dressing, hygiene and grooming, etc., are particularly suited to this approach; 90 however, just about any activity or task can be divided into its component parts.

Basic Principles

The basic principles of applied behavior analysis are relatively easy to understand. Within

a short time, most of the fundamental concepts of behavior analysis, and what is termed

operant conditioning, can be grasped. Simply put, behavior analysis focuses on the behavior

of people and the environmental influences that precede and follow the behavior, as

opposed to their thoughts and feelings. We can refer to

these factors as a person’s behavioral

condition. The components of a person’s behavioral condition are the antecedent, the behav

ior, and the consequence. Behavior analysis attempts to explain the relationship between

these components. This relationship is referred to as a contingency. For example, reinforcers

are delivered “contingent” upon performance of a certain behavior.

Antecedent

To begin with, all target behaviors (those behaviors to be modified) are preceded by some

event in the person’s environment. This preceding event is called the antecedent. This

event can be a broad-based condition that influences behavior (setting event) or a more

specific stimulus (stimulus event). In a manner of speaking, the setting event “sets” the

stage for the occurrence of the behavior, e.g., fatigue resulting from lack of sleep may be

a setting event for behavior problems the next day. 91 Stimulus events are more discrete.

For example, a phone ringing means that a behavior (answering the phone) will be

reinforced (talking to someone). The antecedent may be an event occurring externally to

the person (e.g., lighting, noises, instructions) or internally to the person (e.g., headache,

flu, seizure, medication). One word of caution — even though one has to take into

consideration internal antecedents to behavior, the focus of behavior analysis is always

on those factors external to the person. Internal

antecedents to behavior (e.g., vestibular

sensitivity, headache) are best dealt with via medical and therapeutic disciplines within

the rehabilitation regimen.

It is important for staff members to realize that external antecedents are under staff

control. Tone of voice, body language, therapeutic demands, and physical setting are some

of the variables that staff can adjust to decrease the likelihood of a behavioral episode. 92,93

Necessary tasks, however, should not be avoided simply because they can, at times, be

antecedents to behavioral episodes. Continued progress toward independence is often

reliant on the person's participation in such tasks at a very intense level of rehabilitation.

Avoidance of difficult therapy tasks to reduce "problem" behaviors can be very seductive

to staff, but it may simultaneously teach the client to exhibit more negative behavior as a

means of escaping the rigorous demands of therapy. 94 Therapists and behavioral program

mers need to survey all environmental antecedents and weigh the advantages and disad

vantages of the therapeutic regimen before eliminating or modifying any requirements.

Lowering therapeutic expectations because of potential acting-out by the person may

negatively impact the person's long-term independence.

Likewise, internal antecedents should be evaluated for other potential treatments that

may assist in the person's behavioral improvement. These should not be viewed as reasons

to avoid implementation of a behavioral program. Let us say, for example, that a person

has a vestibular lesion that causes him to be quite sensitive to motion. One day, after a

motor vehicle trip, the person is not feeling well and, during therapy, is quite escalated

and trying to avoid participation. He strikes a staff member. Some therapists would be

inclined to believe that the individual did not feel well and that the therapist who was

struck should not have persisted in treatment. While this reasoning may seem sound, it

is limited by the fact that under no circumstances is it acceptable to strike another person.

Thus, the behavioral program would include recognition of the contribution of the vesti

bular component but would also include a means for de-escalating behavioral agitation

and for responding to physical aggression.

Behavior

An antecedent event is followed by the occurrence of a behavior. If the behavior has been

chosen for modification, to either increase or decrease, it is referred to as the target behavior.

People with traumatic brain injury can exhibit a wide variety of behaviors that require

intervention. A target behavior must be observable and immediately recordable. The target

behavior must also be very clearly defined in terms of observable actions. 95 This is known

as an operational definition. Two therapists, for instance, can have very different ideas about

what constitutes a behavior. For example, take the behavior of physical aggression. Does

it include spitting or threatening? What about self-injurious behavior? Should throwing

or breaking objects be included? Clear and concise definitions of target behaviors are critical

to identifying the behaviors and to implementing programs consistently.

People with traumatic brain injury can exhibit a number of maladaptive behaviors.

Behavior disorders (Table 14.1) can be categorized as those of excess (occurring too often),

those of deficit (not occurring often enough), and those of stimulus control (not occurring

in the correct context).

Excess behaviors tend to be the most noticeable and, thus, receive the most attention

from other persons. Examples of excess behavioral disorders typically seen with the

traumatically brain injured are noncompliance, 96 angry language, 97 hoarding, escaping, 98

physical aggression, 99 socially inappropriate talk, 100 impulsivity, and tardiness. 101 Some

other excess behaviors that may be exhibited are sexually aberrant behavior, perseveration,

self-abuse, stealing, property destruction, and overfamiliarity. These behaviors can be

disruptive to other clients, can frighten others, and/or increase the risk of injury during

treatment, thus increasing exposure to legal liability. If severe enough, they can result in

a person not receiving proper therapeutic services or, worse yet, being isolated from family,

friends, and community in an institutional setting.

Common deficit behaviors of people with traumatic brain injury are activities of daily

living, 102 communication, 103 social skills, 104,105 and initiation. Rehabilitation of these skills

is of paramount importance in a client's progress toward more independent living. It is

also important that excess behaviors that have been eliminated or reduced through struc

tured behavioral programming be replaced with more appropriate behaviors occurring at

a proper rate. Such behaviors will allow the client access to a wider range of naturally

occurring reinforcers, thereby increasing the opportunity for successful generalization and

maintenance of skills.

Stimulus control disorders can occur with any behavior that occurs in the wrong situ

ation (e.g., brushing teeth, hugging another person, etc.). For example, the behavior may

occur at the wrong time or place, or with the wrong person. The problem of stimulus

control as a behavioral disorder has not been fully explored in TBI literature even though

there are indications it is a very common problem with this population. Most people with

traumatic brain injury are adults who have already acquired many life skills. Their injury

does not necessarily result in loss of the skill but, seemingly, loss of knowledge of the

more abstract "situation" in which the behavior should occur. Antecedent or stimulus

control behavior programs are tailor-made to positively

impact these disorders.

Consequence

Target behaviors are followed by a consequent event that is going to affect the future rate,

duration, and/or intensity of the behavior. Consequences are either “reinforcing” or TABLE 14.1 Behavior Categories and Examples Excess Deficit Stimulus Control Noncompliance Angry language Socially inappropriate talk Disinhibition Physical aggression Escaping Hoarding Tardiness Impulsivity Sexually aberrant Perseveration Self-abuse Stealing Property destruction Overfamiliarity Compliance Self-control Social skills Timeliness Initiation ADLs Overfamiliarity Public sexual behavior Public grooming behavior Public discussion of private events Undressing in public

“punishing.” Reinforcers will increase and punishers will decrease the future occurrence

of the target behavior. Consequences do not inherently possess the quality of being either

a reinforcer or a punisher. The effect of the consequent event on the frequency of a target

behavior (i.e., whether it increases or decreases the target behavior) defines it as a reinforcer

or a punisher. Let us use chocolate as an example. For a person who likes chocolate, its

use after the occurrence of a behavior may increase the frequency of that behavior, thereby

defining it as a reinforcer. For a person who dislikes chocolate, its use may actually decrease

the frequency of a target behavior, thus defining it as a punisher.

There are two types of positive reinforcers: primary and secondary. Primary reinforcers

do not require any type of special training to develop their value. Food and water are two

examples of primary reinforcers. Secondary reinforcers have

gained their value through

learning. Examples of secondary reinforcers are praise and money. Secondary reinforcers

can be developed by pairing them with a primary reinforcer; for example, if praise is not

a reinforcer for a person and food is, food can be paired with praise during behavioral

procedures until praise serves as a reinforcer. Food can then be discontinued as a reinforcer.

There are also two types of punishment. One type involves presenting an aversive event

following the behavior and the other removes a positive event following the behavior. For

example, getting a ticket for speeding can be an aversive event while having your driver’s

license taken away after three tickets is the removal of a positive event.

One of the most misunderstood concepts of behavior analysis is negative reinforcement;

it is important that those who work with people with traumatic brain injury understand

this term. Negative reinforcement increases the occurrence of a behavior by eliminating

the aversive event after the behavior has occurred. 106 In TBI rehabilitation, being allowed

to “escape and avoid” therapeutic tasks is a common example of negative reinforcement.

Another basic principle of behavior analysis is extinction. Extinction does not involve

either presenting or taking away consequences to behavior, but rather discontinues the

reinforcement of a behavior. Not reinforcing the behavior eventually decreases or elim

inates the occurrence of the behavior. “Ignoring” is probably the best example of an

extinction procedure. Ignoring behaviors that were previously given attention (e.g., com

plaining, yelling, etc.) can be an effective technique when combined with reinforcement

of positive behaviors.

It is recommended that reinforcement programs (or reinforcement combined with extinc

tion) be attempted before implementing a punishment program. Reinforcement programs

that teach people “what to do” are generally more effective for long-term maintenance of

the desired behavior, and do not elicit many of the negative side effects inherent to

punishment programs.

Prompting and Fading

Teaching behaviors involves prompting to help initiate the behavior. Instructions, gestures,

and modeling are all examples of prompting. They are antecedents to the target behavior.

The way in which prompting is utilized can have significant impact on how easily a client

learns. A person with language deficits will have difficulty following verbal prompts. In

this case, using physical gestures and cues can be more effective. Different types of prompts

can be combined to facilitate the desired behavior. Shaping and chaining procedures rely

on competent use of various prompting techniques (e.g., backward and forward chaining)

to teach new skills.

The goal is for the behavior to occur independently without prompting. The method

for accomplishing this is called fading. Fading is the systematic and gradual removal of

prompting. If prompting is ended too quickly, the behavior may not continue. A more

gradual reduction in prompting is recommended until the behavior is performed inde

pendently or with as little prompting as possible. For example, teaching a person with

traumatic brain injury a showering sequence may start with actual physical guidance

through many of the steps. Next, some of the physical cues can be reduced to gestures

(e.g., pointing) and then to verbal cues. Later, a written checklist can be placed in the

shower, listing each step of the showering sequence. The checklist can then be removed,

allowing the client to perform the task independently.

Generalization

Like fading, generalization is an important procedure in developing the independence of

a person with traumatic brain injury or transferring responsibility to primary caregivers

and other environments for long-term care, etc. 107 There are two types of generalization

— stimulus generalization and response generalization. Whereas fading involves decreas

ing a behavior’s dependence on prompts, stimulus generalization reduces a behavior’s

dependence on the conditions under which it was learned. Most people would agree that

rehabilitation takes place in a restricted environment. It

is the goal of stimulus generali

zation that behaviors learned under these conditions be transferred to other settings. For

instance, the goal of learning to read in a clinic setting is that it will generalize to reading

the newspaper at home or the grocery list at the supermarket. Learning to control physical

aggression in the clinic, to give another example, is not as important as the ability to

control aggression in the community.

Response generalization involves behaviors rather than the conditions under which they

occur. In other words, reinforcing or punishing a specific behavior will also affect similar

behaviors. We have seen this occur with clients. A behavior treatment plan that focuses

on reducing the most problematic behavior at the same time decreases other less severe

behaviors. This experience lends support to the saying, “Worry about the big things and

the little things will take care of themselves.” Target the most severe behaviors first and

the small ones may never require treatment.

Behavioral Diagnostics

Prior to writing a behavioral treatment plan, it is essential that a comprehensive assessment

of the client’s history, current status, and future goals be performed. The success of a

behavior program depends as much on an accurate evaluation of the client’s behavior as

on the intervention plan itself. 108 The evaluation must analyze all the potential factors

contributing to a client’s behavior. The three basic behavioral diagnostic tools are: (1) a

historical survey, (2) a current status evaluation, and (3) a functional assessment.

Historical Survey

Collecting historical information helps the behavior programmer understand how the

client may respond to the rehabilitation process, and what he or she expects to gain from

treatment. 109 The first half of a historical survey covers a range of demographic data. This

includes information on age, sex, marital status, children, parents, friends, religious pref

erence, living conditions prior to the injury, education, work history, and recreational

interests. Information we have found to be particularly important is that concerning eating

characteristics. Many behavior problems can be averted with an understanding and appre

ciation of a client’s lifestyle prior to the injury. Requiring the client to conform to unfamiliar

schedules, foods, people, and situations that can be reasonably modified creates a potential

setting event. 110 As we explained in the previous section, a setting event increases the

likelihood of a problem behavior occurring. This can happen when facilities develop

schedules that are easier or less expensive to manage. This inflexibility can contribute to

unnecessary behavior problems that are actually more difficult and expensive to manage.

The second half of the historical survey concerns medical and rehabilitation history. It

can be helpful for the behavior programmer to know the location and etiology of injury,

the elapsed time since injury, and the course of treatment that has been provided. This

furnishes the programmer with an idea of the client's rate of recovery. Additionally,

knowledge of a client's medical history can be beneficial. For example, any diseases, major

illnesses, or substance abuse problems that may have occurred before the injury may

contribute to the client's current behavioral status and future prognosis.

Most of the above information can be gathered from medical records, discussions with

the previous treating staff, and an interview with the client and/or significant others, such

as family and friends. Contact with prior treatment facilities provides insight into behav

iors exhibited by the client since the injury, under what circumstances the behavior

occurred, and staff response. Interviews with the client and/or significant others help to

determine the client's preinjury behavior pattern which, in part, determines his or her

response to the demands of rehabilitation and life after a traumatic brain injury.

Current Status

Traumatic brain injury usually involves more than just damage to the brain. Many medical

and psychological complications can result from TBI. These complications can also be

setting events for behavior problems. For example, if a person is in pain or constantly

dizzy, his or her behavioral control will likely be diminished. This is why a comprehensive

evaluation of a client's current status is important.

A current status evaluation reviews a client's medical and psychological status and

therapeutic testing results, and examines the relationship of these to behavioral issues. A

comprehensive review of the medical status involves looking at the cardiac, vascular, and

respiratory systems, orthopedic and muscular capability, the sensory system, bowel and

bladder functioning, and other areas of physiological functioning. Of all possible medical

problems, medication usually has the most direct relationship to behavior. Medications

can profoundly affect behavior, thus programmers need to be educated and informed on

the subject.

A traumatic brain injury has an impact not only on the client, but family and friends

as well. It is important that programmers understand the dynamics between the client

and significant others. After discharge from rehabilitation, family or friends may be

required to carry out behavioral procedures with their loved one or, at the very least,

maintain an environment which is conducive to continued learning and development.

One of the most important assessments of current status is a functional skills evaluation.

How well is the client able to perform activities of daily living such as hygiene, grooming,

dressing, and toileting? Is the client able to cook meals

and clean the house? What about

community mobility, driving, and shopping? Is the client able to manage his money? All

of these issues are fundamental to levels of independent functioning. They will prescribe

the type of living arrangement and level of assistance the client will require. Also,

relearning functional skills can help to replace maladaptive behaviors while reducing the

need for aversive procedures.

A review of therapeutic testing results completes the current status evaluation. Standard

therapeutic testing includes cognitive, physical, and psychological evaluations, as well as

a neuropsychological examination. A client's cognitive level can dictate the type of behav

ioral procedure that is implemented. Clients with severe cognitive impairment, for

instance, will probably not participate in a "contracting" program because it requires more

abstract thinking. Physical issues can also directly affect the treatment plan. For example,

overcorrection or contingent restraint procedures can be especially ill suited for clients

with orthopedic concerns. The neuropsychological examination brings all of the client's

skills and deficits into focus, helping the behavior programmer to design an appropriate

treatment plan.

Functional Assessment

A functional assessment is central to the design of the treatment plan. Its purpose is to

identify the function that each target behavior serves. 111 A functional assessment can be

composed of three parts: (1) describing the behavior and its surrounding events, (2)

predicting the factors that control the behavior, and (3) testing the predictions by manip

ulating the identified factors.

A descriptive analysis begins by describing the behavior. This is accomplished by inter

view and/or direct observation. Direct observations should constitute the primary source

of information because anecdotal reports from interviews can be clouded by subjective

perceptions. The observations should also occur in a wide range of settings and situations.

Nevertheless, in cases where direct observations are not possible, interviews may be the

only method for gathering the information needed to start a treatment plan. Interviews

are conducted with those who have direct contact with the client such as family members,

caregivers, therapists, or paraprofessionals. The interview consists of identifying the target

behavior, the conditions under which it normally takes place (antecedent or setting events),

what events occur following the behavior (consequence), and what function the behavior

serves (e.g., communicating needs). Some behavior problems can be reduced by simply

improving the function that the behavior is attempting to perform. 112 If behavior problems

are being caused by an inability to effectively communicate ones needs, for example, then

improving a client's communication skills may decrease the problem behaviors. Although

indirect assessments, such as interviews, are important to functional assessment, if possi

ble, they should be a secondary source of information.

Functional assessment is usually based on direct observations. The most precise method

for collecting observational data is by recording the events surrounding behavioral epi

sodes. An excellent form for organizing this information was designed by O'Neill, Horner,

Albin, Storey, and Sprague. 113 Figure 14.1 is a modified version of this form. It includes a

place to write in the time of each behavioral event, possible setting events (e.g., difficult

task, demands, etc.), the perceived function of the behavior (e.g., attention, avoiding activ

ity, etc.), and the consequence to the behavior. The completed form can then be analyzed

for patterns of behavior and the conditions in which they most frequently occur. From this

analysis, hypotheses can be formulated regarding conditions maintaining the behavior.

The last step is a functional analysis to test the conclusions drawn from the interviews

and direct observations. 114 This involves manipulating specific conditions and observing

the level of the behavior occurrences. The idea is that, by changing the consequences to

a behavior, one may be able to determine the condition maintaining the behavior. Once

the conditions have been identified, then a treatment plan can be developed. For example,

if physical aggression occurs with a client 25% of the time while in therapy, but only

during 5% of the time before starting therapy, one may try allowing the client “alone time”

after completing a specified amount of therapy.

Of course, the time and financial constraints of rehabilitation may make it difficult to

always complete this last step of a functional analysis before implementing a treatment

plan. However, identifying the conditions that maintain behavior and monitoring the effects

of changing these conditions can, at the very least, be utilized during the treatment plan.

Behavior Plan Format

A behavior treatment program includes four major components: (1) short- and long-term

goals, (2) operational definitions of target behaviors, (3) data collection system and mate

rials needed, and (4) staff procedures (Figure 14.2). The behavior programmer must syn

thesize diagnostic data (historical information, current status, and functional analysis)

with goals of the client, family, treating staff, and payer to create an individualized

treatment program. The treatment plan should be written as clearly as possible and in an

“easy-to-follow” structure. The programmer has to strike a balance between including all

the necessary information and, at the same time, presenting it in a way that is concise and FUNCTIONAL ASSESSMENT Time

Behaviors

Antecedent/Setting Events Demand/Request Difficult Task

Perceived Functions Get/Obtain Attention Desired
Item/Activity Escape/Avoid Demand/Request Activity Person

Consequences

FIGURE 14.1

Functional assessment form. BEHAVIOR TREATMENT PLAN

Client Name: C.G.

Program Start Date: 11-30-03

Implemented By: Clinical therapists and staff aides

GOALS:

Short-Term Goal: To decrease physical aggression by 5% of total intervals from last month

Long-Term Goal: To increase Independent Living Scale (ILS) score to more than 80/100 pts. (min.–mod. supervision)

Evaluation of Goals: Weekly summary of interval data

TARGET BEHAVIORS:

Primary:

Physical Aggression (PA) — attempting to and/or striking out with an object or body part; may include hitting,

kicking, pinching, grabbing without permission, scratching, throwing items at someone, etc.; includes attempted

or actual contact; does not include verbal threats or invasion of personal space.

Property Destruction (PD) — ramming, throwing, tearing, striking, or breaking property (even if accidental or only

attempts have been made to do so); property does not have to be damaged.

No Cooperation (None) — did not participate in therapy at all and exhibited at least one target behavior. May be in

therapy area, yet did not attempt any activities.

Secondary:

Angry Language (AL) – cursing, yelling, threats, hostile language, demands delivered with increased volume (above

conversational level) lasting more than two seconds.

Refusal to Work (R) – active or passive statements or actions meant to evade start, interrupt, or stop therapy tasks

or directives; must be more than 1 min; does not include slow processing time or lack of ability.

Escaping (E) – attempted to and/or left place of required activity.

Partial Cooperation (Part) – attempted and/or completed some therapy tasks as directed. Displayed one or more

target behavior(s), but was able to be redirected to task or attempted the task prior to any behavior episode

Full Cooperation (Full) – attempted and/or completed all therapy tasks as directed. No target behaviors displayed.

MATERIALS AND DATA COLLECTION:

1. 15-min interval data sheet

2. 2-min therapy chart

3. 2-min board with countdown timer

TREATMENT PROCEDURES:

Outline – This program will consist of several key components including: (1) a 2-min fixed interval DRO, (2)

primary target behaviors of PA and PD, (3) a reward contingent upon completion of the five 2-min blocks of therapy

with no occurrence of the target behaviors, (4) a graduated guidance program contingent on the occurrence of

noncompliance, and (5) relaxation practice each hour.

Relaxation – Begin each hour with 2-min of timed relaxation practice. Tell C.G. to "take a couple of minutes to relax."

Ask him to close his eyes, take a deep breath, and let his mind and muscles relax. Make every effort to keep the

surrounding therapy area quiet during his relaxation time.

DRO – Following the relaxation period, post the 2-min board on a straight back chair near the task area where

C.G. can see it clearly. Inform him that when each of the boxes has an "X" in it, he can go outside. Set the timer

for 2 min and begin therapy. Each time the timer sounds and C.G. has not exhibited a primary target behavior, "X"

out a box on the board, quickly reset the timer, and continue therapy. Try to keep therapy tasks flowing comfortably

while maintaining awareness of the timer. Immediately after the final (fifth) box has been "X'd", state to C.G. "Great,

you stayed calm; we can go now" and take him for a short walk outside. Have C.G. walk himself during the walk

unless he asks for assistance. Reflect to him that this is his time and he has earned it. After about 3 to 5 minutes,

redirect C.G. back to therapy. Do not allow him to manipulate or slow his return to therapy. Assist as needed.

Immediately reset the timer and repeat the above sequence.

Graduated Guidance – If C.G. displays noncompliance (i.e., refusing to start a task), immediately provide hand-over

hand guidance. Have tasks available that C.G. can be physically guided through. For example, tasks requiring

pointing, reaching, touching, etc. As soon as noncompliance begins, start prompting the current task or immediately

switch to an activity requiring motor involvement. Provide guidance until C.G. begins complying, then fade

physical prompting. Once guidance has been discontinued, return to the task and/or approach used before the

behavior occurred.

FIGURE 14.2

Example of a behavior treatment plan.

readable. The degree of staff behavioral training will dictate the level of sophistication

with which the program can be written and followed with consistency. However, the

reality of most rehabilitation environments, whether acute, postacute, or in the home, is

that there is a wide range of behavioral competence. The Behavior Analyst Certification

Board (BACB)* was created to develop, promote, and implement a voluntary national

certification program for behavior analyst practitioners. However, even after extensive

training, there are significant differences in the degree of “natural” ability among staff to

carry out effective behavioral treatment. This being the case, a “step-by-step” procedural

outline, combined with close monitoring of staff performance, is the most practical format

with which to run behavior treatment plans.

Goals

Behavior treatment goals are separated into short- and long-term goals. Short-term goals

are objectives that define the desired measurable change in the target behavior. A specific

time frame for accomplishing the objective should be clearly stated. For example, physical

aggression (the target behavior) will be reduced to 5% of the total recorded intervals within

30 days. Short-term goals help the client and staff focus on tangible achievements while

continuing to strive toward long-term goals.

Long-term goals, on the other hand, describe the projected functional outcome of the

treatment plan. For example, the client will increase independent living to a minimal

supervision level (group home) or will be able to work in a part-time volunteer employ

ment position. Long-term goals are to be defined by the client, family, caretakers, funding

source, and other responsible parties.

All goals and objectives should include three parts: (1) how they will be assessed, (2)

how often they will be reviewed, and (3) what type of report will be generated. Many

accrediting or regulating agencies, such as the Commission on the Accreditation of

Rehabilitation Facilities (CARF), require these guidelines for accreditation. The assess

ment of goals can be accomplished by many public or in-house rating systems, for

example, long-term goals of disability level can be gauged by the Disability Rating

Scale. 115 Short-term goals can be evaluated by a standard data collection system (e.g.,

frequency count, time-sampling, etc.). Short- and long-term goals should include a state

ment concerning the frequency of review (e.g., weekly, bi-weekly, monthly) and what

type of report will be produced.

Target Behavior

Target behaviors are the focus of the treatment plan. They are the behaviors that are

interrupting therapy, impeding progress, endangering others, disrupting activities, or

otherwise interfering with a person's ability to live independently in the community. They

can be behaviors of excess (e.g., physical aggression), deficit (e.g., hygiene and grooming),

or stimulus control (e.g., public sexual behavior).

Each target behavior must be operationally defined. The operational definition describes

what the behavior "looks like" in objective, observable terms. For example, labeling a target

behavior "physical aggression" without an operational definition leaves it wide open to

interpretation. The more interpretation is allowed in a behavior program, the less consistent

it will be. Not only does an operational definition describe what a behavior "is," it also

describes what it "is not." For example, physical aggression could be defined as any

attempted or actual hit, strike, kick, pinch, or grab by the client, not including spitting.

Operational definitions sometimes require that the context in which the target behavior

will occur be identified. For example, "hand waving" is only a problem when it interferes

with writing activities. The definition may also need to include the duration or rate at

which the behavior must occur before it is considered a

target behavior. For example,

refusing to participate in therapy for more than 30 seconds may be the minimum criteria

for “noncompliance.”

Materials and Data Collection

The third section of a behavior treatment plan outlines all the materials required to carry

out the prescribed procedures and the data collection system for tracking the rate and/

or duration of the target behavior. Many behavior treatment plans require specific mate

rials for implementing procedures. For example, a stopwatch may be needed for a “dif

ferential reinforcement of other behavior” program that calls for reinforcing the client after

a specified period of time in which the target behavior does not occur. Any supplies or

items that are used to implement the treatment plan (e.g., timer, tokens, tape recorder,

etc.) need to be described in this section.

The second half of this section describes the data collection system. All behavior pro

grams should have a procedure for gathering information that will be used to determine

the effect of the treatment plan. The data collection and graphing section of this chapter

details methods for systematically recording and analyzing behavioral data. Without

consistent data collection, it is difficult to ascertain whether or not the program is working.

Anecdotal reports (i.e., verbal feedback from staff) are usually not reliable enough, due

to their subjectivity, to make important decisions concerning the effectiveness of behavior

programming. Frequency, interval, duration, or time-sampled data of operationally

defined target behaviors gives the behavior programmer ample information which,

together with staff feedback, will allow for better treatment decisions.

Treatment Procedures

The procedures section of the treatment plan describes the steps of the behavior program.

It outlines the staff's response to the target behavior (consequence) and arranging of

environmental conditions prior to the behavior (antecedent). The section on behavior plan

procedures details a variety of behavior treatment plans.

The treatment plan describes each step a staff member is to take before and after the

occurrence of the target behavior. Every step needs to be described in clear, concrete terms

that can be understood by a wide range of people, including the client, staff, and family.

More often than not, the success of a program rests on the ease with which the procedures

can be followed. Figure 14.2 is an example of a completed treatment plan.

Behavior Plan Procedures

The staff member responsible for writing behavior programs has many designs from which

to choose (Table 14.2). The types of behaviors exhibited by the client, the setting for

implementing the program, and the level of staff skills and experience are all factors to

be considered in choosing the most suitable behavior program. Once these factors have

been identified and weighed, one can then choose a treatment procedure that is accelerative

(designed to increase the frequency or duration of a target behavior), decelerative (designed

to decrease the frequency or duration of a target behavior), or complex (having character

istics of both accelerative and decelerative programs). Combinations of these procedures,

in a multicomponent approach, can also be used simultaneously to increase the speed of

and maintain behavioral change. 116

We will outline procedures for the most common behavior programs and provide

illustrations (for most procedures) of actual cases encountered in behavioral treatment.

Some of the techniques we will not be covering in this chapter are group-based programs,

peer-administered contingencies, biofeedback, and cognitively-based treatment (e.g.,

stress reduction, problem-solving skills, self-statements, etc.). These methods are either

not often used, not practical for people with traumatic brain injury (e.g., group-based

programs, peer-administered contingencies), or fall more into the realm of counseling (e.g.,

cognitively-based treatment).

Accelerative Programs

Positive Programming

Positive programming is nothing more than teaching individuals new skills through the

use of reinforcing consequences. 117 Activities of daily living, functional communication,

and social skills training are all examples of positive programming. This technique is

familiar to most of us since we have been exposed to learning new skills (e.g., reading)

and being rewarded for our performance (e.g., grade).

An advantage of positive programming is that it is constructive in nature. It teaches

people “how to do something.” Positive programming helps to reduce undesirable behav

iors that are incompatible with the new skill (e.g., the social skill of shaking hands is

incongruous with hitting). 118 Generalization and maintenance of skills taught through

positive programming are also often supported by naturally occurring contingencies (e.g.,

learning to verbalize allows one to express and receive one’s needs).

A disadvantage of positive programming can be its lack of quick results — positive

programming takes time. Because of the tremendous costs involved in rehabilitation of

people with traumatic brain injury, pressures are exerted on rehabilitation programs to

bring about behavioral change as quickly as possible. This does not infer that positive

programming should be excluded, rather that efficient programming must be developed

to meet the needs of payers. To help accomplish this, positive programming can be

integrated with other behavior programs that focus on decreasing undesirable behaviors.

The result should be increased efficiency and rate of behavioral change. TABLE 14.2 Behavior Program Treatment Procedure Designs Accelerative Decelerative Complex Other Positive Programming Shaping and Chaining DRI DRO DRL: Overcorrection Stimulus Change Stimulus Satiation Time-Out Contracting Stimulus Control Token Economy NCR Case Illustration H.H. was a 32-year-old male injured in a motor vehicle accident. H.H.'s physical and cognitive skills were severely impaired. Expressive language, in particular, was extremely difficult. Most of his severe behavior, which included physical aggression and self-injurious behavior, occurred when his wife would leave for home at the end of his day at the clinic. When she would inform him she was leaving, he would start yelling, attempt to attack her or anyone intervening, and throw himself out of his chair. On one occasion, he even stabbed himself with a pencil that was lying nearby. The program for reducing his aggressive behavior was to replace it with more appropriate social and communication skills. H.H. was taught to wave goodbye to his wife before she departed for the evening. This was accomplished by having the client, during counseling sessions, practice saying goodbye to a videotaped presentation of his wife. If he completed the sequence correctly, and without any negative behavior, he was allowed to color in one section of a black and white drawing of his house. The drawing was divided into seven sections. When he completed coloring in the seven sections, he earned a supervised weekend home visit. Once he succeeded at the videotape presentation, and earned a visit home, the client practiced saying goodnight to his wife in person. The same reinforcement procedure was used again. Seven successful trial sessions resulted in a weekend home. H.H. successfully completed both training procedures within approximately 30 days and never presented the problem again during the rest of his stay in rehabilitation. The more appropriate social skills of saying goodnight and waving goodbye had replaced the maladaptive behaviors of physical aggression and self-injurious behavior.

Shaping

Shaping refers to the reinforcement of gradual approximations to a target behavior and

is generally used with behaviors that do not require urgent change. For example, if a

therapist wants a client to remain seated during the therapy session, she may start by

reinforcing the client for remaining seated for 5 continuous minutes at a time. Once the

client is able to accomplish this consistently, the time can be increased to 10 minutes, and

so on, until the client remains seated the entire session. Although shaping is used primarily

for skill building (e.g., learning a single step of a dressing procedure — pulling one's shirt

all the way down), it can also be used to modify maladaptive behaviors. For example, if

a client is constantly late for therapy, he or she could be reinforced for approximating

closer correct arrival times to therapy.

Chaining

Chaining, often confused with shaping, involves teaching a sequence of steps to a task. 119

The basic sequences in which such a task may be taught are termed forward chaining,

backward chaining, and whole task method. 120 For example, putting on a pullover shirt would

involve teaching a person the steps of: (1) putting his arms through the sleeves, (2) pulling

the shirt over his head, and (3) pulling the shirt down over his body. In forward chaining,

one would begin teaching with the first step (putting arms through the sleeves), then

combine steps one and two, and finally connect the sequence of steps one through three.

In backward chaining, one actually begins teaching the last step first (e.g., pulling shirt

down), then combines step three and two, and finally steps three through one. In whole

task method, the most common teaching technique, the entire sequence (step 1 to step 3)

is taught each time. Evidence is not clear as to which of these methods is most effective;

however, backward and forward chaining is usually used if one is trying to reduce the

number of errors produced by the client during learning. Case Illustration K.T. was a 38-year-old female who was injured in a motor vehicle accident. The injury left K.T. with severe cognitive and behavioral problems. Her most difficult

behavior was an intense motor restlessness and inability to sustain attention. She

was constantly moving her legs and arms, and would exit from therapy every

few minutes. A shaping program was introduced to try to increase her ability to

sit in a chair and participate in therapy. The procedure started with having K.T.

sit on the floor for 30 seconds. If she completed this successfully, she was allowed

up and a poker chip token was placed in a circle on a board with ten total circles.

When all ten circles were filled with a token, K.T. was taken for a walk around

the clinic or outside. After she mastered floor sitting for 30 seconds with minimal failures, she was instructed to sit in a chair for 30 seconds. The same procedure was repeated. The 30-second time period was systematically increased over several weeks, with the structured introduction of “table-top” activities, until she could sit at a therapy table for 45 minutes and work on therapeutic tasks without exiting. K.T.’s ability to sit quietly and work on cognitive activities had been shaped to a length commensurate with most clients participating in rehabilitation. The same program was used with K.T. in her living environment to help her sit at the dining table and finish eating a meal.

Decelerative Programs

Differential Reinforcement of Incompatible Behaviors (DRI)

DRI involves reinforcing behaviors that are topographically different from, or incompat

ible with, the target behavior. 121 For example, the behavior of keeping one's hands in the

lap or to the side is topographically different from hitting oneself. The production of the

topographically different behavior actually competes with, or disallows, the production

of the target behavior. Thus, reinforcing the client for keeping his hands in his lap or to

his side is said to differentially reinforce an incompatible behavior.

Careful monitoring of behaviors during a DRI program is required to make certain that

the target behavior is actually decreasing and not only that incompatible behaviors are

increasing. Using the above example, one could imagine that the client's time with hands

in his lap or to this side (incompatible behaviors) could increase and self-hitting (target

behavior) could remain unchanged. If this occurs, use of a differential reinforcement of

other behaviors (DRO) program may be more effective. Case Illustration E.N. was a 43-year-old male who was injured in a motor vehicle accident. E.N. exhibited a variety of tick-like behaviors. He would touch or pick at his nose and face and grab his crotch area constantly throughout the day. As you can probably guess, social interaction with others was severely limited by these behaviors. A differential reinforcement of incompatible behaviors (DRI) was implemented to help reduce these socially unacceptable behaviors. During therapy sessions, E.N. was reinforced with tokens for keeping his hands either on the table or engaged in hand-involved therapeutic tasks. The tokens were exchangeable for certain privileges in his living

environment. Over a period of several months, E.N.'s "ticlike" behaviors decreased to a socially acceptable level. His inappropriate behavior (i.e., touching nose, face, or crotch) had been replaced by incompatible behaviors (i.e., hands on table or engaged in a task). It was not possible for E. N. to exhibit both behaviors at the same time.

Differential Reinforcement of Other Behaviors (DRO)

DRO is defined as reinforcing any behavior other than the target behavior for a specific

interval of time. 122,123 For example, if the target behavior is physical aggression, the ther

apist would reinforce the client at the end of every designated time interval in which the

physical aggression was not exhibited. One can keep the time intervals absolute (e.g.,

every 15 minutes) or relative (e.g., resetting the clock after every occurrence of the target

behavior). If the client exhibits physical aggression, the clock is reset for another 15

minutes. Once there is an increase in the number of intervals in which aggression does

not occur, or when it is occurring at a pre-determined lower rate, the interval size can be

systematically lengthened and eventually eliminated.

There are, however, a few precautions to take when implementing a DRO program.

DRO programs are not designed to reduce high-rate behaviors. High-rate behaviors do

not allow enough time to reinforce the client between episodes of the targeted inappro

priate behavior. Also, by their nature, DRO programs reinforce any other occurring behav

iors. Therapists need to be aware that they may inadvertently reinforce another

undesirable behavior. 124 As with many decelerative programs, DRO procedures do not

teach people new skills and, thus, are more effective if implemented in concert with

positive programming. Case Illustration C.I. was a 27-year-old male who was injured in an industrial explosion. As a result of the accident, C.I. had severe cognitive deficits and could not ambulate independently. He also had severe aggressive behavior problems that were significantly interfering with all rehabilitative therapy. C.I. exhibited hitting, kicking, biting, yelling, exiting, and noncompliance in therapy. A DRO program was started to reduce the above-mentioned behaviors. C.I. was required to participate in the therapy task for a total of 2 minutes without any of the target behaviors. If he was successful, an “X” was marked over one of five squares on an erasable dry ink board. A picture of an outdoor scene was attached to the board at the end of the five-square sequence. Any time C.I. displayed one of the target behaviors, the clock was reset to zero and a new 2-minute interval would begin. As soon as five squares were marked, C.I. was taken for a walk outside of the clinic (the identified reinforcer). When he was able to complete 2-minute intervals approximately 80% of the time without resetting, the time was increased to 5 minutes, and then to 10 minutes. Eventually, C.I. was able to participate in therapy for a full 45 minutes before taking a break. He was being reinforced for any behaviors “other” than the target behaviors.

Differential Reinforcement of Low Rates of Behavior (DRL)

DRL programs provide reinforcement if a specified interval of time has elapsed since a

target behavior last occurred or if a specified number of occurrences of the target behavior

have occurred during the interval. 125 For example, if the target behavior is yelling, a DRL

program may state that a client is to be reinforced for each 15-minute interval of time that

passes since yelling last occurred or for each time interval in which the target behavior

occurs below a certain rate (e.g., five occurrences or less of yelling every 15 minutes). The

time intervals can then be lengthened (e.g., from 15 minutes to 30 minutes) or the number

of occurrences allowed can be decreased (e.g., five occurrences to two occurrences every

15 minutes) until the target behavior is eliminated or reduced to an acceptable level.

Baseline data must be collected to determine either the initial time interval length or the

initial number of occurrences to be allowed for the client to receive a reinforcer. For

example, if a behavior is occurring four times per hour, an appropriate interval length

may be 15 minutes, or reinforcement for every 15 minutes that the behavior occurs only

once. This interval length will assure initial success by the client and help develop rein

forcer strength.

Some of the advantages of DRL programs are that interval times can be adapted to fit

therapy sessions (e.g., 45-minute sessions can be divided into 15-minute intervals) and

high-rate behaviors, for which DRO programs are not designed, can be systematically

reduced. Like DRO programs, however, DRL programs do not teach new skills. Instead,

the focus is on reduction of maladaptive behaviors. DRL programs, therefore, should be

supplemented with positive programming of some type. Case Illustration K.C. was a 36-year-old male who was injured when the bicycle he was riding was hit by a car. K.C. presented several behavior problems, including verbal and physical aggression. If he displayed any target behavior, the DRL program stated he must go to his kitchen and remove

one of four keys hanging on a corkboard. If, at the end of 3 days, he still had one key remaining, he could unlock a box and choose one of several available reinforcers (e.g., $10). When K.C. was able to earn his 3-day reinforcer three consecutive times, the reinforcer period was increased to 4 days, and so on, until it reached a 1-week reinforcer time period. The number of keys was then reduced until only two keys were available. This meant he could only exhibit one target behavior per week and still earn a reinforcer. K.C.'s target behaviors had been systematically reduced to lower rates.

Overcorrection

There are two types of overcorrection procedures, restitutional and positive-practice over

correction. 126 Restitutional overcorrection requires that a person returns the environment

(e.g., therapy room) to a state better than before the behavioral episode. For example, if

an agitated client knocks over a chair, he or she is required to pick up not only that chair,

but to straighten all other chairs in the room as well.

Positive-practice overcorrection requires repeated practice of an appropriate behavior.

For example, if a client walks with poor posture, he or she may be asked to practice

walking with upright posture for specified periods of time.

Overcorrection can be an alternative to other, more punitive punishment procedures.

The disadvantages are that overcorrection can be time-consuming and can elicit aggres

sion in circumstances where overcorrection requires physical guidance to obtain

compliance. Case Illustration O.H. was a 42-year-old female who was injured in a motor vehicle accident. She had spent approximately 1 year in a locked psychiatric institute on multiple psychoactive medications prior to admission for rehabilitation. She exhibited behaviors of yelling,

hitting, stripping, exiting, and noncompliance with therapy. Although continent of bowel and bladder, O.H. would periodically urinate small amounts on furniture during therapy. A restitutional overcorrection program was implemented to reduce this behavior. If O.H. urinated on a chair, she was required to change her clothing, put the dirty clothes in the wash, clean the chair that was soiled, and wipe off all other chairs in the room. O.H.'s inappropriate urination ended within a few weeks. Case Illustration S.D. was a 29-year-old female who fell into a diabetic coma and suffered anoxia. S.D. displayed yelling and noncompliance to therapy, and was also incontinent of bladder. A positive-practice overcorrection program was started to reduce her incontinence. If S.D. was incontinent between her scheduled bathroom visits, she was required to go to the bathroom and practice a series of five correct "toileting"

sequences (i.e., adjust clothing, sit on toilet, clean self, get up, adjust clothing,

wash hands). After several months, S.D. was continent of bladder and able to live in a supervised group home.

Stimulus Change

Stimulus change is the sudden introduction of an unrelated (nonfunctional) stimulus, or

change in stimulus conditions, that results in a temporary reduction of the target behav

ior. 127 For example, clapping loudly once while a client is engaged in yelling, or suddenly

shouting the client's name if he is engaged in aggressive behavior, may cause a lapse in

the behavior.

An advantage of stimulus change programs is that their effectiveness can be determined

very quickly. There is no need for any long-term assessment of the program. The disad

vantage of a stimulus change program is that its effect may be temporary (startle effect)

and/or the client may quickly adapt to the stimulus event

and return to the maladaptive

behavior. Stimulus change programs are almost exclusively used as “emergency” pro

grams to quickly stop destructive behavior.

Stimulus Satiation

Stimulus satiation programming allows unrestricted access to the reinforcer of an unde

sirable behavior. 128 The unconditional availability of the reinforcer will eventually weaken

its relationship to the target behavior. Stimulus satiation weakens the reinforcer through

the process of satiation (complete satisfaction) and deprivation of other reinforcers. 129 Case Illustration C.F. was a 32-year-old male who, while working on a rooftop, was electrocuted and fell. C.F. exhibited a number of severe behavior problems; however, one unusual behavior was his obsession with staying on the toilet. When cued to leave the bathroom, C.F. would become extremely agitated and start yelling. If anyone tried to help him out, he would become physically aggressive. His time in the bathroom was becoming increasingly longer and his behavior more severe. A stimulus satiation program was implemented to reduce his time in the bathroom. The program allowed the client to stay in the bathroom, and on the toilet, for as long as he desired. Over a period of 2 weeks, C.F.’s time on the toilet increased to over 19 consecutive hours in 1 day. The following 2 weeks saw his time in the bathroom decrease gradually to what would be considered “normal” lengths of time. Unlimited access to “toilet-time” eventually weakened its reinforcement quality (i.e., satiation).

Time-Out

Time-out procedures (also known as contingent withdrawal) can be either nonseclusionary

or exclusionary. Nonseclusionary time-out involves withdrawing attention from a person

while remaining in his/her presence. Exclusionary time-out consists of removing the

person from a reinforcing environment following the occurrence of a target behavior. For

example, when a client exhibits verbal threats, one can either ignore the statements (non

seclusionary) or remove the client from the area (exclusionary). Time-out procedures are

more effective if the reinforcer sustaining the behavior is attention from others. A third

type of time-out procedure, seclusionary, involves the use of a time-out room when the

client exhibits a specific target behavior. Strict guidelines need to be followed to safely

operate seclusionary time-out procedures. 130

- The duration of seclusionary time-out should be as brief as possible (e.g., 1 to 5 minutes).

- The room should be well lit, ventilated, and free of dangerous objects (e.g., light fixtures).

- The room should have provisions for visually monitoring the person.

- The room should not be locked, only latched.

- Records should be kept for each use of the time-out room. At a minimum, records should include the client's name, description of the behavioral episode, and start/ end time of the procedure.

An advantage of time-out procedures is that they are easy for staff to understand. The

disadvantage is that, in reality, time-out procedures can be very difficult for staff to

implement. It is extremely difficult for staff to completely ignore a client's target behavior

(e.g., threats, cursing) 100% of the time. If the target behavior is not ignored, it can be

inadvertently intermittently reinforced. Intermittently reinforced behavior is actually

strengthened. Also, a client should not be removed from the therapy area as part of an

exclusionary time-out procedure if the behavior is to escape and avoid therapy. Time-out

procedures should always be combined with positive, skill-building procedures (e.g.,

positive programming, shaping) to develop functional skills to replace the behavior being

extinguished. Case Illustration L.I. was a 24-year-old male who was injured in a motor vehicle accident. L.I. exhibited behaviors of verbal aggression, threatening behavior, and noncompliance. He had sustained a mild traumatic brain injury. If L.I. did not want to participate in a therapeutic activity, he began by arguing, then escalated to yelling and threatening physical aggression. A nonseclusionary time-out procedure was started to reduce his aggressive behavior and increase his compliance with therapy. Attention from staff was the identified reinforcer. Any time that L.I. began arguing and refusing to follow instructions, therapists were instructed to inform L.I. that they were going to their office and would return when he was ready to stop yelling and cooperate. Other staff members were also instructed to ignore L.I. if he was not with his therapist during therapy time. Cooperation increased to an acceptable level over a 2-week period.

Complex Programs

Contracting

Contracting is a technique that involves a written agreement between the client and another

person. 131 A key to behavioral contracting is that the elements of the contract are agreeable

and understandable to both parties. Contracting can shift the focus of therapy away from

the demands of a therapist to one of cooperative problem solving. Clients may be more

likely to follow therapeutic guidelines when they feel part of the decision-making process

and can see behavioral steps and reinforcers outlined in a written format. Contracting

should include a definition of the target behavior or goal, how the behavior or goal will

be measured or monitored, rewards for following the contract, and the signatures of both

parties. Contracting can work well for behaviors such as tardiness, cooperation, and quality

of performance, which are typically thought of as involving “higher” levels of self-control. Case Illustration T.K. was a 36-year-old female who, while working as a junior high teacher, was injured when hit in the head by a student. T.K. was diagnosed as having “mild” head injury. Most of her symptoms were related to psychological functioning and high-level abstract thinking. One specific symptom that caused her difficulty was

a sensitivity to light. Following the injury, she could not tolerate bright light,

including indoor florescent lighting. She developed a habit of wearing dark

glasses, both outdoors and indoors. As therapy progressed, she still felt the need to wear dark glasses indoors. T.K. stated that she wanted to stop wearing dark glasses inside; however, she could never fully cooperate. Various procedures were attempted to reduce her dependence on dark glasses, but none worked. Contracting was finally adopted. T.K. signed a contract stating she would cooperate with systematically reducing her time wearing glasses based on gradually increasing periods without “dark glasses on.” Once the goals were outlined and the contract signed, full cooperation from T.K. was achieved. She completed her rehabilitation and was discharged without the need to wear dark glasses indoors.

Stimulus Control

Stimulus control programming involves bringing the target behavior under the control of

a specific stimulus or set of conditions. 132 Many behaviors are deemed acceptable, or

unacceptable, based on the circumstances under which they occur. Sexual intimacy, for

example, is considered an acceptable behavior if it occurs between consenting adults in

the privacy of their home. If it occurs at the supermarket or on a public bus, however, it

would not be considered acceptable. The goal of stimulus control programs, then, is to

bring behaviors that may be occurring at the wrong time, place, or frequency into more

appropriate, or more easily controlled, stimulus conditions. 133 Behaviors are brought under

stimulus control by reinforcing the target behavior at the time and/or location where the

behavior should naturally or acceptably occur (e.g., masturbating in the bedroom rather

than in public). Behaviors can also be brought under a specific stimulus control that is

then progressively reduced, decreasing the frequency of the behavior as access to the

stimulus decreases. Stimulus control programs are considered positive in nature because

the behavior is being reinforced, in most cases, for occurring in a more appropriate

environment or time.

It is not recommended that stimulus control programs be used with more violent or

destructive behaviors (e.g., physical aggression, self-injurious behavior). Severe behaviors

are potentially dangerous to the client and others and, thus, are not acceptable even at

low rates of occurrence or in selected settings. Case Illustration D.K. was a 37-year-old male who was injured in a motor vehicle accident. As a result of severe brain

injury, D.K. displayed physical and verbal aggression, exiting, and noncompliance with therapy. His verbal behavior (i.e., threats, cursing, and yelling) was his predominant problem. A stimulus control program was implemented to reduce verbal agitation. A therapy room was set aside as the stimulus control environment. A lamp, with a blue incandescent light bulb, was placed on the table to increase the uniqueness of the room. To begin with, all therapy sessions were done in this room. If D.K. exhibited any verbal target behaviors, he was reinforced with a variety of edibles and verbal praise. To insure a high reinforcer rate, if D.K. did not exhibit a target behavior within 60 seconds, he was prompted by the staff to "please yell." In contrast, when D.K. was outside of the room (for walks, bathroom breaks, etc.), all target behaviors were ignored. After 3 weeks of using the stimulus control room exclusively for therapy, D.K. was systematically moved to conventional rooms at a rate of one per week. Again, he was reinforced for exhibiting target behaviors only in the stimulus control room, whereas target behaviors were ignored in all other conditions.

Token Economies

Token economies require the use of secondary reinforcers (tokens) that a person has earned

and which can be traded later for something of value to the person. 134 For example, plastic

poker chips are commonly used as tokens that are earned for positive behaviors such as

compliance with therapy. Clients can then trade in the chips daily, weekly, etc. (depending

on the reinforcement interval length required) for any activity, privilege, or item identified

as a reinforcer (e.g., dining out, movies, money). One can also include a response-cost

aspect to a token program. This involves losing tokens for exhibition of specific behaviors.

For example, a client may earn tokens for compliance with therapy and lose tokens for

exhibiting any physical aggression.

The most difficult aspect of a token program is deciding the value of each token and

how often the client can earn it. Baseline data on the frequency of the target behavior is

necessary to determine the potential earning power of the client. Token programs should

be neither too easy nor too difficult for a client. An earning rate of about 70 to 80% is

probably a good rule of thumb. Advantages of token programs are that they provide for

structure, concrete feedback, delay of gratification, and ease of use across many settings

(e.g., therapy room, community, home). Case Illustration S.X. was a 28-year-old male who was hit by a motorist while working as a motorcycle highway patrolman. S.X. suffered a severe brain injury that left him with significant cognitive and physical deficits. With the exception of physical therapy, S.X. was limited to using a wheelchair for mobility. While sitting, S.X. would let his head fall forward and begin drooling. He would also let his left hand pull up to his chest, instead of keeping it in a more neutral position on his lap. A token program was started to decrease the above-mentioned behaviors. He could also earn bonus tokens for each 15-minute interval in which he added inflection to his “monotone” voice. A response-cost element was added to decrease his habit of transferring out of the wheelchair without supervision. He was given a “transfer ticket,” which cost him tokens if anyone witnessed him transferring without another person present. Tokens were earned on a 15-minute interval basis (determined by baseline data on the rate of target behaviors) and could be cashed in for food outings and extra walking time. By time of discharge, S.X.’s drooling and hand position had been resolved and he was placed in a semiindependent living environment and a part-time position with the police force as an office clerk.

Other Programs

Noncontingent Reinforcement (NCR)

Noncontingent reinforcement (NCR) procedures involve the delivery of reinforcers on a

time schedule that is not contingent upon the subject's behavior. 135 This is different from

a traditional, contingency-based model of reinforcement. For instance, if "attention from

others" is the identified reinforcer, attention will be delivered to the client on a fixed

schedule (e.g., every 15 minutes), independent of the client's behavior. Whether the client

acts inappropriately or appropriately, the reinforcer "attention" will be given to the client

every 15 minutes.

NCR has some advantages over other reinforcement programs. It requires little in the

way of monitoring, whereas other programs require constant observation of the client's

behavior. This can be an important factor in situations where staffing levels are less

intensive, such as long-term care environments or programs that don't offer one-to-one

therapy-to-client treatment ratios. Case Illustration C.I. was a 40-year-old male with traumatic brain injury participating in a longterm care program. C.I. suffered a brain injury as a result of a motor vehicle accident 13 years prior to his admission. Although suffering from severe cognitive deficits, C.I.'s aggressive behavior toward others and himself was of primary concern. C.I. participated in structured individual and group oriented activities during the day and in a residential setting during the evenings and weekends, relearning activities of daily living. Physical aggression and self-injurious behavior were identified as the target behaviors and "attention" as the maintaining reinforcer. Attendants delivered attention every 30 minutes, independent of behavior, for the client's waking hours. The attention sequence consisted of spending 3 minutes in social conversation with C.I., after which he was redirected to an activity. Implementation of the NCR program resulted in physical aggression occurring four times less often and selfinjurious behavior two and a half times less often than prior to the program.

Summary

The design of an effective behavioral program may require combining a number of the

procedures just described. No single design can be used universally. Consequently, it is

often necessary to begin with one procedure and switch to another when the first plan

fails or loses its effectiveness.

Recent studies have also stressed the importance of contextual control in choosing

treatment plans. 136 Contextual control recognizes the role that context (stimulus setting)

plays in altering the effect of behavior programs. A treatment plan designed to modify

behavior in one environment may not be effective in another. 137

Data Collection and Graphing

Behavior programming requires a procedure for systematically recording and graphing

behavior data. Decisions regarding the effectiveness of treatment plans should be data

based and this demands comprehensive data collection. When possible, collect data

throughout the entire day and evening — not just in structured settings. Behavior data

from the home and community are just as important as those from a school or rehabili

tation facility. Long-term maintenance is questionable if behavior changes do not gener

alize to other, more natural environments. This section will cover methods of data

collection, graphing and analysis of data, and the use of

computer technology to assist

in data management. Although comprehensive data collection and graphing can be time

consuming and somewhat rigorous to implement, there are a number of important reasons

to collect data on a consistent basis.

• Provide baseline information prior to starting a behavior program – before beginning any behavior program, it is recommended that data be collected on the person's target behaviors. Baseline data provides the behavior programmer and staff with a clear picture of the frequency of maladaptive behaviors being exhibited by the person. This information bears directly upon the design of the treatment plan. For example, if, after baseline data analysis, it is determined that the target behavior rate is extremely high, then one would not choose to implement a DRO program which is suited for low-rate behaviors.

• Method for judging the ongoing effectiveness of the behavior program – systematic collection and graphing of data is important in tracking the progress of a treatment plan. Trends in data can be analyzed to support any changes necessary to the initial program. Modifications to the program should be "data-driven" and not based on anecdotal staff reports alone.

• Feedback to family, staff, payers, and client – behavior data provide important information to those responsible for the client's well being and/or funding. People typically respond more favorably to observationally-recorded data of behavior, rather than statements such as "They are behaving better." Graphs, based on collected data, help the client, staff, and others visualize and understand the impact of the behavioral intervention plan. Graphs can also assist the client in developing self-monitoring skills.

• Valuable information for research and program development – if the person is in a school or rehabilitation program, systematic collection of behavior data assists those responsible for clinical research, conference presentations, preparation of professional manuscripts, and program development. These activities require the support of reliably collected data.

Data Collection

There are many methods for collecting data. The three most common and practical meth

ods are event recording, interval recording, and time-sample recording. These three data col

lection methods are known as direct observational recordings (Table 14.3).

TABLE 14.3

Direct Observational Data Collection Methods Method Definition Considerations

1. Event Recording Tally each occurrence of target behavior. Requires constant observation. Difficult to judge beginning and end of behavior.

2. Interval Recording Record each occurrence or nonoccurrence of target behavior during each interval. Requires constant observation. Results in approximations of behavior duration and frequency.

3. Time-Sample Recording Record occurrence or nonoccurrence of target behavior at the end of each interval. Broad approximation of behavior duration and frequency.

Event Recording

Event recording (Figure 14.3) is probably the easiest direct observational recording system.

The only requirement is to mark on a piece of paper each time a specific target behavior

occurs. Hand-held devices, such as golf counters, can be used to make counting easier for

high-frequency behaviors. The drawback to event recording is that it can be difficult to

judge when one occurrence of a behavior ends and another occurrence begins. In tallying

angry language, for example, if a person is yelling for several minutes, it would be difficult

to judge how many instances of angry language actually occurred. The person recording

would have to decide whether to count the entire period as one event or try to tally each

statement as a separate occurrence. In addition, high-frequency and long-duration behav

iors are more difficult to count because of the amount of attention required. Event record

ing requires constant observation of the client so all occurrences of the target behavior are

recorded, thus making it one of the most time-consuming of the data collection procedures.

Interval Recording

Interval recording (Figure 14.4) eliminates the task of judging the beginning and ending

of behavioral episodes and tallying high-frequency or long-duration behaviors. Instead,

interval recording divides the therapy session (or observation period) into equal time

intervals (e.g., 15-minute periods) and requires the person recording to mark whether or

not the target behavior occurred during each interval. It does not matter how many times

Client Name: John Williams Date: 4-14-03 Time: 1–2 pm

Therapist Name: Mary Smith Therapy: OT

Instructions: Tally the number of occurrences of each target behavior. Target Behaviors Tallies Total

1. Physical Aggression

Definition — attempting to and/or actually striking

an individual with an object or body part l l 2

2. Angry Language

Definition — cursing, threats, or any hostile language

delivered with increased volume l l l l l 5

3. Property Destruction

Definition — attempting to and/or actually

damaging property l 1

4. Refusal

Definition — not starting, interrupting, or

stopping therapy or instructions > 60 sec l l l l l l l 7

5. Escaping

Definition — attempting to and/or leaving the

place of required activity l l l 3

FIGURE 14.3

Example of an event recording sheet.

the behavior occurred during the interval, only that it occurred at least once. Interval

recording requires choosing an appropriate interval size. Time intervals should approxi

mate the frequency rate of the behavior. High-rate behaviors require short time intervals

(e.g., 5 minutes) and low-rate behaviors need long time intervals (e.g., 15 minutes). For

example, if a person uses angry language approximately once every 10 minutes, an

observation interval of 10 or 15 minutes would capture most of the variability in the

behavior. If the interval size is too long, the rate of behavior may change and not be

reflected in a measurement of percent of interval change. When the intervals are extremely

short (e.g., 30 seconds), every other interval should be used for marking the data sheet.

This achieves greater accuracy because the observer does not miss occurrences of behavior

while attending to the recording sheet. If several target behaviors are being tracked

simultaneously, the use of behavioral codes is recommended to simplify the procedure.

At the end of each interval, the person recording marks the behavioral code (e.g., PA =

physical aggression) for those behaviors that occurred during the interval. As in event

Client: John Williams Day: Monday Date: 4/14/03

Instructions: Every 15 min you are to mark any target behaviors and level of cooperation listed below that occurred during

that period by circling the letter corresponding to the behavior. The interval begins at the listed time (e.g., mark in the 2:00 period

behaviors seen from 2:00 to 2:15). Note any observations and comments in the space provided.

Target Behaviors: PA = Physical Aggression, AL = Angry Language, PD = Property Destruction, R = Refusal to

Work, E = Exiting

Cooperation: None = No cooperation (with behavior), Part = Partial cooperation (with behavior), Full = Full

cooperation (no behavior)

Therapy SP

Target Behaviors > Cooperation > 9:00 a.m. PA AL PD R E None Part Full 9:15 a.m. PA AL PD R E None Part Full 9:30 a.m. PA AL PD R E None Part Full 9:45 a.m. PA AL PD R E None Part Full

Comments/Other >

Therapy OT

Target Behaviors > Cooperation > 10:00 a.m. PA AL PD R E None Part Full 10:15 a.m. PA AL PD R E None Part Full 10:30 a.m. PA AL PD R E None Part Full 10:45 a.m. PA AL PD R E None Part Full

Comments/Other >

Therapy ED

Target Behaviors > Cooperation > 11:00 a.m. PA AL PD R E None Part Full 11:15 a.m. PA AL PD R E None Part Full 11:30 a.m. PA AL PD R E None Part Full 11:45 a.m PA AL PD R E None Part Full

Comments/Other >

Therapy PT

Target Behaviors > Cooperation > 1:00 p.m. PA AL PD R E None Part Full 1:15 p.m. PA AL PD R E None Part Full 1:30 p.m. PA AL PD R E None Part Full 1:45 p.m. PA AL PD R E None Part Full

Comments/Other >

Therapy RT

Target Behaviors > Cooperation > 2:00 p.m. PA AL PD R E None Part Full 2:15 p.m. PA AL PD R E None Part Full 2:30 p.m. PA AL PD R E None Part Full 2:45 p.m. PA AL PD R E None Part Full

Comments/Other >

Therapy SP

Target Behaviors > Cooperation > 3:00 p.m. PA AL PD R E None Part Full 3:15 p.m. PA AL PD R E None Part Full 3:30 p.m. PA AL PD R E None Part Full 3:45 p.m PA AL PD R E None Part Full

Comments/Other >

FIGURE 14.4

Example of an interval recording sheet.

recording, interval recording requires the undivided attention of the person recording. It

is necessary to track both interval time and occurrence of target behaviors.

Time-Sample Recording

The last data collection method to be covered is time-sample recording (Figure 14.5). Time

sample recording is similar to interval recording except that it does not require constant

attention by the person recording. Behavior is only periodically sampled. A therapy session

(or observation period) can be divided into equal or variable (random) periods at the end

of which (during a brief time-sample) the person recording marks the occurrence or

nonoccurrence of the target behavior. The advantage of this method is that the person

recording does not have to continuously monitor the client's behavior and it is minimally

intrusive on any activities, which also makes it ideally suited for monitoring high-fre

quency behaviors. It does require a device such as a timer to signal the end of each time

period. The disadvantage is that time-sample recording results in an even broader approx

imation of behavior frequency than does interval recording.

Computer Management of Data

With the advent of powerful and affordable personal computers, a number of spreadsheet

programs have been made available which are well suited to managing and graphing

behavior data. If a facility handles a fair number of clients with behavior difficulties, it is

highly recommended that one of these programs be used. Organizing data is a time

consuming task that can be streamlined with the help of computer technology. Spreadsheet

Client Name: John Williams Date: 4-14-03
Time: 2–3 pm

Therapist Name: Mary Smith Therapy: OT

Instructions: At the times listed in the left column, observe the client for 30 sec then put an “X” under Yes if the target

behavior occurred, or under No if the target behavior did not occur. Target Behavior Definition

Angry Language Cursing, threats, yelling, or any hostile language delivered with increased volume. Time Yes No Time Yes No 9:00 X 9:32 X 9:03 X 9:35 X 9:10 X 9:40 X 9:15 X 9:47 X 9:23 X 9:51 X 9:25 X 9:56 X

Data Calculation:

Total Yes’s = 5 Total Yes’s/ Total Samples = 5/12

Total No’s = 7

Total Samples = 12 = 42% of time-samples

FIGURE 14.5

Example of time-sample recording sheet.

programs, such as Excel∗, are very useful for this purpose. They typically include both

spreadsheet functions and graphing capabilities. Figure 14.6 is an example of a computer

summary sheet covering 1 week of interval data. It includes columns for the date, day,

each target behavior (e.g., PA = physical aggression), and the total number of intervals

recorded. All that is required is to write simple formulas for each of the percent calculations

and design a master form that can be retrieved for each new client.

Another option, especially for high-volume data collection, is electronic forms. Most of

us are familiar with survey forms and questionnaires that we receive in the mail. After we

fill them out, we either fax or mail the completed forms to the survey company. Behavior

data can be collected in the same fashion. Behavior data sheets can be created in an available

program, such as Teleform**, and the results scanned and organized electronically.

Graphing

Due to its single-case structure, behavior analysis does not lend itself to statistical proce

dures to judge the effectiveness of treatment interventions. Graphs are the traditional

means of accomplishing this task. They provide an overall visual impression of behavior

that is easy for staff, families, clients, and others to understand. As it is common for

behavior problems to accelerate before decreasing after the introduction of the treatment

intervention, graphs are an easy way to track learning curves. Graphs can be produced

by hand or with one of the numerous commercially available computer graphics programs

or with a spreadsheet program, such as Excel.

There are two fundamental concepts to remember when graphing. Firstly, what infor

mation goes with the vertical line (ordinate, or y-axis) of the graph and, secondly, what

information goes with the horizontal line (abscissa, or x-axis) of the graph. Figure 14.7

labels all the basic components of a graph.

For event-recorded data, the ordinate indicates the number of occurrences of the target

behavior (e.g., physical aggression) and the abscissa indicates the time across which the

behavior was recorded (e.g., days, weeks). For example, if one were graphing the number

PA = Physical Aggression, AL = Angry Language, PD = Property Destruction, R = Refusals, E = Exiting,

T = Total Intervals

John Williams

Week 1 PA AL PD R E T 4/10 1 5 0 2 1 24 4/11 0 2 0 1 0 20 4/12 3 5 1 3 1 24 4/13 1 1 0 0 0 20 4/14 2 4 1 2 1 24

Total 7 17 2 8 3 112

Percent 6.25 15.18 1.79 7.14 2.68

FIGURE 14.6

Example of computer summary data sheet.

* Microsoft Excel 2000, Copyright 1985–1999 Microsoft Corporation.

** Teleform, Cardiff Software, Inc., Copyright 1991–1998.

of occurrences of physical aggression on a weekly basis, the graph would look something

like Figure 14.8.

In addition, choose the maximum value for the ordinate scale based on a number that

is slightly higher than the highest frequency that has occurred with the person. For

example, if the highest number of occurrences of physical aggression in a week was four,

then choose five as your maximum value for the ordinate scale.

For interval or time-sample recording, the ordinate of the graph indicates the percentage

of intervals (or time-samples) in which the target behavior has occurred. The abscissa of

the graph represents the time period during which the behavior was recorded. For

FIGURE 14.7

Components of a graph.

FIGURE 14.8

Example of an event graph.

example, if one were graphing the percentage of intervals for physical aggression on a

weekly basis, the graph would look something like Figure 14.9.

Choose the maximum percentage for the ordinate scale based on a slightly higher

percentage than the maximum that has occurred with the person. For example, if the

highest percentage of intervals with physical aggression in a week was 20%, then choose

25% as your maximum value for the ordinate scale.

Interpreting graphs can sometimes be very difficult. Behavior that is either highly

variable or changes very little can make analysis a challenging proposition. One can look

for a general trend or slope, or one can begin grouping data and comparing means

(averages) to help detect changes in behavior.

A graphing technique we have found to be extremely useful in situations where inter

pretation is difficult is called trend graphing. This graph

is tedious to complete by hand,

but most spreadsheet programs now have the ability to calculate a “line of best fit” graph.

If we take a behavior (e.g., physical aggression) and create a trend graph, it will show us

the future projected change of physical aggression based upon the current observed rate

of change. Figure 14.10 is an example of a trend graph. It clarifies the effect of the treatment

and indicates when a target behavior might be expected to reach a projected goal. Of

course, there are numerous variables that can have an impact on goal attainment, so care

must be taken when interpreting trend graphing.

Crisis Prevention and Intervention

Assaultive behavior, such as physical aggression, is common in the field of traumatic brain

injury rehabilitation. 138 All of the planning and programming described in the previous

sections cannot always prevent or predict the occurrence of assaultive behavior by a client.

In some cases, behavioral programming may even elicit aggression when it exerts control

over sensitive aspects of a client’s environment. Assaultive situations can be a frightening

FIGURE 14.9

Example of an interval or time-sample graph.

experience. People can be combative during the acute phase of recovery as they reorient

themselves to the world around them and during postacute rehabilitation (i.e., when a

person has reached medical stability) as they develop

awareness of functional deficits.

Severe behavior is a reality of the rehabilitation process and staff can learn to take mea

sures, when possible, to prevent its occurrence. However, if a crisis situation does occur,

staff should also be equipped with techniques to de-escalate the client and decrease the

likelihood of injury to the client and others.

This section will cover some basic models of the assault cycle, common reasons for

assaultive episodes, techniques for preventing the development of crisis situations, and

useful interventions if a crisis cannot be prevented. However, this chapter is not a replace

ment for a certified course in crisis intervention or management of assaultive behavior.

There are a number of training programs available to train staff directly or to certify staff

members as instructors. We highly recommend that all facilities, schools, or families that

work with people with traumatic brain injury with behavior problems incorporate this

training as standard practice. The content, structure, and training methodology of these

courses, including the practice of self-defense and restraint techniques, is an effective

means of comprehensively equipping a person to safely handle assaultive situations.

Models of Assault

Paul Smith, 139 founder of Professional Growth Facilitators and author of Professional Assault

Response Training (PART) ® *, has proposed seven models of assaultive behavior. They are

the Common Knowledge Model, Stress Model, Communication Model, Environmental

Model, Legal Model, Developmental Model, and Basic Needs Model. We will only concern

ourselves here with the first five. The developmental and basic needs models are not

typically related to the field of TBI rehabilitation.

FIGURE 14.10

Example of a trend graph.

* Registered Trademark of Professional Assault Response Training, Citrus Heights, CA, 1983.

Common Knowledge Model

Smith 139 believes that the underlying reasons as to why people attempt to injure one

another are relatively simple and that one can apply intervention techniques to effectively

respond to these events. He states that assaultive incidents can be reduced to four common

motives: fear, frustration, manipulation, and intimidation.

When people are afraid, or feel that their safety is threatened, their behavior may escalate

to physical aggression as a means of defending themselves. To reduce fear, staff can

respond to the client with a relaxed posture, use slow and natural gestures, keep a safe

distance from the client, stand off to the side, position oneself below the client's eye level,

use a firm, yet reassuring voice, stay logical, and encourage calm reflection.

When a client's behavior escalates as a result of frustration, staff members need to follow

different guidelines than those used with a fearful client. Staff should demonstrate control

with a more commanding posture, use forceful gestures such as pointing, stay directly in

front of the person but just out of reach, keep the tone of voice quiet, yet forceful and

confident, and repeat commands.

If a client is escalating behaviorally as a means of manipulation, a role of “detachment”

is the technique recommended by Smith. 139 This method involves maintaining a closed,

yet relaxed, posture, mild gestures of disapproval (e.g., finger tapping), positioning far

enough away from the client to show noninvolvement, turning slightly away from the

client, using a detached, slightly “bored” tone of voice, and quiet, repetitive commands.

If the client is attempting to intimidate through escalated behavior, the technique

Smith 139 advises is “identifying consequences.” The basic premise is that clear communi

cation of the consequences of an assaultive act will reduce the probability that the episode

will occur. Staff should be poised and ready to react (without giving the impression of

fear), keep gestures to a minimum, position oneself for protection (e.g., behind a chair or

desk), maintain a monotone, emotionless tone of voice, and give clear and direct state

ments of consequences.

Stress Model

The stress model views assaultive behavior as a reaction to extreme stress. The rehabili

tation process, as we know, is an extremely stressful situation for a person. When a client

perceives a threat to his well being (e.g., daily confrontation of deficits), he can either fight

or flee from the situation. In TBI rehabilitation, we see both of these responses. Some

clients try to escape the stress of their condition by either escaping or avoiding therapy.

Others become combative when stressed. Each client has specific responses to stress, which

can be detected and recognized as predictable patterns. A common tool for visualizing

these response patterns is “The Assault Cycle” graph (Figure 14.11). It is divided into five

separate phases. They are: (1) triggering event, (2) escalation, (3) crisis, (4) recovery, and

(5) postcrisis depression.

The triggering event is any stimuli or event that exceeds the client’s tolerance for stress

(e.g., demands for compliance, being touched, etc.). This begins the assault cycle. Any

prevention techniques (e.g., arranging of environment, level of demands, etc.) would have

to occur before the triggering event. The escalation stage is characterized by increasing

levels of agitation or changes in the normal (i.e., baseline) behavior of the client. De

escalation techniques are used during this phase to try to help the client return to a baseline

level of behavioral activity. The sooner de-escalation techniques are used during this stage,

the less likely more restrictive measures will have to be implemented. The crisis stage is

characterized by the client's physically "acting out." At this point, de-escalation techniques

have failed and physical intervention may be necessary. During the recovery phase, the

client's level of activity is decreasing. Once the person regains self-control, decrease any

external control that may have been introduced. The last stage, postcrisis depression, is

characterized by activity that falls below baseline levels. The client may require a short

period of rest or less active tasks until recovery occurs.

Communication Model

The communication model focuses on the balance of communication between the therapist

and client. On one end of the spectrum is "withdrawal" and on the other end "assault."

Smith 139 believes that the best means for achieving a "balance" that decreases the chances

of triggering an assaultive cycle is with assertive communication. Smith states that the

communication model takes into account client manipulation and intimidation. When

staff members respond with either intimidating aggressiveness or submissive nurturing,

they contribute to an imbalance of communication and increase the opportunity for an

assaultive situation. Smith 139 emphasizes that, "by using assertive communication,

employees (or clients) reduce the chance that an assault will occur" (Chapter 4, p. 13).

Environmental Model

Smith 139 describes the environmental model from the

perspective that assaultive behavior

is, for the most part, a product of the circumstances in which it occurs. This is the model

that most closely fits the fundamental philosophy of behavior analysis. Although Smith

does not discuss consequences to behavior as part of his model, he does emphasize the

role of antecedents and setting events in triggering or setting the stage for assaultive

behavior. Such things as weather conditions, level of sound, crowding, and scheduling of

activities are given as examples of events that can "predispose people to assaultive behav

ior." The important point to make concerning the environmental model is that staff is in

control of most environmental antecedents to behavior. Schedules, noise level, tone of

voice, etc., are usually under the control of the staff. Staff can take advantage of this

opportunity to prevent "trigger events" and minimize assaultive behavior.

Legal Model

Assaultive behavior can be separated into legal categories. They are: (1) simple assault,

(2) assault and battery, and (3) aggravated assault. The staff can legally protect itself against

these varying degrees of assault, but is limited to using only "reasonable force." As Smith 139

states, "A reasonable amount of force is just enough for effective self-protection …" For

example, with simple assault (i.e., threatening gestures or speech), communication

FIGURE 14.11

The assault cycle. (From Smith, P., Professional Assault Response Training (PART), Workshop Syllabus, Citrus

Heights, CA, 1983. With permission.)

techniques would be the maximum force that could be legally applied. With assault and

battery (i.e., use of physical force and threats), evasive self-defense would probably be the

maximum reasonable force allowed. If aggravated assault (i.e., attempt to cause serious

bodily harm) occurs, a controlling self-defense (i.e., restraint) and physical intervention

would be reasonable. The use of physical techniques for self-defense and other interven

tions requires intensive training. Unless a staff member has completed this training, he

should have limited contact with clients exhibiting severe behavior disorders.

General Techniques and Methods

There are many techniques for preventing a crisis situation or intervening once it has

started. We have covered many of those methods in the previous section. Smith's 139

recommendations regarding body posture, tone of voice, content of speech, and use of

gestures are invaluable aids to dealing effectively with a crisis episode. There are other

techniques that can be added to this list.

To help prevent a crisis situation from being "triggered," review the guidelines outlined

in the General Management Guidelines section of this chapter. These included (1) increasing

rest time for the client, (2) keeping the environment

simple, (3) keeping instructions simple,

(4) giving feedback and setting goals, (5) staying calm and redirecting the client to task, (6)

providing choices, (7) decreasing chances of task failure, (8) varying the type of activities,

(9) over-planning, and (10) utilizing task-analysis procedures. If one can implement these

environmental controls and combine them with sensitivity to patterns of interaction and

sharpened observational skills, most assaultive events can be prevented. For those that are

unavoidable, intervention techniques for de-escalating the client must be employed.

Once the escalation phase of an assault cycle has begun, measures by staff change from

one of prevention to one of intervention. The intervention techniques used during the

escalation stage are an attempt to de-escalate the client before the cycle reaches the crisis

stage. The earlier the intervention, the less restrictive the measures will need to be to

control the situation. If the client progresses to the crisis stage, de-escalation techniques

will not be useful and may, in fact, prolong the crisis. Physical intervention by staff,

unfortunately, becomes likely.

Some of the most effective de-escalation techniques staff can utilize are active listening,

orientation, setting limits, redirection, withdrawal of attention, and contracting.

• Active listening — a technique incorporating a variety of listening skills. 140 Active listening begins on a “nonverbal” basis. The staff member should make eye contact with the client, maintain a relaxed posture that shows

interest, and use natural gestures. Once this nonverbal basis has been established, verbal statements can be utilized. These consist of paraphrasing, clarifying, and perception checking. Paraphrasing is a method of restating the client's message in fewer words. Its purpose is to indicate to the client that you are trying to understand his message. Clarifying focuses on the more abstract messages from the client. The staff member admits confusion about a statement and tries a restatement or asks for clarification; for example, "'I'm confused, is what you are saying …?" Perception checking involves asking the client for verification of your perception. For example, "You seem to be very mad at me. Is that correct?"

• Orientation – memory deficits are one of the most common consequences of a TBI. People can experience periods of severe disorientation. Disorientation has been found to be a key factor in the severe behavior of people with traumatic brain injury. Orienting a client to the time, to his location, and to whom he is with can sometimes help to de-escalate a client. It helps the client feel less threatened by the environment when he can understand where he is and why he is there.

• Setting limits – as stated earlier, setting limits can be a useful technique. This is especially true for clients who are trying to intimidate staff by threatening severe behavior. Although these can be frightening experiences, escalation can be curtailed if the staff member remains calm and confident and outlines the consequences of the threatened behavior. For example, "If you throw that chair at me, you will be restrained by four other staff members until you are calm."

• Redirection – also known as topic dispersal, is useful when a client is in the early stages of escalation. Staying calm and redirecting a client to another task or activity can interrupt the escalation phase and refocus the client on something else. It also decreases the opportunity for inadvertently reinforcing the client with attention that may be the behavior problem's maintaining reinforcer.

• Withdrawal of attention – this technique is the opposite of active listening. Whereas active listening provides undivided attention to the client during escalation, withdrawal of attention discontinues any attention during escalated behavior. Withdrawal of attention is usually more effective with "manipulative" types of behavior. Clients exhibiting this type of behavior thrive on attention from others. Withdrawing attention for brief periods of time

when they begin to escalate helps establish a relationship between “attention” and cooperative, calm behavior.

• Contracting — like other de-escalation techniques, this is a skill that takes some practice. The reason, however, is that contracting has the potential for being misused. If used incorrectly, it becomes a method of “buying” good behavior that may lead to further behavior problems from the client. For example, if a client is escalated over completing an unpleasant task and you “contract” with him that he does not have to finish the task if he calms down, you have set yourself up for future problems when the client does not want to complete a task. You may have reinforced the escalated behavior. A more constructive response may be to tell the client that he can switch to another task for the moment and finish the difficult task later in that session. This teaches the client that he can let you know when he has reached his limit of frustration with an activity and would like to work on something else for a while.

The models of assault, as outlined by Smith, 139 provide us with a structure in which to

view crisis episodes. Techniques for prevention should be the first line of defense in dealing

with severe behavior problems. Behavior treatment plans should always include instruc

tions for controlling antecedents and setting events to help prevent problem behaviors

from occurring. If they do occur, the treatment plan outlines the consequences to the

behavior and provides procedures for staff to follow. All crisis situations, however, cannot

be predicted or prevented by a behavior program. This is why it is important for staff to

be trained in techniques and methods of crisis intervention. Hopefully, the techniques

described in this section, although not a substitute for direct training, will at least assist

staff and family members with basic approaches to crisis intervention. Recommended Training Professional Assault

Response Training (PART) Professional Growth Facilitators P.O. Box 5981 San Clemente, CA 92674-5981 (949) 498-3529 pgfsc@aol.com Crisis Prevention Institute, Inc. (CPI) 3315-K North 124th Street Brookfield, WI 53005 (800) 558-8976 or (262) 783-5787 www.crisisprevention.com

Staff and Family Training

A fundamental component to the implementation of a sound behavioral treatment plan

is staff training. To be successful in treating people with traumatic brain injury with

behavioral difficulties, rehabilitation facilities must be committed to providing adequate

staff training and support. This commitment is not only one of allocating the time and

financial resources for training but also of providing philosophical support of behavioral

principles, use of its techniques, and sufficient staffing levels to effectively carry out

behavior programs. Without this foundation, it would be very difficult for a facility to

realize the full benefit of behavioral programming. These issues aside, training consists

of the following steps:

• Basic principles — training must begin with an understanding of basic behavioral principles. Staff should be able to identify environmental influences (antecedents and setting events) and responses (consequences) that help to maintain target behaviors. It is especially important for staff and families to understand the importance of consistency in implementing treatment plans and in responding to the client behavior.

• Data collection — staff members require training to enable them to accurately observe client behavior and reliably record data. This can include training to criteria. For example, staff can observe client behavior on video tape and fill out data sheets until they are within 90% agreement of preestablished scoring.

• Behavior procedures — it is important for staff and families to understand the structure of behavior treatment design, for example, the differences between accelerative programs (e.g., positive programming), decelerative programs (e.g., DRO), and complex programs (e.g., token economy). Staff members are better able to consistently follow programs that they understand.

• Ethical issues — it is recommended that staff and families be informed of current ethical issues and guidelines regarding the use of behavior programs. Applied behavior analysis can be a powerful and controversial intervention for behavioral change. The procedures must be implemented with great care, understanding, and sensitivity.

• Environmental validity and generalization — staff and families need to understand the concept of environmental validity (the teaching of skills at the proper time and in a natural setting) and generalization (the transfer of skills from one setting to another). Skills are not useful if they cannot be performed in the correct context or cannot be transferred from a clinical setting to the home and community. For example, being able to dress in a clinic treatment room at 11 a.m. is not the same as being able to dress at 7 a.m. in your own bedroom.

• Team approach — training should emphasize the importance of a team approach to applied behavior analysis. Assisting one another in crisis situations or helping when a client or staff member is not “having a good day” are just a couple of situations which illustrate the need for staff to act as a team. Staff members are more confident at implementing behavior programs when they know that others are there to help if the circumstances warrant it.

• Management of assaultive behavior — even the most effective behavior programs may not always prevent a crisis situation. Several courses provide training in management of aggressive behavior and crisis intervention. They typically include methods of observation, de-escalation, self-defense, and physical restraint. This training, in our experience, affords one of the best means for instilling confidence in staff to effectively work with behaviorally-difficult clients. It provides for a systematic approach to aggression and a structure in which all behavioral interactions and interventions can be gauged. These courses tend to emphasize early intervention in the client’s “assault cycle,” before it reaches a crisis stage that requires physical intervention. This training

also provides a useful means for ensuring adherence to the legal requirements of balancing the restraint of clients and self-defense.

• Behavior staffings — staff members require a forum to openly address and discuss current behavioral issues. Weekly behavior staffings, of at least 1-hour duration, are a minimum requirement for keeping abreast of the latest behavioral concerns. They also provide an excellent venue for continuing staff education on behavior methodology.

• Family training — many clients continue to have behavior problems that persist after being discharged from a facility. Those people who will play a significant role in the client's life after rehabilitation will need training in the proper use of behavior analysis and access to behavior specialists for ongoing support. Facilities can provide families with the same training as their staff. Family members can practice behavior procedures (with the client) under the guidance of the facility. Without this training, behavioral stability after discharge from a facility is less likely to be maintained.

Putting It All Together

This chapter has described the basic components of effective behavior program designs.

However, each component does not stand alone. All of the steps are integrated and must

be systematically completed in order to reach the desired behavioral outcome.

• Perform behavioral diagnostics — first, a thorough assessment must be performed. This consists of reviewing historical information about the client that helps the behavior programmer understand how the client may respond to rehabilitation and what he or she expects to gain from treatment. It involves evaluating the client's current functional skills and analyzing clinical test results that can dictate the type of behavioral procedure that is implemented. Most importantly, a thorough behavioral assessment includes a functional analysis that identifies the function served by each target behavior.

• Identify potential conditions maintaining the behavior — the result of behavioral diagnostics should be the identification of conditions that might be supporting the target behavior. Is there an antecedent or setting event to

the behavior? Are there responses to the behavior that are reinforcing? What function might the behavior be serving? The three parts of a functional analysis are (1) identification of the target behavior and its surrounding events, (2) predicting the factors that control the behavior, and (3) testing of the behavioral hypothesis by manipulating those factors.

• Collect baseline data — once the assessment is complete, the target behavior defined, and the maintaining conditions identified, baseline data can be collected. Baseline data will provide valuable information concerning the frequency and duration of the target behavior and a means for judging the effectiveness of the treatment procedure. The behavior programmer can choose an event, interval, or time-sample recording method based on the characteristics of the target behavior. Event recording is better suited to discrete behaviors (i.e., those with a clearly defined beginning and end). Time-sample recording is more appropriate for highrate behaviors that are ill-suited to constant observation, and interval recording works for general-purpose data collection.

• Design and implement treatment procedures — after baseline data has been collected, a treatment plan can be designed and implemented. The behavior program should include short- and long-term goals, clear operational definitions of the target behavior, a list of any materials needed, a description of the data collection system, and procedures for staff to follow. Procedures can be accelerative (designed to increase the target behavior), decelerative (designed to decrease the target behavior), or complex (having characteristics of both accelerative and decelerative programs). Effective behavioral programming may even require combining more than one of these procedures simultaneously.

• Continue data collection — once the treatment plan has started, data collection should continue as a means of monitoring the progress of the client. Data recording sheets should be completed on a daily basis in as many environments and conditions as possible. Systematic data collection allows the programmer, staff, client, family, and others to be kept abreast of the client's progress. People typically respond more favorably to observationally recorded data of behavior than statements such as "They are behaving better."

• Graph and analyze behavior data — behavior data should be routinely summarized and graphed. Graphing is one of the

best means for analyzing the effect of a treatment plan. It provides an overall visual impression of behavior that is easy to understand and, also, an effective way of tracking learning curves. The behavior programmer can then base any modifications to the treatment plan on more objective data rather than anecdotal reports.

• Modify treatment procedures — treatment procedures should be altered only when there is sufficient evidence in the data to indicate a failure in the procedure's effectiveness, or when the data indicates a need for a transition to a less structured approach. This can happen when the original behavior problem has been resolved. In this situation, the use of trend graphing can be useful. Trend graphs show the future projected change in a behavior based on the current observed rate of change.

• Plan for generalization and maintenance of changed behavior — treatment plans are not successful if a behavioral change is not generalized to other environments and conditions and maintained over time. As treatment and recovery progress, procedures require modification, for example, thinning a reinforcement schedule or decreasing dependence on prompts. If the client will be living with others after rehabilitation, training of these individuals in basic principles and treatment procedures is essential for a successful outcome. Long-term maintenance of behavior changes can hinge on the ability of family and friends to continue the treatment plan after a client has been discharged from a facility.

Concluding Remarks

As the field of traumatic brain injury rehabilitation grows beyond its infancy, behavioral

treatment procedures are being recognized as an essential component of successful client

outcome. Applied behavior analysis provides the structure and consistent feedback

required by people with traumatic brain injury. Although many facilities understand the

concepts of behavior analysis and recognize the need for its implementation, the authors

have seen very few facilities actualize this ideal. Usually, this is a result of a division

between a behavioral approach on the one hand and a therapeutic approach on the other.

Behaviorally-oriented staff focus primarily on the behavior of a client, whereas therapists'

main concern is with recovery of lost cognitive and physical skills. Both need to work

together, recognizing the contribution each makes to the total rehabilitation of the client.

The result of any such division is that behaviorally-challenged clients are under-treated,

not able to progress to their highest level of independence, and, in many cases, placed in

a long-term restrictive environment.

Reductions in the use of aversive procedures and emphasis on nonaversive techniques

are forthcoming. Legal and ethical concerns related to the use of aversive procedures are

making these programs increasingly more difficult to implement, which, in our opinion,

will be an unfortunate and impractical consequence. The full spectrum of behavior tech

nology can be properly utilized with comprehensive ethical guidelines and monitoring.

Applied behavior analysis is an essential component in helping people with traumatic

brain injury rebuild their lives. Helping these individuals reintegrate into the home,

community, and work settings presents a great challenge to the field of rehabilitation.

Behavior analysis provides an effective means of achieving this goal.

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15

Management of Residual Physical Deficits

Velda L. Bryan, Christie Byrd Depner, and Prudence Gensman

CONTENTS

An Historical Perspective

Since World War II, an internationally scattered group of occupational therapists (OT) and

physical therapists (PT) have developed and advocated theories and treatment procedures

to address sensorimotor deficits in the neurologically-impaired patient. 1–7 However, until

the early 1980s, training and practice of these techniques were usually found only in

specialty clinics and in advanced professional workshops. The majority of general practice

therapists were neither trained in nor practiced a therapeutic approach based on neuro

physiological or developmental principles. Among those with training, some therapists

were strong advocates of only one approach while others were applying bits and pieces

of all the then-known treatment approaches. Their patients were usually of cerebral palsy,

stroke, multiple sclerosis, and other neurological etiologies.

Survivors of traumatic brain injury (TBI) prior to the 1970s were encouraged to use

functional extremities, were put into wheelchairs and braces, and were eventually sent

home or to an institution. Treatment was usually dictated by medical personnel who were

not rehabilitation oriented. An early entry into the therapy department was rare and

usually awaited the TBI patient’s ability to respond or cooperate.

Most ICUs were not familiar territory for therapists until the mid-1980s when it was

realized that early consistent range of motion and positioning would later enhance general

care and rehabilitation outcome. As early as the 1960s, Bobath 1 advocated that nurses and

therapists should develop cooperative relationships at the ICU and acute floor levels.

Building a bridge of understanding and cooperation between nurses and therapists

required careful diplomacy and patience. Despite graphic instructions on the walls over

patients’ beds, continuity of positioning care was poor. Abnormal postures became habit

ual and the limitations of contractures hindered mobility long down the rehabilitation

road. Today, it is not uncommon to see multisensory stimulation programs undertaken

by the rehabilitation staff in the ICU. In fact, it is generally accepted that this practice is

beneficial overall, though there may be some question as to what physiological or bio

chemical benefit is derived for persons with severe diffuse TBI. 8

The “brain injury unit,” as an important, separate, and distinct unit, was not prevalent

in general or acute rehabilitation hospitals prior to the 1980s. A focused, comprehensive

team approach was absent and vital supportive components were missing. The various

therapy departments represented distinct territories, each treating a designated anatomical

portion of the person. Speech and occupational therapists often bickered over the territory

of oral feeding programs. Physical and occupational therapists did battle over the upper

extremity and some were concerned when a speech therapist would attempt to ambulate

or transfer a person during a session.

Physical rehabilitation essentially focused on strengthening the “good” side and rarely

challenged the impaired or “bad” side. We neglected the potential of the person as a

“whole.” Bobath 1 warned of the inherent failure of this “compensatory rehabilitation”

approach. Many therapists made assumptions about a person’s skills from the narrow

view of the clinical setting rather than from a broader real world perspective.

Severe cognitive and perceptual deficits and inappropriate behaviors often over

whelmed the physical rehabilitation effort and these people were usually discharged due

to “lack of progress,” “lack of motivation,” or as “uncooperative.” Behavior modification

training to support the treating staff was nonexistent. Therapies were frequently further

hindered by use of psychoactive medications. People with TBI were often discharged to

nursing homes or to locked psychiatric hospitals or, without other options, many were

discharged to frightened families. TBI was puzzling and many wrong assumptions were

made about the sequelae of brain injury. In the process, the notion that the person with

acquired brain injury could not appreciably benefit from rehabilitation was perpetuated.

Meanwhile, emergency neurotrauma and neurosurgical technology dramatically

improved as a result of the Korean Conflict and the Vietnam War. By the mid-1970s, the

TBI survivor population was increasing and institutionalization became more and more

unacceptable. Although early, aggressive involvement of therapists in the acute facility

had not yet captured great enthusiasm, therapists began to question the old points of view

and began to be truly challenged by people with TBI. By the late 1970s, a handful of

therapists dedicated themselves to organizing a postacute

TBI rehabilitation environment.

These people knew inherently that they could expand horizons for this special population

and, soon, their vision became a reality. A chance for “life after head injury” was coming

into view.

In the early 1980s, professional attendance at the first TBI conferences and response to

initial publications revealed an intensified international interest. Jennett and Teasdale 9 and

Rosenthal, Griffith, Bond, and Miller 10 brought the broad scope of TBI into clearer view

and the idea of continuity of care to our attention. During this time, many postacute

admissions presented with unnecessary contractures, unattended heterotopic ossification,

misdiagnosed or ignored vestibular and oculomotor deficits, poorly defined cognitive

deficits, and polypharmacy for aggressive behaviors. Until the mid-1980s, many postacute

TBI clients lost valuable time, at tremendous expense, due to the fact that they required

“reconstructive therapy.” This loss ultimately reflected a less-than-optimal outcome.

Although it was a frustrating time for clients and therapists, many knew that more could

be accomplished.

During this time, the expansion of a continuity of rehabilitation care from the acute

through the postacute directed many therapists to reflect on the seemingly obscure lessons

of the past. New enthusiasm for Bobath’s 1 teachings and Ayres’s 7 concept of sensory

integration emerged. The notion of hierarchical development in the human being was

revisited. Therapeutic intervention was noted to be more successful when directed in the

appropriate developmental order. The complex nature of TBI residuals requires, and was

recognized to benefit from, an organized, integrated, progressive approach which utilizes

theories and treatments from all rehabilitation disciplines. 11 Alternative views regarding

posture and movement control emerged and gave therapists fresh avenues through which

to evaluate and treat balance and movement deficits. 7,12–14

By 1990, increasing involvement of therapists during the acute stage was evidenced.

Recent authors point out that good preventative care must begin at the acute level for the

severely brain-injured patient. 15–17 As a result, early consistent positioning, use of inhibitory

and facilitatory techniques, and orienting activation of the TBI patient are provided. 18,19

Greater focus is now placed on treatment team communication and cooperation. The

“brain injury unit” offers a more structured and less distracting rehabilitation environment

within the acute setting. Supportive systems to address aggressive and other inappropriate

behaviors now assist staff in the acute rehabilitation facility. The results of all these efforts

are reflected in the patient’s subsequent improved status when discharged from the acute

phase and admitted to the postacute neurological rehabilitation program.

Sazbon and Groswasser 20 reviewed TBI sequelae in relationship to the length of post

comatose unawareness (PCU) relative to physical rehabilitation. The review of 72 patients

with postcomatose unawareness periods of greater than 1 month showed that approxi

mately 1 / 3 of all patients achieved full ambulation, 38.9% achieved aided ambulation, and

27.8% required wheelchairs for mobility. The patients were classified, according to length

of postcomatose unawareness, into four groups. Of those patients in PCU for 31 to 60

days, 55.2% progressed to full ambulation, 34.2% to aided ambulation, and 10.5% to

wheelchair mobility. Conversely, of those patients who fell into the PCU group of 91 to

180 days, only 10% progressed to full ambulation, 20% to aided ambulation, and 70% to

wheelchair mobility. Since PCU is, essentially, a manifestation of severity of injury, it can

be seen that the more severely injured individuals were, not surprisingly, the individuals

most likely to present in physical therapy and occupational therapy departments with

ongoing postacute neurorehabilitation needs. These patients were also the most likely to

have significant problems with aphasia, speech disorders, visual deficits, behavior distur

bances, and cognitive disturbances.

It is becoming common practice for physical and occupational therapists to consult with

pharmacists and physicians about medications administered to their patients. With feedback

from therapists about the positive or negative impact of medications on therapeutic efforts,

physicians have been able to make better choices. For example, they have found that, in

many situations, the sedating effect of antispasticity or psychoactive medications can be

avoided with appropriate treatment approaches by well-trained and supported therapists, 18,21

except in cases of severe spasticity, flaccidity, or behavioral disturbance. Severe spasticity

which is not amenable to therapeutic or conventional pharmacological management has

been demonstrated to respond well to intrathecal Baclofen (Lioresal ® *) management. 22 Flac

cidity may be treated successfully with conventional techniques, EMG/biofeedback, 23 and,

in some cases, administration of dopaminergic medications such as Sinemet ® .** 24–26 (See

Chapter 14 for information on behavior management.) Cooperative effort between physi

cians, nurses, psychologists, and therapists has greatly enhanced patient progress.

As people with TBI are provided excellent early acute rehabilitative care, they move

into the postacute phase as “clients” with greater potential for progress. Now, the level

of expectation of both the postacute therapist and the client with TBI has been raised. The

therapeutic approach (how) and the environment (where) become influential factors to

successful outcomes. In this process, the ultimate exchange occurs as the client learns and

teaches as much as the therapist teaches and learns.

The postacute neurorehabilitation experience is at its best when provided in environ

mentally valid settings with comprehensive neurorehabilitation-experienced teams work

ing with the client and family toward a common goal. With a broader and more realistic

scope of treatment settings, therapists are allowed to more fully challenge their clients.

Intensified treatment, with graded structure and proper generalization of skills, translates

into shorter lengths of stay, reduced costs, and more favorable outcomes.

* Watson Laboratories, Corona, CA.

** Dupont Pharma, Wilmington, DE.

Purpose and Focus

A truly experienced comprehensive postacute TBI rehabilitation program is qualified to

admit a broad range of clients, and therapists must treat clients with severe, moderate, or

mild levels of disability. A severely-impaired client may have significant sensorimotor,

perceptual, visual, vestibular, language/communication, and cognitive deficits and may

be wheelchair-bound, have a gastrostomy, and be incontinent, along with multiple other

deficits. A severe level of disability can also include the ambulatory, physically-functioning

client who is significantly confused and behaviorally difficult. The moderately-impaired

individual may have some perceptual, visual, vestibular and cognitive deficits while being

capable of independent ambulation and performance of simple

ADLs with supervision.

The person suffering sequelae from mild traumatic brain injury (MTBI) may not rou

tinely appear as an early referral to the TBI rehabilitation program. It is more likely that

this client will be first referred to and treated by an orthopedic therapist for commonly

associated musculoskeletal complaints. Comments about changes in routines or bizarre

complaints regarding symptoms should be questioned. Subtle changes in daily routines

occur as a result of unrecognized deficits. For example, driving habits may change in

response to deficits in visual and cognitive processing. Driving at night may be gradually

avoided and more lighting is used in the house after sundown. An astute therapist will

pick up on these clues from the client and recommend referral for appropriate assessments

to define the core cause and to direct effective treatment. This cooperative effort will

prevent a comparatively minor injury from becoming a catastrophic one.

Brain-injured persons may be postinjury 2 weeks or 2 years, or more, upon admission to

postacute neurorehabilitation programming. They may be directly admitted from the acute

hospital or may come from home, a psychiatric hospital, a nursing home, or another

postacute program. TBI may be combined with various levels of spinal cord injuries, unre

solved orthopedic/neurosurgical injuries, and diseases or dysfunctions of various systems.

Consequently, the evaluative process and the management of residual physical deficits need

to be thorough and capable of addressing neurological, musculoskeletal, psychological,

visual, vestibular, cognitive, and behavioral influences to physical functioning.

The purpose of this chapter is to offer some practical information to physical and

occupational therapists treating TBI clients at the postacute rehabilitation level. The focus

is to address the continuum of evaluation and management of residual physical deficits

which complicate the postacute phase of recovery. Although it may appear that specific

areas of evaluation and treatment have been designated to the PT or the OT, there is no

intent to imply that these designations are, necessarily, as described. The important point

is that every area must be appropriately evaluated and aggressively treated by the best

therapist for the task.

The Evaluative Process

The purpose of a complete evaluation is to identify both obvious and subtle deficits in

order to set the stage for an effective continuum of treatment and achievement of realistic

goals. It is important to not only evaluate problem areas, but to evaluate all systems for

proper identification and treatment of specific deficits within those systems. 11 The therapist

must be able to identify which part(s) is missing during the client’s attempt to perform a

task or what is interfering with the client’s ability to

complete the task. It is not uncommon

in the TBI population to encounter persons with seemingly more advanced skills than are

actually present. A good example can be found in the person who is able to ambulate

reasonably well when certain challenges are not present; however, when balance is chal

lenged, delayed protective reactions may be revealed. Such a person is in greater jeopardy

for reinjury following a loss of balance or a fall.

In an efficient admission to the postacute TBI rehab program, the therapeutic team will

be informed in advance about the client's injury, medical and early rehabilitation histories,

and will be given a glimpse into the preinjury history and lifestyle prior to the commence

ment of the individual's therapy. Recommendations, pertinent factors to explore, and

discussion of possible discharge options should be reviewed prior to admission. The

collection and presentation of this information should be provided by experienced field

evaluators (see Chapter 20 on field evaluation).

All therapists should be able to recognize the influence of various cognitive deficits

which impact the client's ability to problem solve, organize, and sequence motor acts. The

rehabilitation team needs to understand impairments in perception and integration of the

senses influencing movement, balance, and position in space.

Agitation or otherwise inappropriate behaviors can seriously hinder progress. There

fore, proper staff training and effective approaches to behavior management should be

expected in a comprehensive TBI program (see Chapter 14). Behavioral deficits are a

fairly common sequelae in TBI. Many persons are tactilely defensive and/or easily

overstimulated by even modest amounts of stimuli. Disorientation adds to the likelihood

that verbal or physical aggression or withdrawal from treatment will occur. The proximity

of physical and occupational therapy treatments, together with the factors above, makes

it quite likely that therapists in physical rehabilitation will require substantial behavioral

intervention.

Behavioral programming should be superimposed on treatment in either physical or

occupational therapy. Application of defined behavioral strategies and programs can be

best achieved in tandem with physical rehabilitation programming. Occasionally, it will

be necessary for behavioral programming to supplant other programming; however, care

ful monitoring should be conducted to ensure that rehabilitation programming is under

taken as soon as possible. It is not realistic, nor necessary, for behavioral issues to be

completely resolved prior to initiation or continuation of rehabilitation programming. In

fact, there are very few instances where rehabilitation programming should be deemed

“nonfeasible” due to behavioral deficits.

Emotional problems may manifest in problems with

cooperation or motivation. Hope

fully, a team member is available to assist in the address of such problems; however, the

physical or occupational therapist may become the de facto counselor to the brain-injured

person. Often, the intimacy of the physical rehabilitation treatment setting allows for the

breakdown of psychological defense mechanisms or allows the development of a level

of trust and understanding which will allow access to the person's emotional status.

Overall, discussion amongst team members will allow for all aspects of the clinical

presentation to be shared and treatment approaches to be developed by the appropriate

discipline.

As the person enters the initial PT and OT evaluation sessions, the therapist should

explore him/her as a whole. There should be no assumptions made about functional skills

despite the report of previous diagnoses, treatment records, or initial appearances. Such

premature assumptions can lead to inappropriate or absent treatment. 27

Evaluation should be performed in a variety of clinical, residential, and community

settings. Although personal lifestyle and medical histories were introduced in the pread

mission information, the initial session should still allow time for getting acquainted.

During this interaction, trust and understanding should be nurtured. To signify respect,

the therapist should attempt to explain the purpose of each

test or exercise and relate it

to tasks in daily life. Most clients will respond to this type of interaction and will probably

attempt to rise to a realistic level of expectation. A vital aspect of the therapist’s role is

that of motivator.

The evaluation should be thorough and well-documented in quantitative and qualitative

terms. Utilization of video tape is an excellent tool to assist in recording the person’s

performance progress from evaluation throughout treatment to discharge. If the person

is unable to follow directions or is uncooperative, document observations of how the

individual functions. For example, in an evaluation of a person who was heavily medi

cated, depressed, and unable to respond to usual evaluative techniques, the person was

asked to tie his shoe. After a significant delay, presumably for processing, the individual

sat down in a chair, slowly brought his left leg to his right knee, and tied the shoe.

Observation allowed for comment about probable range of motion impairments, at least,

for the observed joints in movement, dexterity, trunk flexibility, strength of the left hip

and knee flexors, fine and gross motor coordination, visual-motor integration, proprio

ception, and antigravity muscle groups during standing. There were no obvious impair

ments of gait, other than speed. Flexibility of the trunk was demonstrated by reaching to

tie the shoe during sitting. Obvious impairments of

dexterity, possibly related to medica

tion, were observed as well. It was also obvious that the individual was able to respond

to a verbal command, was able to follow through, did not demonstrate evidence of apraxia,

and was cooperative within his capabilities. When the ability to respond becomes more

appropriate, more conventional testing can be performed and documented. 28–31

The neurological rehabilitation field is currently responding to an increasing demand

for assessment tools to provide better documentation of functional skills and out

comes. 29,32,33 Such assessments as the Barthel Index, 34 the Disability Rating Scale, 35 the Tuft's

Assessment of Motor Performance (TAMP), 36 the Tinetti Performance-Oriented Assess

ment of Mobility, 37 and the Functional Independence Measurement (FIM) 38 have been

utilized. More recently, "functional status measurements" are being developed to measure

performance during daily activity which includes cognitive, social, and psychological

functioning. 27 Therapists should be acquainted with a variety of measurement tools and

should choose the most appropriate tool for the level of client and the information desired.

Rating systems provide ongoing comparative data to review the flow of progress.

Additional information can be obtained from pertinent family members. 39,40 Their

insights about the individual's previous lifestyle and their perception of changes since the

injury can reveal information which may help the therapist to understand and, perhaps,

enhance motivation. Also, in appropriate situations, the family can be included in treat

ment sessions so as to educate and prepare them as potential participants in the person’s

future discharge environment.

During the initial interview, the therapist may wish to expand upon preadmission

information by exploring the person’s perception of the accident. Indications of retrograde

or anterograde amnesia may be detected. If available, the family may provide their per

ceptions or additional insights for a confused or otherwise noncommunicative person.

Documentation should include review of preinjury and postinjury history of fractures,

surgeries, medications, and visual and/or auditory dysfunctions.

The subjective review should also include the individual’s perception of current symp

toms and any changes in activity levels which may be related to endurance, musculosk

eletal complaints, sensorimotor deficits, pain, or vestibular dysfunction as they impact the

person’s quality of life. The person should also be asked to provide the therapist with an

understanding of both short- and long-term goals for treatment. As the individual relates

problems in a given area, it may be helpful to provide a checklist (Figure 15.1) to further

elicit information about the nature of the problem prior to evaluation. Further research

has been performed to develop comprehensive client-centered methods for recording

goals. The Canadian Occupational Performance Measure (COPM) is one such interview

procedure that focuses on the individual’s different occupational goals based on the arenas

of self-care, productivity, and leisure skills. 41

Range of Motion and Dexterity

A thorough evaluation and documentation of active and passive hip, knee, ankle, and

cervical/lumbar spine ranges of motion must be conducted. Evaluation should also review

upper extremity ranges of motion, including the shoulders, elbows, wrists, and fingers.

Documentation of flexibility (Figure 15.2) should include an assessment of the hamstrings,

the gastrocnemius (with the knee extended), Thomas test, long sitting, trunk extension in

the prone position, and trunk flexion from a seated position. Assessment of ITB (iliotibial

band) flexibility should be included.

When evaluating upper extremity and hand function, hand dominance should be doc

umented. Observe the person’s ability to control gross grasp and release and perform

A. VESTIBULAR SYMPTOMS CHECKLIST 1. Current symptoms:

B. SELF-PERCEPTION: 1. Self-Reported Deficits:

C. OTHER PERTINENT INFORMATION:

FIGURE 15.1

Vestibular Symptoms Checklist used to collect initial evaluative information about the nature of problems from

the client’s perspective.

lateral pinch, tripod pinch, and palmar prehension. Upper extremity and hand function

are further observed for the ability to hold, stabilize, and carry a variety of both light and

heavy objects. Gross motor coordination of the upper extremity can be documented during

timed performance testing via the Box and Blocks Test of Manual Dexterity. 42

Fine motor coordination and selective movements are assessed during timed perfor

mance tests (e.g., the Nine Hole Peg Test 43) and through functional task observation. Such

tests as the Purdue Pegboard 44 and the Minnesota Rate of Manipulation 45 can be used for

advanced client testing. If desired, additional prevocational assessments of dexterity, cog

nitive, and perceptual functions can be attained with such tests as the Crawford Small

Parts Dexterity Test 46 and the Bennett Hand Tool Dexterity Test. 47 Objects which are

pertinent to the client’s lifestyle should be used in the functional task evaluation (e.g.,

razors, toothbrushes, combs, buttons, zippers, eating utensils, pencils/pens, kitchen tools,

cards, and work tools). Any complaints of pain, or observations of edema, tremors, or

changes in muscle tone, should be documented.

The Neurological Examination

While the comprehensive neurological examination takes place in the initial field evalu

ation and, subsequently, by other treatment professionals

(see Chapter 1), this does not

relieve the need for further assessment by the OT and the PT. A focused neurological

examination is necessary to look at those components that will eventually be addressed

by the OT and the PT.

Sensation and Proprioception

Although the structure of documentation varies in each clinical setting, a complete sensory

evaluation should be performed (Figure 15.3). Tactile sensation is tested for light/firm

and sharp/dull discrimination and hot/cold temperature discrimination. Responses

should be recorded as intact or hyper/hypo sensitive. Proprioception testing includes the

ability to name movements, mirror movements, and detect vibration. Graphesthesia (the

ability to identify numbers written on the skin by the examiner’s finger) and stereognosis

(the ability to identify objects by touch) should be tested and documented. Record

responses to proprioceptive testing as intact or impaired.
FLEXIBILITY EVALUATION LEFT RIGHT

A. HAMSTRING _____ _____

B. THOMAS TEST _____ _____

C. GASTROCNEMIUS (knee extended) _____ _____

D. LONG SIT TEST _____

E. PRONE TRUNK EXTENSION _____

F. SEATED FLEXION _____

G. ILIOTIBIAL BAND (ITB) _____ _____

FIGURE 15.2

Flexibility Evaluation Form used to document information about the lower extremities and trunk.

Deep Tendon Reflexes and Pathological Reflexes

These reflexes influence responses to movement. Record responses to the patellar, Achilles,

biceps, brachioradialis, and triceps reflex tests as hyper (3+), normal (2+), hypo (1+), and

absent (0) (Figure 15.4). The Babinski reflex should also be tested and recorded as present

or absent.

Cerebellar Tests

Cerebellar reflexes have significant influence on the performance of smooth movements.

Tests should include performances of (1) finger-to-finger, (2) finger-to-nose, and (3) heel

to-shin. Record findings as normal, hypermetric, ataxic, or with intention tremor (Figure

15.5). Diadochokinesis is tested symmetrically and asymmetrically and is recorded as

normal, ataxic, or unable.

Urbscheit 14 discussed the frustration encountered by many therapists in the evaluation

and treatment of cerebellar deficits. Many therapists are unable to adequately diagnose

and treat cerebellar dysfunction. Swaine and Sullivan 48 reviewed interrater reliability for

measurement of clinical features of finger-to-nose testing and reported fairly poor NEUROLOGICAL EVALUATION

I. SENSATION UPPER EXTREMITY LOWER EXTREMITY LEFT RIGHT LEFT RIGHT A. Light/Firm Intact Hyper Impaired Intact Hyper Impaired Intact Hyper Impaired Intact Hyper Impaired B. Sharp/Dull Intact Hyper Impaired Intact Hyper Impaired

Intact Hyper Impaired Intact Hyper Impaired C. Hot/Cold Intact Hyper Impaired Intact Hyper Impaired Intact Hyper Impaired Intact Hyper Impaired

II. PROPRIOCEPTION UPPER EXTREMITY LOWER EXTREMITY LEFT RIGHT LEFT RIGHT A. Naming Movements Intact Impaired Intact Impaired Intact Impaired Intact Impaired B. Mirroring Movements Intact Impaired Intact Impaired Intact Impaired Intact Impaired C. Vibration Intact Impaired Intact Impaired Intact Impaired Intact Impaired D. Graphesthesia Intact Impaired Intact Impaired Intact Impaired Intact Impaired E. Stereognosis Intact Impaired Intact Impaired Intact Impaired Intact Impaired

FIGURE 15.3

Neurological Evaluation Form used to document sensory and proprioceptive functions.

interrater reliability for determination of the presence of dysmetria. The therapist working

with this population must become proficient in cerebellar evaluation and treatment.

The individual must be observed for hypotonicity, dysmetria, difficulty with rapid alter

nating movements, and movement decomposition. These deficits may be observed in gait,

pace of gait, and activities of daily living (ADL) (e.g., brushing teeth, stirring food, eating,

or trying to walk at a fast pace). Complaints of difficulties with vision while the individual

is in motion may be related to cerebellar dysfunction as well as vestibular dysfunction.

The Manual Muscle Test, Tone, and Muscle Endurance

Muscle testing is performed not only to evaluate a muscle group’s ability to produce force

against gravity, but also the person’s ability to isolate a muscle’s movement and force.

Manual muscle tests document strengths in musculature of the neck, shoulders, arms,

hands, hips, knees, ankles, abdominals, and trunk extensors. In some situations, the

manual muscle test may not be appropriate. For example, in the presence of spasticity, a REFLEX TESTING

I. DEEP TENDON REFLEXES A. Patellar Left Right Hyper (3+) Hyper (3+) Normal (2+) Normal (2+) Hypo (1+) Hypo (1+) Absent (0) Absent (0) B. Achilles Left Right Hyper (3+) Hyper (3+) Normal (2+) Normal (2+) Hypo (1+) Hypo (1+) Absent (0) Absent (0)

II. PATHOLOGICAL REFLEXES A. Babinski Reflex Left Right Absent Absent Present Present

FIGURE 15.4

Reflex Testing Form used to document reflex testing information. CEREBELLAR TESTS

A. Finger–Finger Left Right Normal Normal Hypermetric Hypermetric Ataxic Ataxic Int. Tremor Int. Tremor

B. Finger–Nose Left Right Normal Normal Hypermetric Hypermetric Ataxic Ataxic Int. Tremor Int. Tremor

C. Heel–Shin Left Right Normal Normal Hypermetric Hypermetric Ataxic Ataxic Int. Tremor Int. Tremor

D. Diadochokinesis Symmetrical Asymmetrical Normal Normal Ataxic Ataxic Unable Unable

FIGURE 15.5

Cerebellar Tests Form used to document cerebellar functions.

forcefully opposing muscle group will increase muscle tone and assessment of the ability

to perform an isolated muscle contraction will not be valid.

Muscle tone may remain a factor significantly influencing movement. In initial obser

vations, many people seem to have minimal to nil abnormal tone. However, the individual

should be closely observed during active functional movements. This is another reason

for evaluating the individual while performing functions in various environments. The

evaluation should begin with an analysis of the motor control present in each extremity.

The Modified Ashworth Scale for Grading Spasticity 49 provides an accepted tool for initial

0 = No increase in muscle tone.

1 = Slight increase in muscle tone, manifested by slight catch and release or by minimal resistance at end of ROM when affected part(s) is moved in flexion or extension.

1+ = Slight increase in muscle tone, manifested by slight catch and release or by minimal resistance throughout the remainder (less than half) of ROM.

2 = More marked increase in muscle tone through most of ROM, but affected part(s) easily moved.

3 = Considerable increase in muscle tone, passive movement difficult.

4 = Affected part(s) rigid in flexion or extension.

Observations pertaining to lack of movement or minimal movement, in particular, in

cases where the dopaminergic system may have been impacted by the injury, may suggest

the application of dopaminergic medication to enhance motor function. Conversely, per

sons who present with significant spasticity will generally not benefit from such an

approach. The response of spasticity to stretching, relaxation, positioning, and medication

will need to be explored, together with an appraisal of the likelihood of response to

chemical neurolysis and casting. Spasticity should be differentiated from rigidity in the

hypertonic patient. Rigidity may respond to dopaminergic

drugs whereas spasticity may

be worsened. The PT and OT can provide quite valuable information to the physician in

these arenas. The influence of emotion, pain, fatigue, and varying demands of motion and

posture should be considered in evaluation of movement.

Muscle endurance of the trunk and lower extremities is also assessed by the PT. Trunk

endurance (Figure 15.6) testing documents the maximum number of sit-ups performed in MUSCLE ENDURANCE

1. TRUNK ENDURANCE Sit-Ups _____ repetitions (1 min) Push-Ups _____ repetitions (maximum) Bridging _____ seconds (norm: 1 min) Hyperextension _____ seconds (norm: 30 sec)

2. LOWER EXTREMITY ENDURANCE Wall Slide (90˚/90˚) _____ seconds (norm: 1 min)

FIGURE 15.6

Muscle Endurance Form used to document trunk, lower extremity, and cardiovascular endurance.

1 minute and the maximum number of push-ups the individual is able to produce.

Bridging and hyperextension are each sustained as long as possible (Figure 15.6). Accept

able performance is considered to be 1 minute for bridging and 30 seconds for hyperex

tension. Cardiovascular endurance can be tested with a standard or modified Bruce™

test 50 (Figure 15.7 and Figure 15.8), based on the individual’s level of conditioning. It is

very important to monitor heart rate and blood pressure during this exercise. Do not forget

to document the client’s current medications which may affect vital signs at rest and

during exercise. Advanced endurance testing, such as a physical capacity evaluation, may

be performed to address back-to-work potential.

Differential diagnosis of cardiorespiratory endurance problems and vestibular dysfunc

tion cannot be undertaken completely at this point in the evaluation; however, findings

of nystagmus during testing may point to vestibular dysfunction and should be noted for

consideration during subsequent vestibular testing.

Mobility, Posture, and Gait Evaluations

Although the majority of severely disabled TBI persons may have become quite mobile

during the acute rehabilitation stay, there will be an occasional need for full evaluation of CARDIOVASCULAR ENDURANCE BRUCE'S LOW LEVEL TREADMILL TEST (Modified Shefield-Bruce Submaximal Protocol ™)

STAGE TIME SPEED GRADE METS DATE DATE DATE DATE DATE

Rest HR xxxxx xxxxx xxxxx xxxxx

Rest BP xxxxx xxxxx xxxxx xxxxx

Stage 1 min 1 min 2 min 3 1.7 mph 0% 2.3

Stage 2 min 4 min 5 min 6 1.7 mph 5% 3.5

RPE xxxxx xxxxx xxxxx xxxxx

Stage 3 min 7 min 8 min 9 1.7 mph 10% 4.6

Stage 4 min 10 min 11 min 12 2.5 mph 12% 6.8

RPE xxxxx xxxxx xxxxx xxxxx

Recovery

_____ min xxxxx xxxxx xxxxx xxxxx

Recovery

_____ min xxxxx xxxxx xxxxx xxxxx

Recovery

_____ min xxxxx xxxxx xxxxx xxxxx

FIGURE 15.7

Cardiovascular Endurance Form — Bruce’s low level treadmill test.

bed mobility, transfers, tub/shower, and wheelchair skills. In the residential setting, most

people will be able to sleep in standard double size (or larger) beds. Bathrooms should

be an appropriate size and equipped for wheelchair, walker, or cane mobility.

Beyond the expected physical components for bed mobilization and bed/tub/toilet

transfers, other areas which impact mobility, such as cognitive abilities, safety judgment,

impulsivity, visual deficits, and systems impacting postural control, should be observed

and documented. The evaluation should document the person’s ability to perform the

tasks independently or with assistance and include notation of the quality of performance. CARDIOVASCULAR ENDURANCE BRUCE’S STANDARD TREADMILL PROTOCOL

STAGE TIME SPEED GRADE METS DATE DATE DATE DATE DATE

Rest HR xxxxx xxxxx xxxxx xxxxx

Rest BP xxxxx xxxxx xxxxx xxxxx

Stage 1 min 1 min 2 min 3 1.7 mph 10% 4–5 hr

Stage 2 min 4 min 5 min 6 2.5 mph 12% 6–7 hr

RPE xxxxx xxxxx xxxxx xxxxx

Stage 3 min 7 min 8 min 9 3.4 mph 14% 8–10 hr

Stage 4 min 10 min 11 min 12 4.2 mph 16% 11–13 hr

Stage 5 min 13 min 14 min 15 5.0 mph 18% 14–16 hr

Stage 6 min 16 min 17 min 18 6.0 mph 20% 17–19 hr

RPE xxxxx xxxxx xxxxx xxxxx

Recovery

_____ min

HR

BP xxxxx xxxxx xxxxx xxxxx

Recovery

_____ min

HR

BP xxxxx xxxxx xxxxx xxxxx

Recovery

_____ min

HR

BP xxxxx xxxxx xxxxx xxxxx

FIGURE 15.8

Cardiovascular Endurance Form — Bruce’s standard treadmill protocol.

Bed mobility (Figure 15.9) explores scooting up and down as well as to the right or left

sides. Is the person able to turn to either side and attain sitting and supine positions? A

useful method to provide objective measurement of bed mobility is to time the task and

document any observation of asymmetries between right and left sides. Note if the indi

vidual includes the hemiparetic side or is using

compensatory strategies during move

ments. Is the person using tone to achieve movement? For example, extensor thrust may

be used to complete rolling. Note differences in bed mobilization abilities on gym mat vs.

soft bed. Quality of movement should be emphasized. Wheelchair mobility (Figure 15.9)

assessments include the client’s ability to mobilize on even and uneven surfaces, inclines

and declines, through doorways, and over curbs. Note the approximate height of the curb

and time to cover specific distances.

Document the person’s preparation for transfer (Figure 15.9). Record any need for verbal

and/or physical cues, as well as the need for physical assistance. Note performance in

transferring from the wheelchair to a level surface, an elevated surface, the floor, and floor

to wheelchair. MOBILITY EVALUATION

I. BED MOBILITY Assist Quality A. Scooting 1. 2. 3. 4. Up Down Left Right _____ _____ _____ _____ _____ _____ B. C. D. 1 / 2 Rolls 1. 2. Left Right _____ _____ _____ _____ Attain Sitting Attain Supine _____ _____ _____ _____

II. WHEELCHAIR MOBILITY Assist Quality A. Even Surfaces _____ _____ B. Uneven Surfaces _____ _____ C. Inclines _____ _____ D. Declines _____ _____ E. Doorways _____ _____ F. Curbs _____ inches _____ _____

III. TRANSFERS Assist Quality A. Preparation _____ _____ B. Wheelchair to level surface _____ _____ C. Wheelchair to elevated surface _____ _____ D.

Wheelchair to floor _____ _____ E. Floor to wheelchair _____ _____

IV. AMBULATION Assist Quality A. Sit to stand _____ _____ B. Assistive device _____ _____ C. Indoors _____ _____ D. Outdoors _____ _____ E. Uneven terrain _____ _____ F. Inclines/declines _____ _____ G. Curbs _____ _____ H. Stairs _____ _____

FIGURE 15.9

Mobility Evaluation Form used to collect information on bed, wheelchair, transfer, and ambulation activities.

Observations of the general ability to ambulate should be documented (Figure 15.9)

whether the individual has detectable mobility problems or appears quite normal. The

evaluation should include observations from clinical, residential, and community settings.

Observe and document ambulation indoors, outdoors, on uneven terrain, on inclines and

declines, and negotiating curbs and stairs. Document the ability to rise from sitting to

standing. Note the need for assistance and the use of any supportive devices. The Timed

“Up and Go” Test 51 is a quick and objective gait test (Figure 15.10).

When evaluating ambulatory skills, an initial impression of minimal or no obvious

abnormalities may change when the situation moves from a well-lit, even-surfaced, clinical

setting to a less ideal environment with low light and uneven terrain (i.e., darkened room

with plush carpeting or evening time on grassy/rocky terrains). Impairments in sensorim

otor and/or vestibular system-related performances may be revealed under more realistic

and demanding circumstances. The evaluation may even be extended to include move

ment onto or off of escalators and into or out of elevators. Watch for a tendency to avoid

or complain about tasks in noisy or busy environments. Subtle changes in fluidity of body

movement during ambulation can point to vestibular or oculomotor problems.

During ambulation evaluations, document reduced or absent reciprocal arm swing,

slowed pace of walking, reduced head turning or visual scanning, drifting or “wall walk

ing,” and slight or obvious hesitancy when changing directions. It is also important to note

subjective complaints of dizziness, nausea, or feelings of drunkenness or light-headedness

when walking. These may be additional indicators of visual and/or vestibular disturbances.

Notations should be made regarding the client’s posture during sitting and standing

activities, as well as any gait deviations. 52 Observations should also note apparent influ

ences from muscle weakness, leg length discrepancies, pain, vestibular, cerebellar, or ocular

dysfunctions, cognitive/perceptual deficits, poor endurance, loss of flexibility, and impair

ments in somatosensory functions. 13,14,18,53,54

As emphasized in NDT (neurodevelopmental theory), 1,55 observations of postures

should include the position of the scapula, pelvis, rib cage, and spinal column. Position

of the trunk may vary greatly so also note the conditions under which observations are TIMED “UP AND GO” TEST

Equipment: Chair (without arms) and stop watch.

Criteria: Individuals must be able to ambulate at least 200 feet with/without any type of assistive device.

Description: Individuals are asked to rise from a chair (without arms) on the signal “Go,” walk 10 feet, turn, walk back to chair, turn, and sit down. The total time to complete the test is recorded in seconds. The goal is to complete the test in the shortest time possible.

Scoring: Practice Trial:_____ Test Trial 1:_____ Test Trial 2:_____ Test Trial 3:_____ Mean Time:_____

Interpretation of Results:

1. <20s

2. 20s - 30s

3. >30s Functionally independent in basic ADLs “Grey area,” variable functional abilities. Functionally dependent in basic ADLs.

FIGURE 15.10

Timed “Up and Go” Test.

made. For example, is the individual sitting on a solid surface or on a bed or standing?

Note if the person is able to recognize and maintain midline with head and trunk positions.

Neurodevelopmental Sequence Evaluation

To gather a baseline on a variety of movement patterns, the neurodevelopmental sequence

is a good place to start. Assessment of the motorically-intact individual is just as important

as assessing the motorically-impaired person. Omission of this evaluation for people

functioning at a high level may prevent observations of subtle deficits in sensorimotor

integration. Observe closely for inefficient movement patterns.

The ability to perform independently or with assistance is recorded as well as the quality

of performance. Video recording of this initial evaluation further documents quality of

performance. Of course, recording is repeated at various intervals throughout the treat

ment process.

The evaluation follows a very basic sequence of movement patterns (Figure 15.11). It

begins with log rolling to both sides. Next, observe the ability to assume and maintain a

prone-on-elbows position, followed by the quadruped, or all-fours, position. Contralateral

(Figure 15.12A) and ipsilateral (Figure 15.12B) positions are assumed next and the main

tained positions are timed. Reciprocal crawling is observed forward and backward. Tall

kneel position is observed for the ability to assume and maintain the position as well as

the ability to weight shift. Knee walking is also observed in forward and backward. The

half-kneel position is assumed and maintained for both sides. The half-kneel-to-stand

position is also observed from both sides.

Vestibular Evaluation

It has already been pointed out that an important aspect of the evaluation is to identify

subtle deficits impacting upon ADL task performances.

Proper identification of the core

cause leads to a better choice of treatment avenues. The therapist should be trained in the

assessment and treatment of various vestibular dysfunctions, though much of the training

in this subject is available largely through postgraduate courseware. 12,13,56–58 Lingering

problems related to balance, postural control, and spatial orientation can disable any TBI

client. The reader is directed to Chapter 5 where assessment and treatment approaches

are excellently reviewed and clearly demonstrated and, therefore, not discussed herein.

Additional tools for the therapist may include the Motion Sensitivity Quotient 59 (Figure

15.13) and the Functional Reach Test 60 (Figure 15.14). Despite the fact that the Functional

Reach Test was developed for the geriatric population, it provides a quick and easy balance

test for most age groups. Age appropriate norms for both male and female populations

are included.

Sensorimotor Integration and Dynamic Balance Evaluations

In a normal central nervous system, purposeful activity of the extremities depends upon

the stabilization of the trunk. When postural control is maintained, significant influence

is exerted on limb tone, range of motion, and control. 52 However, the individual with

moderate to severe sensorimotor impairment may find that extremity movement is less

than functional when selective movement is reduced to gross movement patterns influ

enced by primitive reflexes.

The ability to maintain standing balance in static or dynamic conditions requires the

complex interaction of several systems — vision, vestibular, and somatosensory systems.

However, these systems must be coupled with appropriate motor programs, muscle con

tractions, body alignment, and ranges of motion to allow for smooth and well-coordinated,

purposeful movements.

The sensorimotor integration evaluation considers the manner in which postural control,

reflexes, and feedback from vision, vestibular, and proprioceptive systems impact upon

motor control and programming. The evaluation should, therefore, document postural

control in sitting and standing (Figure 15.14). In the sitting position, observe body align

ment. While sitting, note responses to weight shifting in lateral and anterior/posterior NEURODEVELOPMENTAL SEQUENCE EVALUATION Assist Quality

I. LOG ROLLING A. Left _____ _____ B. Right _____ _____

II. PRONE ON ELBOWS A. Assume _____ _____ B. Maintain _____

III. QUADRUPED A. Assume _____ _____ B. Maintain _____ _____

IV. CONTRALATERAL BALANCE A. Left Knee _____ _____ sec B. Right Knee _____ _____ sec

V. IPSILATERAL BALANCE A. Left Knee _____ _____ sec B. Right Knee _____ _____ sec

VI. RECIPROCAL CRAWLING A. Forward _____
_____ B. Backward _____ _____

VII. TALL KNEEL A. Assume _____ _____
B. Maintain _____ _____ C. Weight Shift
_____ _____

VIII. KNEE WALK A. Forward _____ _____
B. Backward _____ _____

IX. HALF KNEEL A. Assume Left Knee _____
_____ Right Knee _____ _____
B. Maintain Left Knee _____ _____ Right
Knee _____ _____

X. HALF KNEEL TO STAND A. Left Foot _____
_____ B. Right Foot _____
_____

FIGURE 15.11

Neurodevelopmental Sequence Evaluation Form used to
document information on various movements through

the sequence.

directions. While the individual orients the head, rights
the trunk, or resumes the vertical

position, note the direction of shift. Notice responses to
dizziness, disequilibrium, and

protective responses.

The Tinetti Performance-Oriented Assessment of Mobility 37
includes an assessment of

balance deficits in more impaired clients during movement
in functional tasks. The assess

ment calls for observation of the client during sitting,
arising, standing, and walking.

Balance reactions are also observed while the individual
turns around (360 degrees), sits

down, and attempts single-foot support. The test provides a
scoring system for compar

ative data. As the client reaches scoring criteria, he/she

can be advanced to more appro

priate tests.

People without severe impairments to postural control and balance/coordination may

also benefit from evaluation of sensorimotor integration (Figure 15.15). 61,62 In the standing

position, balance skills can be evaluated through observation of postural control strategies

used during both active and induced weight shifts as well as standing one-foot balance

evaluation. Observation of active weight shifts (initiated by the person) to anterior/

posterior and lateral positions assesses the use of ankle, hip, stepping, or other types of

postural control strategies. Presence or absence of dizziness is noted. Induced weight shifts

(imposed by the examiner) measure the same positions.

Standing one-foot balance is measured by the length of time maintained and the postural

control strategy utilized (i.e., ankle, hip, stepping, or other) should be noted. Undertake

two to three trials and average the times. Sensory organization, that is, the integration of

proprioceptive and vestibular input, is measured by timing and the amount of sway with

eyes open and eyes closed on a firm surface and on a foam surface. Care should be taken

to disallow any potential for orientation which might be available from a continuous light

or sound source during balance and sensorimotor testing (Figure 15.15).

FIGURE 15.12A

Illustration of contralateral position in the neurodevelopmental sequence. (Photo courtesy of James E. Eaton.)

FIGURE 15.12B

Illustration of ipsilateral position in the neurodevelopmental sequence. (Photo courtesy of Lynda R. Eaton.) MOTION SENSITIVITY QUOTIENT

Client Name: _____
Date: _____

Baseline Symptoms:

Intensity Score Duration Score Intensity Score 0 — least 5 — most 0-5 sec 6-10 sec 11-30 sec >30 sec = 0 = 1 = 2 = 3 +Duration Score

MOVEMENT INTENSITY DURATION SCORE (I+D) 1. 2. 3. 4. 5. 6. 7. 8. 9. 10. 11. 12. 13. 14. 15. 16. Sit to supine Supine to right side Supine to left side Supine to longsit Right Hallpike Return to sit Left Hallpike Return to sit Sitting - nose to right knee Return to vertical Sitting - nost to left knee Return to vertical Head rotation × 5 Head flex/ext. × 5 Standing 180 degree turn right Standing 180 degree turn left

MSQ = Total Score × number of provoking positions divided by 20.48. Total Score: _____ MSQ: _____

SCORE KEY: 0-10% = Mild 11-30% = Moderate >30% = Severe

FIGURE 15.13

Motion Sensitivity Quotient. FUNCTIONAL REACH NORMS NORMS MEN (inches) WOMEN (inches) 20-40 years 16.7 +/-1.9 14.6 +/-2.2 41-69 years 14.9 +/-2.2 13.8 +/-2.2 70-87 years 13.2 +/-1.6 10.5 +/-3.5

FIGURE 15.14

Functional Reach Norms.

The dynamic balance evaluation (Figure 15.16) again documents the type of postural

control strategy (ankle, hip, stepping, falls) used in dynamic gait activities, heel-toe ambu

lation, balance beam ambulation, winding strip ambulation, and step-ups. The dynamic

gait activity task involves walking forward for 12 feet to an abrupt stop. Note the postural

control strategy utilized and complaints of dizziness. Next, have the individual walk

forward for 12 feet and then sharply pivot to the right. Repeat to the left. Note the strategy

utilized and any complaint of dizziness. The final dynamic gait activity task involves

walking with the head first moving horizontally and then repeated with the head moving

vertically. Note the strategy utilized and any complaint of dizziness. SENSORIMOTOR INTEGRATION EVALUATION

I. POSTURAL CONTROL

A. Sitting: 1. Alignment:

B. Standing: 1. Active weight shifts: a. b. c. Anterior/posterior: Lateral: Dizziness: ANKLE ANKLE YES HIP HIP NO STEPPING STEPPING OTHER OTHER d. Comments:

FIGURE 15.15

Sensorimotor Integration Evaluation Form used to document postural control in sitting and standing positions.

Heel-toe and balance beam ambulation evaluation should document required assistance

levels and the quality of performance for going forward, backward, sideways, and during

Carioca or braiding step maneuvers. The winding strip ambulation test (heel-toe walking

following a piece of string or fabric laid out in a curvilinear fashion on the floor) (Figure

15.17) is conducted for forward, backward, and sideways walking. Step-ups are repeated

20 times, first leading with the left and, then, with the right. Note the time needed to

perform this task. The careful notation of the times will provide a window on the progress

of the improvement as it occurs.

Quick Reciprocal Movement Evaluation

For evaluation of higher level balance and coordination disorders, movements to be

assessed include straddle jumps, straddle crosses, reciprocal jumping, pendulum, slalom

(forward/backward), four-point, shuffling (left/right), running Carioca (left/right), skip

ping, and reciprocal marching (forward/backward) (Figure 15.18).

In regard to higher level balance and coordination skills, the admonition “never assume”

comes into play. We have observed many young men who initially present as very DYNAMIC BALANCE EVALUATION

I. DYNAMIC GAIT ACTIVITIES: Strategy: A = Ankle H = Hip S = Stepping F = Falls Strategy Dizziness A. Walk 12 ft stop abruptly _____ _____ B. Walk 12 ft pivot sharply 1. 2. Left Right _____ _____ _____ _____ C. Walk with head motion 1. 2. Horizontal Vertical _____ _____ _____ _____

II. HEEL-TOE AMBULATION: Assist Quality A. Forward _____ _____ B. Backward _____ _____ C. Sideways _____ _____ D. Carioca _____ _____

III. BALANCE BEAM AMBULATION: Assist Quality A. Forward _____ _____ B. Backward _____ _____ C. Sideways _____ _____ D. Carioca _____ _____

IV. WINDING STRIP AMBULATION: Assist Quality A. Forward

_____ _____ B. Backward
_____ _____ C. Sideways
_____ _____

V. STEP-UPS (20 repetitions) Assist Time A. Left
_____ _____ B. Right
_____ _____

FIGURE 15.16

Dynamic Balance Evaluation Form used to document performances during dynamic activities.

FIGURE 15.17

An illustration of the Winding Strip Ambulation Test. (Photo courtesy of Caryn Murphy.) QUICK RECIPROCAL MOVEMENT EVALUATION Assist Quality

I. STRADDLE JUMPS: _____ _____

II. STRADDLE CROSSES: _____ _____

III. RECIPROCAL JUMPING: _____ _____

IV. PENDULUM: _____ _____

V. SLALOM: A. Forward _____ _____ B. Backward _____ _____

VI. 4-POINT: _____ _____

VII. SHUFFLING: A. Left _____ _____ B. Right _____ _____

VIII. RUNNING CARIOCA: A. Left _____ _____ B. Right _____ _____

IX. SKIPPING: _____ _____

X. RECIPROCAL MARCHING: A. Forward _____ _____ B. Backward _____ _____

FIGURE 15.18

Quick Reciprocal Movement Evaluation Form used to document performance of quick reciprocal movements.

functional in mobility assessments but show significant deterioration of skill performance

when higher level demands are requested. The importance of going a step further to

assess higher levels of balance is related to the hopeful achievement of as near premorbid

levels of functioning as possible. These quick movement demands arise in various sports

activities or in certain driving conditions. The same requirement for high level coordina

tion skills may arise in various vocational duties involving coordinated quick upper and

lower extremity movements.

Straddle Jump

The straddle jump is performed beginning in a standing position with the feet together.

The individual jumps from the feet-together position and lands with the feet separated

via hip abduction, as in a jumping-jack exercise (Figure 15.19).

Straddle Cross

The straddle cross is performed beginning in the same position as the straddle jump;

however, rather than separating the feet while in the air, the individual crosses the feet

and lands in a legs-scissored position. The second straddle cross reverses the front leg

position with the back leg position (Figure 15.20).

Reciprocal Jumping

Reciprocal jumping is accomplished by beginning in a standing position with the feet

together. The individual jumps and lands with one foot outstretched in a forward, hip

flexed position while the other foot is in a backward, hip-extended position. The arm

FIGURE 15.19

Illustrates the ending position of the straddle jump. (Photo courtesy of James E. Eaton.)

swing should be reciprocal as in normal walking. The second reciprocal jump reverses

the leg and arm positions (Figure 15.21A and Figure 15.21B).

Pendulum

The pendulum maneuver is accomplished by beginning in the standing, feet-together

position. The individual jumps, kicking one leg into hip abduction, keeping the foot in

the air, and landing on the opposite foot. The second pendulum swing is accomplished

by jumping and reversing leg/foot positions (Figure 15.22).

Slalom

The slalom exercise begins with standing in the feet-together position. The feet are kept

together as the individual jumps and lands. The first jump places the feet off to the left

and the second places the feet off to the right, while maintaining an upright torso. The

knees should be flexed and pointed forward. The feet positions are similar to those used

in parallel turns while downhill skiing (Figure 15.23A, Figure 15.23B, and Figure 15.23C).

Four-Point

The four-point jump is initiated in the standing, feet-together position. The individual

jumps using both feet, but moves one foot forward, via hip flexion, to toe-touch the floor

in front of the individual in harmony with the other foot returning to the floor. On the

next jump, the foot which was moved to the forward toe-touch position is moved to the

side toe-touch position via rotation of the hip to a hip-abducted position. On the third

jump, the foot is moved to the rear toe-touch position, via hip rotation to a hip-extended

FIGURE 15.20

Illustrates the cross position of the straddle cross. (Photo courtesy of James E. Eaton.)

FIGURE 15.21A

Illustrates the beginning position of the reciprocal

jump. (Photo courtesy of James E. Eaton.) FIGURE 15.21B Illustrates the change of leg positions during the midjump phase of the reciprocal jump. (Photo courtesy of James E. Eaton.)

FIGURE 15.22

Illustration of the pendulum position. (Photo courtesy of Caryn Murphy.)

FIGURE 15.23A

Illustrates position No. 1 of the slalom activity. (Photo

courtesy of Caryn Murphy.) FIGURE 15.23B Illustrates position No. 2 of the slalom activity. (Photo courtesy of Caryn Murphy.)

FIGURE 15.23C

Illustrates position No. 3 of the slalom activity. The sequence of Figure 15.23 is then repeated a specified number

of times. (Photo courtesy of Caryn Murphy.)

position. The final jump brings the feet back together. The exercise is performed to each

side (Figure 15.24A, Figure 15.24B, Figure 15.24C, and Figure 15.24D).

Shuffling

The shuffling maneuver is initiated with feet together in standing. Separations of the feet

are accomplished via hip abduction followed by quick return to the feet-together position

via hip adduction to produce a rapid sideways shuffle. The maneuver should produce

sideways movement and should be conducted in both directions.

Running Carioca

Running Carioca is a rapid production of the grapevine step or cross step.

Skipping

Skipping should be self-explanatory.

Reciprocal Marching

The reciprocal march is an exaggerated march step with large arm swing and exaggerated

hip and knee flexion during the march.

Each of the above exercises is repeated until the evaluator has a good understanding of

the person’s abilities. Measure assistance required and quality of performance.

FIGURE 15.24A

Illustrates the starting position of the four-point which

is followed by a jump to the next position. (Photo

courtesy of Lynda R. Eaton.) FIGURE 15.24B Illustrates the second position of the four-point with a foot forward. (Photo courtesy of Lynda R. Eaton.)

Rapid Alternating Movement Evaluation

While seated, alternate floor touching with the heel and toe and seated sidesteps are

observed for the number of repetitions performed in 10 seconds. The number of repeated

standing sidesteps are also recorded for a 10-second period. Note quality of performance

(Figure 15.25). These simple tasks can be good indicators of asymmetries or the ability to

mimic a motor pattern, as well as coordination of the lower limb.

FIGURE 15.24C

Illustrates the third position of the four-point with the

foot adducted to the side. (Photo courtesy of Lynda R.

Eaton.) FIGURE 15.24D Illustrates the fourth position of the four-point with the foot posterior to midline. The next jump returns to the starting position in Figure 15.24A and the sequence is repeated a specified number of times. (Photo courtesy of Lynda R. Eaton.) RAPID ALTERNATING MOVEMENT EVALUATION (# repetitions in 10 sec) Left Right

I. HEEL-TOE: _____ _____

II. SEATED SIDE STEPS: _____
_____

III. STANDING SIDE STEPS: _____
_____

FIGURE 15.25

Rapid Alternating Movements Form is a simple format for documenting rapid alternating movements.

Assessment of Smell and Taste

It is imperative that chemosensory or gustatory and olfactory senses are tested, in that

they can be impaired or absent in both the person with MTBI and the severely-impaired

individual. Yet, these functions are often ignored in the evaluation process.

Dysfunction in olfactory and gustatory senses may have gone undetected until the

individual reaches the postacute phase. Anosmia is thought to occur in approximately

5.5% of the TBI population, while over a third of TBI patients have dysosmia. 63,64 As many

as a third of people with TBI may have difficulty with olfactory naming and recognition.

Questions should be raised by complaints of smelling foul odors, poor appetite, or

unawareness of body odor or various household smells, including burning or spoiled

foods. Following a chemosensory screening by OT or PT, alterations in function should

be examined in light of the original injury. The individual will require awareness and

education in ways to detect smoke, gas, other toxic fumes, and spoiled foods. 65,66 A

chemosensory screening may also indicate the necessity to refer for additional clinical

examinations by an otorhinolaryngologist or neurosurgeon.

Evaluation of Vision

The incidence of visual dysfunction following traumatic brain injury is fairly high. Schlag

eter et al. 67 reviewed 51 inpatients within days of admission. They found that 30 (59%)

were impaired in one or more of the following: pursuits, saccades, ocular posturing,

stereopsis, extraocular movements, and near/far eso-exotropia. Since the acute rehabilita

tion experience has become increasingly shorter in duration for this population, relatively

little attention is paid to visual-motor and visual-perceptual remediative efforts. As a

consequence, these deficits are frequently evidenced in postacute rehabilitation settings.

A thorough OT evaluation should include a complete vision screening test. 68 Prior to the

vision screening, preliminary information is collected via the Visual Symptoms Checklist

(Figure 15.26). This questionnaire not only collects subjective responses but provides an

opportunity for objective documentation. For example, the individual may not acknowledge

symptoms. The therapist's observations, however, reveal head tilting, squinting, or closing

an eye, difficulty reading, or bumping into walls or furniture on one side. It is important

to remember that the person may not have any awareness of their visual disturbance.

The purpose of the screening is not to diagnose but to detect potentially unrecognized

visual deficits which may be impacting daily life. The screening should include visual

attentiveness, near and distance acuities, ocular pursuits, saccades, nearpoint convergence,

eye alignment, stereopsis, color identification, and peripheral fields. Changes in acuities

may be reflected in difficulty performing tasks requiring near vision (e.g., shaving or

putting on makeup) or difficulty recognizing environmental cues (e.g., facial expressions).

Smooth ocular pursuits are required for such tasks as reading a line of print or a column

of words or numbers. Saccades provide a rapid but accurate shift of the eye in such visual

tasks as reading to the end of a line of print and rapidly shifting leftward to the beginning

of the next line. The King-Devick Test 69 measures scanning and saccadic function required

to read detailed and structured formats (e.g., reading a bus or train schedule). Evaluation

of visual system integrity may raise suspicion of vestibular or cerebellar dysfunction.

Impairment in nearpoint convergence is another tracking deficit which may be manifested

in double or blurred vision and decreased depth perception.

Strabismus may result in double or blurred vision as the eyes move through the visual

sphere. The ability to visually scan may be impaired in such tasks as reading, writing,

grocery shopping, driving, or reviewing a map. Eye alignment measures horizontal and

vertical alignments to detect possible deviations.

Deficits in stereopsis impact many functions requiring depth perception. The ability to

judge spatial relationships in such eye-hand tasks as threading a needle, targeting food

on a plate, or negotiating stairs is affected by this deficit.

Peripheral and central vision are required for a full field of vision. A loss of the peripheral

field(s) will impact safety for ambulation, awareness of environment, and safe driving and

will require the client’s awareness and ability to compensate with appropriate head-turning.

Following the vision screening, appropriate referrals to the neuro-ophthalmologist or

developmental/behavioral optometrist may be required for further in-depth assessments.

Refer to Chapter 6 and Chapter 7 for an in-depth discussion of evaluative and treatment

options.

People with TBI may or may not complain of visual disturbances. Behavioral evidence

of oculomotor deficits may be seen in problems with reading, writing, driving, playing

video games, or watching television. The person may report that words “jump” around

on the page or that they frequently lose their place while reading. They may complain

that they can read for only short periods of time. They may relate that images move in

strange ways while watching television or while driving. They may experience dizziness,

headaches, or nausea during these activities. Head position adjustments can foretell VISUAL SYMPTOMS CHECKLIST

Prescription glasses: Yes _____ No _____ If yes: Were glasses worn prior to injury?
_____ Since the injury only?
_____
Last vision examination?
_____ New prescription? _____ Date:
_____

Answer yes or no to the following questions: Yes No

1. Do you have blurred or double vision? _____ _____

2. Do you tilt your head to see more clearly? _____
_____

3. Do you squint or close an eye to see? _____ _____

4. Do you get a headache while reading, watching television, riding in or driving a car? Other? _____ _____ _____

5. Do your eyes feel “tired”? _____ _____

6. Do you lose your place while reading? _____ _____

7. Do you hold objects or reading material close to see? _____ _____

8. Do you avoid reading or not read as often as you did before the injury? _____ _____

9. Do you miss words, letters, or numbers while reading? _____ _____

10. Do you have difficulty distinguishing colors? _____ _____

11. Do you avoid dark areas or avoid driving after dark? _____ _____

12. Do you sometimes confuse which direction is right or left? _____ _____

13. Do you reverse letters, numbers, or words? _____ _____

14. Do you have difficulty recognizing road or street signs before it is too late to turn? _____ _____

15. While you are standing still, do objects seem to jump or move? _____ _____

16. While you are walking, do objects seem to jump around? _____ _____

17. Do you bump into objects on one side or the other? _____ _____

FIGURE 15.26

Visual Symptoms Checklist used to collect information on vision from the client.

oculomotor problems, as can observation of dysfluencies of gait, especially in uneven

terrain such as curbs, uneven sidewalks, stairs, or multi-level surfaces. Often, a person

will complain, as well, of neck and shoulder problems that might actually be vision driven

vs. purely orthopedic difficulty.

The field of vision therapy represents a valuable evaluation and treatment process which

has been practiced by too few over the years. It is now being more routinely incorporated

into the clinical practice of neurological rehabilitation.[68,70,71]

Visual Perception and Perceptual Motor Evaluation

Following the vision evaluation, perceptual motor assessments should proceed. Deficits

may impact upon the client's ability to adequately perform normal daily living tasks.

Observations and documentation should be taken from clinical and other environ

ments.[72–74] Clinical assessments may include information from tests performed by both the

OT and the neuropsychologist.

Visual perception examines visual figure-ground, form constancy, spatial awareness or

position in space, depth perception, visual memory, visual sequential memory,

visual-motor integration, and spatial relationships. Visual figure-ground is the ability to

distinguish foreground from background and form constancy explores the ability to per

ceive subtle variations in form. Position in space is the ability to manage such spatial

concepts as in/out, up/down, and front/behind. Spatial

relationships examines the indi

vidual’s ability to perceive positioning of two or more objects in relation to themselves or

other objects. It is easy to understand how frequently the client requires these functions

in everyday living.

Clinical evaluations of visual perception should include such tests as the Motor-Free

Visual Perception Test–Vertical Format (MVPT-V). 75 The MVPT measures the time it takes

to process visual information and react to that information. In vertical, it helps to eliminate

errors that may be caused by hemianopsia or visual neglect. This information applies to

such tasks as reading comprehension, depth perception for ambulation, and driving. Stan

dardized scores are compared among individuals without head injuries, individuals with

head injuries but not a visual neglect, and those with a head injury and a neglect.

Advanced standardized perceptual tests, such as The Test of Visual-Perceptual Skills

(nonmotor)-Revised (TVPS-R), 76 greatly enhance previously available detail and precision.

The norms were based on developmental ages for perceptual skills.

The Hooper Visual Organization Test 77 examines the ability to organize visual stimuli

by showing pieces of an object. These skills are needed to locate items in a grocery store,

refrigerator, or in a cupboard. The Hooper Visual Organization Test is useful in detecting

deficits in the right hemisphere and will determine actual

perceptual deficits aside from

performance.

An evaluation of the ability to perform purposeful movements on command or praxis

is important for all people with TBI. Apraxia or dyspraxia may be obvious or subtle and

may influence physical performances. Even in the person with MTBI, initiation and

sequencing of functional motor acts need close observation for potential disorganization. 78

Skills required to produce a design in two and three dimensions (e.g., assemble various

items from written or illustrated instructions) relate to constructional praxis and block

design. Form perception is assessed via the Form Board and examines the ability to

differentiate variations in form.

Difficulties in identifying body parts, or in right/left discrimination, impact perception

of body self or scheme. The OT can assess these abilities with the Draw a Person, Body

Part Identification, and Body Puzzle tests. 79

Lezak 80 warned that observations must distinguish between perceptual failures, aprax

ias, spatial confusions, motivation, or attention problems. Therapists have more recently

responded to this need for clearer definition of deficits and better direction for treatments.

In this regard, Bowler 73 noted that two assessments are beginning to be utilized to define

perceptual skills and other neurological skills which contribute to overall function. The

Rivermead Perceptual Assessment Battery 81 assesses deficits in visual perception and was

developed for adults with brain injury. The Lowenstein Occupational Therapy Cognitive

Assessment 82 examines orientation, perception, visuomotor organization, and cognition

and provides baseline information for treatment. Although some areas of assessment

overlap, the combined tests view each function from a variety of perspectives to more

distinctly define deficits.

Assessment of Activities of Daily Living

The OT is able to gather quite meaningful information from observations during actual

daily tasks in the residential treatment setting or the person’s home. The structure of some

postacute programs allows a trained rehabilitation assistant to gather appropriately doc

umented data of several specific tasks over several days during the initial assessment. This

documentation continues throughout the program for the purpose of reassessment or as

feedback data. For example, observations of the manner in which the individual organizes

and sequences tasks and manages time can be documented while the person plans the

meal, shops for items, and prepares the meal. This continually collected data directs the

OT along a progression of therapeutic focus, clinically and residentially (Figure 15.27).

Activities of daily living assessment may also include an evaluation of the living envi

ronment where the person resides. Home modifications,

environmental controls, and

adaptive equipment needs should be addressed to maximize independence and safety.

Training and education may be provided concerning energy conservation techniques,

transfers within the home, and emergency alert systems. An evaluation of the community

is also helpful to identify resources for vocational or leisure exploration. Community

transportation needs may also be addressed.

Take careful note of potential dependency behaviors. The family or others may fail to

recognize that tasks are innocently assisted or completely performed by them for the

injured person. If possible, assess ADL skills in a normal living environment, independent

of family interaction. This approach should help to identify true problem areas and can

be a good time to educate the individual and family about observed deficits and needed

intervention for same.

Concomitant Injuries

Orthopedic and Spinal Cord

Therapists will encounter people with TBI who have accompanying orthopedic and/or

spinal cord injuries. Special orthopedic issues, such as heterotopic ossification, must be

appropriately addressed (see Chapter 4). Regardless of the possibility that surgical inter

vention may or may not be involved, the PT and the OT will play a vital role. In a

postoperative situation, therapeutic follow-up will be

necessary to prevent loss of flexi

bility and function. Botte and Moore 83 describe, in detail, the methods for acute orthopedic

management of extremity injuries. They point out the importance of anticipation of uncon

trolled limb movement, avoidance of joint immobilization, and avoidance of prolonged ACTIVITIES OF DAILY LIVING CHECKLIST

ASSISTANCE LEVELS

0

1

2

3

4

5

6 = = = = = = = No assistance required to initiate, continue, or complete task Minimal verbal cues or gestural prompts Intermittent verbal cues or gestural prompts Minimal physical prompts Intermittent physical prompts Guided performance Unable Date:

DRESSING Level Comments

1.

2.

3.

4.

5.

6.

7.

8.

9.

10.

11.

12.

13. Don shirt/blouse/dress Doff shirt/blouse/dress Don underwear Doff underwear Don pants Doff pants Buttoning (small, large) Zipping (tops, pants) Buckle/unbuckle belt Don/doff socks/hose Don/doff brace/splint Accessories on/off Shoes on/off _________ _________ _________ _________ _________ _________ _________ _________ _________ _________ _________ _________ _________
____
____
____
____
____
____
____
____
____
____
____
____
____ Date:
____

GROOMING/HYGIENE Level Comments

1.

2.

3.

4.

5.

6.

7.

8.

9.

10.

11.

12.

13.

14.

15.

16.

17. Use faucets Wash face/hands Use handkerchief/tissue Apply/remove glasses Brush teeth/clean dentures Brush/comb hair Shampoo hair Style hair Shave face/legs Apply deodorant Apply make-up Care for nails Manage clothes at toilet Cleans self at toilet Manages feminine hygiene Bathe/towel dry entire body Skin inspection _____
_____ _____ _____ _____ _____ _____
_____ _____ _____ _____ _____ _____
_____ _____ _____ _____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____ Continued.

FIGURE 15.27

Activities of Daily Living Checklist used to document daily performance of ADLs. This information is used by

staff to produce weekly and monthly reports of the client's progress. Date: _____

HOUSEHOLD CLEANING Level Comments

1.

2.

3.

4.

5.

6.

7.

8.

9. Change sheets/make bed Pick up objects from floor Dust
Sweep/mop/vacuum Transport pail of water Wring out mop
Clean windows Clean refrigerator/stove Put out garbage
_____ _____ _____ _____ _____ _____
_____ _____ _____
_____
_____
_____
_____
_____
_____
_____
_____
_____ Date:
_____

LAUNDRY Level Comments

1.

2.

3.

4.

5.

6.

7.

8. Sort clothes Use washer/dryer Use detergent Hand launder Put clothes on hangers Fold clothes Put clothes away Iron clothes _____ _____ _____ _____ _____ _____ _____ _____
_____ Date:
_____

MEAL PLANNING Level Comments

1.

2.

3.

4.

5.

6.

7. Plan balanced meals Scan kitchen for necessary items Compile grocery list Estimate amount of money needed Get to/from store Locate items in store Retrieve items from shelves _____ _____ _____ _____ _____ _____ _____
_____ Date:

MEAL PREPARATION/CLEANUP Level Comments

1.

2.

3.

4.

5.

6.

7.

8.

9.

10.

11.

12.

13.

14.

15.

16.

17.

18.

19.

20.

21.

22.

23. Read recipe/directions Follow recipe/directions Remove food from refrigerator Remove items from cupboard Organize and transfer items to work area Open packages/cans/bottles Handle pots/pans/utensils Use faucets Pour liquids (hot/cold) Use microwave Use stove Use oven Peel/cut vegetables Break eggs Stir Measure Use timer/clock Set table/clear table Transfer food/liquids to table Wash/dry dishes Load/unload/use dishwasher Wipe stove/microwave/table Put dishes away _________

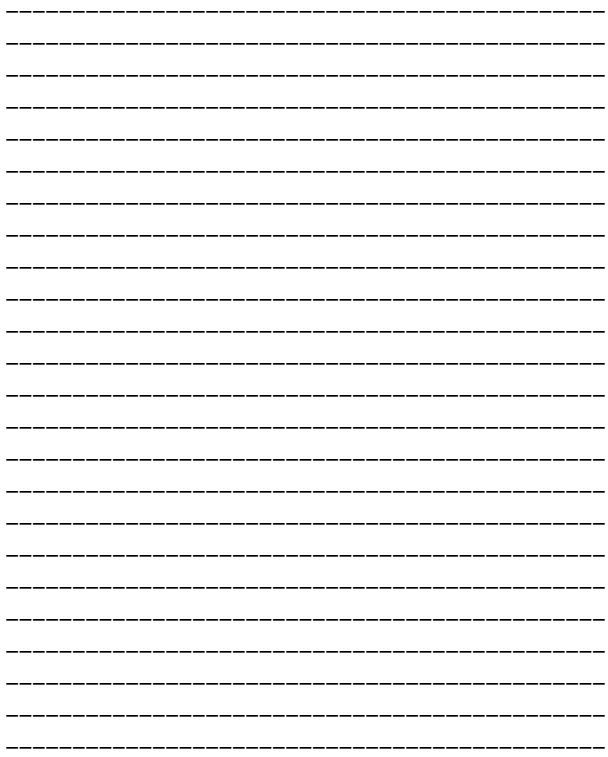

FIGURE 15.27

Continued.

traction methods. In the majority of cases, the acute orthopedic issues will have received

adequate attention from medical staff.

At the acute level, musculoskeletal injuries are missed diagnoses in approximately 10%

of individuals arriving at head trauma units. 84 As people are moved at an increasing pace

through the acute phases of treatment, therapists are faced with greater demands for

orthopedic management. Monitoring of proper positioning, modalities, splinting/casting,

sensation, mobility, and pain management is necessary. The therapists will need to educate

the injured person, family, and other therapeutic staff in

the possible adjustments required

to allow an optimum of function.

Review of frequency of musculoskeletal injury 83 shows that the shoulder girdle, radius,

and ulna are among the most common upper extremity injuries. The elbow must be

watched because of frequent spasticity around the joint, development of heterotopic

ossification, and possible ulnar neuropathy. Fractures of the humerus are relatively rare.

In the lower extremities, fracture of the femur is most common, followed by fracture of

the tibia. Pedestrian accidents will often involve the pelvis. Injuries to the acetabulum and

hip are comparatively rare.

Another frequent concomitant injury is that of the temporomandibular joint (TMJ). TMJ

dysfunction may arise from an associated facial injury or cervical myofascial injury. 85

Mechanisms of injury associated with MTBI can produce minor to severe TMJ dysfunction.

TMJ problems may be manifested by headaches (described as fan shaped in radiation in

proximity to the joint), jaw, neck, or back pain, eating problems, or subtle postural disor

ders. As a matter of awareness and thoroughness in the evaluation process, the PT eval

uation should include a TMJ screening assessment. If the neurological therapist is not

trained in treatment of TMJ dysfunction, appropriate referrals can be made for in-depth

examinations and potential treatment. Many PT’s are trained and work with dentists in

assessment and treatment of TMJ related problems. Although pain behavior related to this

dysfunction can represent a hindering factor to an efficiently addressed TBI rehabilitation

program, TMJ dysfunction is often ignored. It is important to keep in mind that visual

and vestibular deficits may cause pain within the TMJ; therefore, careful screening in all

areas is needed to fully address these complaints.

Pain

Many neurological therapists have noted that pain behaviors, in general, are more fre

quently seen in the person with MTBI than the more severely impaired person. In fact,

the existence of brain injury can actually be hidden by pain behaviors. 86 Headaches are a

common focus of the MTBI client. 87 Pain, whether real, exaggerated, or imagined, is pain

and, along with companion emotional issues, can become a large obstacle to progress.

Perhaps the most frequent complaint of pain arises from headache. 87 Headache, though,

can arise from a number of etiologies. 88 It is important to differentiate headaches arising

from TMJ dysfunction from those arising from sinusitis. Injuries to the head often include

injury to the sinuses. These headaches typically localize around the eyes and maxillary

region in a mask distribution. Headaches which are occipital may represent tension head

aches arising from muscular tension in the neck and shoulder musculature. Sometimes,

these headaches have a frontal regionalization as well. The patient who complains of daily

headache may benefit from review of medications or substances which are known to cause

rebound headache.

Headaches which arise from muscular tension or TMJ dysfunction may be improved

by physical therapy for those problems. Of course, the etiology for the muscular tension

must be determined as to whether it arises from musculoligamentous strain, orthopedic

injury, visual disturbances, or compensatory reaction to vestibular hypersensitivity.

In management of pain, it is very important to utilize a system which allows for the

patient to rate the pain experience throughout the day. Additionally, it is important for

concomitant recording of the degree to which pain impacts the person’s ability to func

tion. These reference points can be utilized by the treating physician and team to deter

mine appropriate medication and therapeutic approaches. Therapeutic approaches

available include thermal treatments, ultrasound, massage, flexibility exercises, strength

ening exercises, and relaxation. In some cases, pain management may be enhanced by

involvement of psychological services for the individual to explore relaxation or hypnosis

as potential avenues of treatment. Fortunately, the vast majority of pain management

programs for TBI respond well to conservative modalities of treatment, either in isolation

or in combination.

It should be understood that the brain-injured person may tend to perseverate on a

painful extremity, cast, etc. The therapist must be sympathetic and pursue appropriate

investigations into potential causes and treatments; however, the therapist should also be

aware that the problem may appear to be larger than it truly is. It is for this reason that

behavioral observation of activity restriction caused by pain can be useful in addition to

the person’s report.

Driving

The person with TBI may appear physically and cognitively able to drive a vehicle and,

yet, there may be problems. The ability to drive can be dramatically impacted by

impairments in or damaged interconnections between the vestibular system, oculomotor

and cerebellar functions, and the somatosensory system. The therapist must carefully

listen during discussions about driving and, when appropriate, driving should be

observed. There may be denial of any problems. Ask a significant other about the

individual’s driving habits or behavior as a passenger. Have any changes occurred? Has

driving at night been significantly reduced or avoided? Does the individual drive only

at specific times to avoid busy traffic? Does he/she frequently become lost or drive only

in certain areas of familiarity? Does the person drive more impulsively, become easily

irritated, or make unsafe judgments? Has driving been abandoned altogether? Many

individuals cannot explain why they have experienced changes and may provide general

comments such as “I just feel weird when driving. It scares me.” They may complain

of motion sickness or headaches while driving. They may be very anxious passengers

and complain that other vehicles are too close or moving too fast. Confusing visual

perceptions, movement imperceptions, and spatial disorientation can produce frighten

ing and disabling effects. 68,89–91

Functioning at Heights

Upon returning home, many people are faced with the need to reach something that is at

a height greater than their own height. Too often, it is assumed that they will be safe

climbing on a kitchen chair, stool, or ladder. It is important for the therapist and family

to be aware of the arrangement of objects within the home to prevent the need to climb,

if the individual is unsafe. An assessment of basic household heights may be appropriate

for some prior to their discharge from therapy.

Some people with TBI may have the potential to return to a vocation. It is generally

recommended that, following TBI, even MTBI, the individual should not be required to

work at heights.

Management of Residual Physical Deficits

Once the evaluative process has been completed and the treatment team has shared their

findings, the individual rehabilitation program begins to take shape. The purpose of treat

ment is to facilitate relearning and continue the momentum of improvement in skills, thus

reducing dependence. The development of a management plan begins with understanding

the factors which limit adequate performance. As is evidenced by the complexity of the

evaluative process, the management program can be expected to be equally complicated.

Neurological rehabilitation differs from other types of rehabilitation in that people who

have sustained neurological damage frequently evidence multiple areas of impairment in

addition to those areas which require physical restoration of function. These individuals

often cannot be left alone to undertake therapy exercises. They require attention for safety,

follow-through, motivation, documentation, and ongoing evaluation. The TBI population

is best treated in one-to-one treatment settings. Therapists must possess adequate knowl

edge of evaluative and treatment techniques and must also possess a repertoire of inter

personal skills which will enable them to motivate the unmotivated, calm the agitated, or

educate the person in denial. There will be times when a therapy session is nearly con

sumed by education or counseling, and others where the session focuses exclusively on

prescribed exercises.

The treatment environment should be such that the treatment can be segregated from

high stimulus environments that distract the individual. Attentional deficits which accom

pany brain injury can make it quite difficult to focus on the treatment session. Overstim

ulation can lead to behavioral problems.

Rehabilitation of physical function requires maximal repetition. As such, the therapist

should attempt to treat in blocks of time which allow for ample repetition of a wide array

of therapeutic tasks that will be required in most treatment plans. Newly emerging positive

responses should be focused upon until they are reliably reproducible, even if this means

continuing a treatment session beyond scheduled times.

The therapist should develop the ability to approach treatment exercises hierarchically,

utilizing task analysis, where necessary, to break larger tasks into smaller ones to accentuate

the learning experience. TBI results in changes in the manner in which a person acquires

new information, so physically restorative therapies may be expected to take longer in the

neurologically-impaired population as contrasted to other populations. To that end, quan

titative measurement of treatment exercises that have been broken into smaller, more

readily learned components can give a clearer picture of slowly progressing improvement.

Therapeutic Measurement

It is now more widely accepted that continued postacute rehabilitation with the traumat

ically brain-injured person can bring about substantial reduction in disability, improve

ment in living status, and improvement in occupational status. 92–97 This was not always

the case, however. In the time when rehabilitation for this population was largely restricted

to the acute rehabilitation experience, it was necessary to develop methods of measure

ment that would allow both the therapist and the consumer access to critical review of

the therapeutic process. Progress could no longer be viewed through the subjectivity of

the therapists' eyes, but instead, a new period of accountability was emerging. Qualitative

summaries of patient performance were no longer acceptable. Many therapists found the

expectation for quantitative analysis to be difficult, but once accomplished, the improved

objectivity about therapist/patient performance, over time, allowed for some major ther

apeutic advances. In fact, quantitative measurement allowed therapists to acquire new

perspectives about breaking therapeutic tasks into hierarchical components so as to better

teach skills to a learning-impaired patient. Therapy became easier to implement and

monitor and patients were better able to benefit from treatment. 11,14

In order to most accurately understand whether a patient is benefiting from treatment,

the therapist must reduce the therapeutic task to its hierarchical components which can

be operationally defined and objectively measured. For

example, in evaluating ambulatory

skills and progression therein, the therapist should refrain from characterization of skills

as follows: “Mr. Smith is able to ambulate short distances with a hemi-cane.” Rather, the

therapist should characterize Mr. Smith’s performance by a statement such as “Mr. Smith

is able to walk 100 feet, with a hemi-cane, in a mean of 2 minutes. This is an improvement

from a mean of 3 1 / 2 minutes for the same distance last week.”

Quantification can generally be achieved fairly readily. The therapist can count repeti

tions of a task, document specific amounts of weight or resistance being used, time

performances, and/or count accurate vs. inaccurate performances to obtain a percentage

correctly performed. Of course, there remains room for subjective observations as well,

but therapy which is quantitatively approached is far easier for all parties to participate

in, enhancing cooperation, motivation, consistency of treatment, and ultimately, progress.

The therapist should keep in mind that the brain-injured person has a number of special

needs. In today’s environment of managed care, it is important to keep the therapeutic

focus on tasks which will translate, quickly and efficaciously, to good functional improve

ment. At the same time, the very measurement which is advocated herein may become

the data utilized to justify continued treatment toward a longer-term goal of improved

functional capability. Outcomes are being viewed, increasingly, from the perspective of

financial risks and benefits. Ashley et al. 92 address the idea that rehabilitation outcome

translates to dollar savings for long-term care costs. These savings have their beginnings

with the daily therapeutic sessions undertaken by the PT, the OT, and their allied health

associates. Another study by Spivack et al. 98 demonstrated a clear relationship between

treatment intensity and rehabilitative outcome. Thus, in order to advocate best for the TBI

person, quantification of treatment will be of critical importance.

During treatment, the therapist must teach all other pertinent staff, clinical and residen

tial, methods that they can use to maximize the individual's learning throughout the entire

day. Management of physical injury residuals cannot be performed in a vacuum separated

from other therapeutic disciplines or from environments which the person will be expected

to function in. Therefore, an important daily goal is to generalize skills into actual activities

in residential and community environments. 29,31 This is where environmentally valid learn

ing takes place. Maximized repetition and structure, performed in sequence and in realistic

situations, maximizes the derived rehabilitation benefit.

Another factor to take into consideration is that the person with TBI is not passively

traveling through the rehabilitation process. In physical and psychological terms, therapy

is difficult work for the person with TBI. Confronting one's weaknesses is never easy.

Early review of the individual's personal history and lifestyle can provide key information

to fuel motivation. Perception of purpose and realization of goal achievement are enhanced

by the therapist's ability to present concrete, appropriately sequenced tasks within the

scope of the individual's interests. Progress requires a constant series of challenges. The

therapist must be a creative motivator.

Mobility

Normal movement cannot be built on abnormal tone and normal behaviors do not sequence

from abnormal ones. 1,11,55 The primary treatment approach toward normalizing functional

mobilization is neurodevelopmental theory or NDT. 1,2 Postgraduate training courses are

available to therapists throughout the United States and other parts of the world. This

technique, often referred to as the Bobath approach, was originated by the husband and wife

team of Karl and Berta Bobath in Sweden in 1943. The initial population served with this

treatment approach was children with cerebral palsy. It is now an accepted treatment for

individuals with acquired brain injury, including stroke and other neurological disorders.

NDT is a means of treating the person with brain injury at, or above, the brainstem

level. Treatment principles emphasize a holistic approach, which requires constant inter

disciplinary communication. Analysis of normal and abnormal

movement is always

important. Trained therapists are able to identify problems interfering with function. The

training enables the therapist to utilize handling techniques to inhibit abnormal tone while

assisting the person in acquiring functional skills. The focus with hemiparesis is to incor

porate the affected side into virtually every activity of daily living. Instead of being

satisfied with compensatory movements or learned nonuse of limbs, the person is assisted

in recovery of symmetry.

Functional mobilization may be influenced by such injury residuals as fractures, periph

eral nerve injuries, general weakness, pain, sensory impairments, visual impairments,

balance and coordination deficits, as well as cognitive and behavioral factors. Each must

be addressed to allow progress to more advanced performance levels. The goal is to

facilitate and normalize movement, which will gradually advance into daily mobilization.

Ranges of motion and adequate strengths to move are among the fundamental require

ments which can usually be conventionally addressed.

Significant motor impairments may require immediate treatment for ongoing hyperto

nicity or a movement disorder (i.e., ataxia) which will be discussed later. Hypertonicity

may refer to spasticity or rigidity. Although these problems are often addressed and

resolved during the acute rehabilitation phase, the postacute therapist will have occasion

to treat these impairments. These issues may be addressed via both a medical consultant

and the therapist. Approaches can range from stretching and positioning to serial casting

and chemical neurolysis. Orthopedic management of spasticity can be efficacious in obtain

ing temporary relief from spasticity. 99 Diagnostic blocks can be utilized to temporarily

eliminate pain and muscle tone to ascertain the degree of motor control present and the

amount of fixed contracture. Therapy is frequently enhanced by application of chemical

neurolysis in that the treatment can focus on nontreated muscles groups, obtaining isolated

contractions in those groups, enhancing awareness of control of those groups, and allowing

for strengthening of those groups.

Mobility can be impacted by reductions in range of motion. Range of motion can be

reduced due to neuromuscular deficits or due to restriction of the joint due to contractures

or heterotopic ossification. Decerebrate or decorticate posturing during coma or neuro

muscular deficits seen most commonly after cortical or brainstem injury which result in

spasticity will frequently result in the development of joint limitations. Restrictions arising

from musculoligamentous contracture should be treated through a multimodal program.

Lehmkuhl et al. 16 advocate early use of such a program to include passive and active

ROM, positioning, serial inhibitive casting, bivalved casts, motor point blocks, and anti

spasticity medication. Elbows and knees were noted by these authors to respond most

quickly to therapeutic intervention, with elbows benefiting most. Increases in joint ROM

can be expected to endure for at least 6 to 9 months. Of course, it should be expected that

joint limitation improvements will be maximized by long-term use of the full ROM

achieved through daily functional activity. 100

It is imperative that mobility be taught in an appropriate progression from bed mobility

to transfers to ambulation. Mobility skills will improve through intense repetition appro

priate to the developmental sequence of movement. The neurodevelopmental sequence

(previously described in this chapter) can become an exercise routine which can be prac

ticed at any level required. For example, the therapist may begin with segmental rolling

to improve body awareness and enhance movement. Rolling should progress to assuming

prone-on-elbows and, eventually, the quadruped position until each is performed inde

pendently. The sequence continues to be practiced, component to component, through

tall-kneel, half-kneel, and standing. Treatment of any difficulty within each component of

the sequence may come from the therapist’s choice of a variety of treatment approaches,

e.g., proprioceptive neuromuscular facilitation (PNF) and NDT. 1,4 The individual continues

to practice, component to component, as the motor tasks are gradually progressed from

the simple to the complex. Besides movement, strength, and flexibility, very basic balance

skills are practiced within the sequenced exercises. The exercises may appear simple,

though they can be quite challenging. Do not skip over sequential components. Do not

assume competence at any level until performance is demonstrated to the therapist.

An emerging gait training strategy uses the concept of partial body weight support

(BWS). The individual is secured in a harness which provides 0 to 50% of support of body

weight. The system may be used on a level ground surface or suspended over a treadmill.

The harness system eliminates risk of falling and the person is able to gradually accept

an increasing amount of their own body weight during standing and/or ambulation. With

no fall risk, gait training can begin earlier in the rehabilitation process. 101–103 Additionally,

the therapist’s hands are free to facilitate normal movement while the person is in the

upright position. A critical component in this treatment technique is the physical cues

provided by a therapist. These cues include weight shifting, stabilizing the trunk, rotating

the pelvis, advancing the affected limb, and so on. Use of the BWS technique during gait

training in hemiplegia produced better results in regard to functional balance, motor

recovery, walking speed, and endurance as compared to gait training with full body

weight. 102 Research has shown that ambulation was

improved with partial weight bearing

protocol, including reduced stance time on the unaffected limb, increased weight accep

tance on the affected limb, increased gait velocity, and improved gait symmetry. 103,104

Studies of people with spinal cord injury have shown that, when provided with the

proprioceptive input of weight bearing during gait, the lumbosacral spinal cord can

generate rhythmic locomotor EMG patterns, even in the absence of supraspinal influ

ences. 105 This indicates that control of the flexion/extension pattern of walking is in the

spinal cord and, in the case of damage to the brain, these central program generators can

be activated to facilitate and improve ambulation. Research on gait training with body

weight support system in the TBI population is extremely limited and is an area in need

of further attention. 105

Treatment of mobility skills is greatly enhanced by daily practice of these skills in the

residential setting. Bed mobility can be practiced every day in the environmentally-valid

routines of getting up and going to bed. A trained staff should be present to assist in

additional home exercises, which should be designed by the clinical staff to ensure the

use of proper techniques. The same is applied to all transfers, toileting, bathing, and early

ambulatory routines. The individual advances through these daily routines from the clinic

to the residence to the community until greater

independence is accomplished.

Pain

In management of pain, it is very important to utilize a system which allows for the person

to rate the pain experience throughout the day. A pain diary provides a way to document

and rate pain. A rating scale of 0 to 10 (0 = none and 10 = most severe) is a simple scale for

the person to use. Headaches or neck and back pain in the brain-injured person can become

a distracting somatic focus and perseveration on pain may hinder progress in several aspects

of the TBI program. An assumption that pain is exaggerated should not be made until

complaints of pain are explored to rule out potential causes which may respond to treatment.

It is important to keep a concomitant recording of the degree to which pain impacts the

person’s ability to function. These reference points can be utilized by the treating physician

and team to determine appropriate medication and therapeutic approaches. The physician

must review all medications taken by the client and determine what modifications, if any,

should be made. Dosage and frequency of medication taken should be included in a diary.

The physician may elect to utilize a controlled reduction of dosages with combined pain

medications. Consultation with an experienced pain management physician may be

required in some cases.

The therapist will have a major impact upon the individual’s understanding of the

various causes of pain. The individual who anticipates pain from movement develops

increased anxiety and muscle tension and, therefore, the potential for chronic pain and

stiffness. A kinesiological orientation in the initial exercise program may be an effective

tool to reduce this anxiety-produced pain and allow the client to begin to move through

and beyond pain. This approach teaches normalizing posture and improving body

mechanics with more efficient movements to reduce pain.

Conventional therapeutic modalities include thermal treatment, ultrasound, TENS (tran

scutaneous electrical nerve stimulation), massage, aquatic therapy, flexibility exercises,

and strengthening exercises. Pain management is best enhanced by involvement of psy

chological services for the individual to explore relaxation or hypnosis as potential avenues

of treatment. The best approach to pain management is to address all deficit areas while

unifying the physician, the treating therapist, and treating psychological team.

Postural Control and Balance

Fisher 52 describes postural deficits commonly seen in people with TBI and contrasts their

postural abilities to normals. In general, the individual with TBI can be observed to tend

toward the relaxed sitting posture of normals, however, on an habitual basis. Trunk

movements tend not to be incorporated into arm movements and, even when attempting

to assume an erect sitting posture, truncal musculature strength and coordination may

make achieving the erect position quite difficult. Not only do truncal weaknesses impact

upper extremity function but transfers can also be impacted. In preparation for arising

from sitting to standing, postural deficits frequently will maintain weight so far posteriorly

as to make the attempt to arise ineffective.

Effective treatment of postural deficits focuses on strengthening of the truncal muscu

lature. In cases where there is concomitant cerebellar dysfunction, strengthening may not

be indicated so much as learning selective utilization of muscle groups with slow, con

trolled muscle activation. In cases, however, where a cerebellar component is not present,

strengthening exercises such as bridging, sit-ups or crunches, or resistive lateral bending

can be helpful. It is important to achieve stabilization at the hips, back, neck, and shoulders.

Activities such as hippotherapy and therapeutic horseback riding are also excellent ways

to retrain the postural system and impact balance along with visual, psychological, and

vestibular enhancement.

For detail regarding treatment of balance impairments related to vestibular dysfunction,

the reader is referred to Chapter 5.

Cerebellar Dysfunction

Many therapists struggle with movement disorders related to cerebellar dysfunction.

Frustrations with ataxia or tremors in the extremities and/or trunk are compounded by

the short period allowed for treatment and often lead a therapist to teach compensatory

techniques (i.e., using the more functional limb or mobilizing from a wheelchair). Minimal

to no time is then spent in therapeutic confrontation of the issue.

When undertaking cerebellar rehabilitation, it is important to keep several important

factors in mind. The first is that muscle strengthening activities can result in exacerbation

of tremor, causing the degree of tremor excursions to increase. The second point is that

the individual must learn to relax selective muscle groups on command to reduce the

excursion of tremor. Tremor results from agonist/antagonist muscle groups firing rhyth

mically. The individual must learn to selectively turn on one muscle, while maintaining

relative electrical silence in the antagonistic muscle. EMG/biofeedback training can be

quite effective in teaching people to control muscles and even specific motor units. 23,106

The third point has to do with the importance of a progression of stabilization of the trunk,

to the neck and head, to the proximal extremities, to the distal extremities. In severe

cerebellar dysfunction, postural tremors may be so severe as to necessitate treatment

commencing in a supine position. It is useful to not only retrain truncal control in this

position, but also to approach proximal extremity musculature control as well. The utili

zation of selective muscular relaxation and activation can be particularly helpful at this

stage, with positioning helpful in teaching the ability of selective relaxation and activation.

Diminished ability with rapid alternating movements, dysmetria, hypotonicity, and/or

movement decomposition are manifestations of cerebellar damage which influence perfor

mance in ADLs (i.e., feeding, brushing teeth, dressing, or gait functions). Reading, or other

skills which require accuracy in visual scanning ability, can be impacted by oculomotor

deficits related to cerebellar injury. A spastic hemiparesis may further complicate an ipsi

lateral or bilateral ataxia in one or more limbs. Acquiring a degree of movement control

and normalizing functions can be frustrating. However, the therapist should pursue proper

identification of the dysfunction and aggressively pursue appropriate treatment. 14,107

Establishment of a stable base of support is the initial focus of treatment. For example,

the performance of any task requiring an ataxic extremity to extend away from the body

requires trunk stabilization. Therefore, goals of treatment are postural stability and accu

racy in extremity movement during functional activities. Treatment must be pursued in

a sequential manner until the individual is independent in each component. That is to

say, head and trunk control must be addressed and established prior to sitting or ambu

latory activities.

If poor head control is evident, initiate treatment with prone-on-elbows positioning or

seated at a table, feet firmly planted on the floor, with weight on the forearms. If there is

poor trunk control, bolsters, wedges, or pillows will assist with support in the prone position.

The neck extensors can be briefly brushed with ice, no more than 5 seconds, followed by a

stretch and then heavy resistance to the extensors. This is followed by downward compres

sion on the shoulders. The goal is to maintain the head in a steady upright position.

Progression to management of trunk control will require a graduated removal of the

pillow supports and an increased demand will be placed on the elbows and shoulders.

Approximation through the shoulders should be provided. Weight shifting should be

practiced until the individual is able to sustain support on one elbow. Additional mat

activities can include the quadruped position combined with joint approximation through

the shoulders and hips and weight shifting. During this phase, trunk rolling and supine/

prone-to-sit exercises can be practiced with graduated mild resistance given by the ther

apist. The person should progress to crawling activity to challenge balance, strength, and

weight shifts in reciprocal patterns.

As head and trunk control improve, sitting can then be addressed. Sitting on surfaces

without benefit of structural supports (i.e., the edge of a mat or chairs without arms or

backs) should be used. Stabilization is promoted by joint approximation at the hips and

shoulders. Weight shifting should be practiced. Another mat activity can include the tall

kneel position. The therapist should provide approximation through the shoulders and

hips and weight shifting can be practiced. Contact support can be initially provided by

the therapist. As stabilization and balance improve, support is gradually reduced.

During progress in sitting and tall-kneel activities, the upper extremities should be

extended from the body to challenge trunk stability. Head and trunk rotations and bending

from the hips can be practiced with one or both arms extended overhead, laterally, or

forward. Realistic movements should be practiced (i.e., reaching for objects overhead, to

the side, or from the floor). Functional upper extremity activities may be practiced while

sitting or tall-kneeling at a table. To progress stabilization, weight may be shifted from

one forearm to the other while the opposing extremity is active. This support is gradually

reduced until two hand activities can be practiced. Mild resistance to the trunk and

extremities for feedback is initially helpful to the client during movements. This can be

provided manually by the therapist or by light wrist weights.

As head and trunk stabilization improves in sitting, supine/prone-to-sit, and tall-kneel

ing, the individual should practice transfers. Initiate

transfers from the most stable position

(i.e., sliding surface to surface) and graduate in degrees of difficulty until the person is

safely independent.

Much of the above activity prepares the person for standing and ambulation. Rolling,

assuming and maintaining the quadruped position, crawling, and tall-kneeling are the

basic neurodevelopmental sequence positions necessary preliminary to standing. Overall

strengths, endurance, and balance must be adequate to launch into the demands of the

upright position. The person should repeatedly practice moving through foot placement,

sliding forward, flexing from the hips, and pushing upward with a sense of center of

gravity and balance. Manual guidance from the therapist and visual feedback from a

mirror can initially assist the individual as extension of the hips and knees move the

individual to the upright position.

Once stability in standing is accomplished, the ambulatory phase can be initiated. A

front-wheeled walker may be the first support device required for ambulation practice. On

occasion, weighted walker legs may be necessary to assist stabilization. If appropriate, tall

poles can be quite effective in developing a sense of rhythm, pace, and reciprocal movement.

Past-pointing or dysmetria will benefit from various techniques such as biofeedback, 108

PNF, 4 and Frenkel’s exercises. 109 EMG biofeedback can be useful during practical activities

(i.e., combing hair, brushing teeth). Aquatic/pool exercises may be beneficial for relaxation

of the person with ataxia.

Sensory Function

There is a therapeutic opportunity to address the sensory impairment of an extremity as

the person is exposed to treatment in clinical, residential, and community activities. Yekutiel

and Guttman 110 documented that somatosensory deficits in the plegic hand can significantly

improve with intensive sensory retraining which incorporates functional tasks. The perfor

mance of basic self-care skills requires an integration of perceptual, cognitive, sensory, and

motor functions. The ability to perform a motor task will depend upon the interactions of

the residual components which are functioning throughout these systems.

An intensive effort should be made to stimulate sensory functions to normalize tactile

sensitivity. 55,74 Keenan and Perry 111 noted that the sensory functions necessary for hand

function included awareness of pain, light touch, temperature, proprioception, and two

point discrimination of less than 10 mm. Assessments will determine the specific deficits

to be addressed. Treatment requires adequate time and opportunities to maximize repeti

tion of stimuli. Also, incorporate visual input into treatment sessions to increase awareness.

If a significant motor impairment accompanies the sensory deficit, improvement of the

motor function is usually addressed first. Tactile stimulation, however, can, and should be,

incorporated into the initial treatment sessions. Weight-bearing on the impaired extremity,

through the palmar surface, on a variety of textured surfaces (i.e., carpet, sand, or smooth

metal) will facilitate motor function, proprioception, and touch. As improvement occurs in

motor and sensory functions, progress to functional two-handed tasks. These tasks may

include weight-bearing on dirt or sand while gardening, holding down paper while writing,

or weight-bearing on the extremity while eating with the functional extremity.

Deficits in touch are addressed by providing a strong stimulus to the extremity. Initial

sessions open with stimulus via rubbing various textures over the extremity. If possible,

have the individual actively move the textured material over his/her own extremity with

the unimpaired hand. Make the person aware of any abnormal positions in the extremity

or hand during activities. This should be immediately corrected to stimulate a sense of

normal touch during movements. Functional tasks in repetitive daily routines can include

washing, rinsing, and drying the hands, dusting, cleaning windows, making the bed, or

folding laundry.

Individuals who have hypersensitivity or sensory defensiveness may be appropriate

for sensory integration techniques such as the Willbarger Protocol. 112 The protocol involves

establishing a set sensory routine that encompasses deep proprioceptive input with active

physical proprioceptive activity. Special training courses are offered to learn and teach

the technique.

It is important to encourage the use of both hands in as many tasks or activities through

out the day as possible. A goal of treatment is to increase spontaneous use of the impaired

side. It stands to reason that, if the impaired extremity is not spontaneously used, then

overuse of the unimpaired side occurs. Eggers 55 suggests a remedy by having the client

wear a glove on the unimpaired hand, which should reduce overuse of the unimpaired

extremity and facilitate increased use of the impaired extremity, called constraint-induced

movement therapy. Protocols for its use have been established primarily for the CVA pop

ulation. Difficulty with the procedure typically involves behavioral compliance and cog

nitive ability to comprehend the treatment.

Proprioceptive deficits should be addressed while performing motor functions. The

impaired extremity is initially guided by the therapist. This is progressed to the individual

moving the impaired extremity through tasks with his/her own unimpaired extremity. If

grip and strength are available, two-handed activities should then be incorporated to

include lifting and movement of various objects (i.e., cans, plastic bottles, a brush, etc.).

Engage activities which will include resistance (i.e.,

sanding or pushing objects). ADL

tasks offer numerous opportunities to maximize therapeutic input for proprioceptive

impairments. For example, dressing with a proprioceptively-impaired upper extremity

should begin with the practice of moving the extremity through sleeves or tubular mate

rials. Have the person guide the extremity with the unimpaired hand and emphasize

visual input as a reference. Progress to functional activities such as dressing. Practice

should initiate with tasks in front of the body and overhead with visual input. As sensory

function improves, progress to tasks without visual reference (i.e., tucking in a shirt,

reaching for a wallet behind the back, or reaching for objects under a table).

Smell and Taste

In cases where impairment of smell or taste is irreversible, the individual and family need

to be made aware of social, dietary, and safety implications of impaired smell and taste.

The person with TBI who will be living and/or working independently in the community

will require training in management of perishable foods and toxic materials. Food prep

aration training must include visual monitoring of food while cooking and identification

of altered seasoning practices which may not be healthy. Structure should be established

to assist by labeling and dating perishable foods. Pet care, if applicable, should be under

taken systematically. Toxic materials should be moved to a

safe place and labeled. Smoke,

carbon monoxide, and gas detectors within the home should be considered and can be

assisted by current electronic detection technology. 66

The work place must, likewise, be considered when treating for olfactory/gustatory

deficits. Education of the employer and coworkers may allow the candidate for vocational

placement a chance for return to work with reduced risk. The vocational rehabilitation

counselor should take these types of deficits into consideration while looking or planning

for vocational placement. 66

Visual Perception and Perceptual Motor Functions

Areas frequently requiring therapeutic intervention are visual inattention, gross ocular

deficits, scanning, figure-ground, visuospatial perception, visual memory, and visual

motor skills.

Appropriately trained rehabilitation assistants can augment the clinical program by

undertaking home exercises, as well as through functional application. Visual perception

deficits, such as figure-ground, can be practiced via homework with work sheets and

home exercises, such as words searches or community scans. It may be helpful to teach

organizational skills and energy conservation techniques to help compensate for residual

deficits. Puzzles, form boards, parquetry blocks, and other appropriate games can keep

the client’s interest while being therapeutic. Visual

scanning while reading or working

word puzzles may be useful. Data should be collected and reviewed over time for progress.

Neistadt 113,114 has indicated that there is an association between functional and construc

tional skills. The presence of constructional apraxia and visuoconstructive disorders has been

shown to impact independent living by difficulties with meal preparation, dressing, changing

a tire, or assembling an object. Bouska, Kauffman, and Marcus 68 discuss the importance of

teaching the individual to approach a visuoconstructive task via sequential planning. For

example, the task should begin first by visually and physically organizing the parts, followed

by construction of the object. The person with apraxia benefits from physical guidance to

initiate and carry out a simple task. With intense repetition, the ability to wash, groom, and

feed should normalize. On higher levels, dyspraxia requires the same touch and guidance

to accomplish more complex activities requiring the ability to plan, arrange, and build.

The neurodevelopmental approach to improving perceptual motor skills has been found

to be effective and provides a guideline to the progression of treatment as the individual

advances. Intensive practice is vital and should be pursued with functionally meaningful

tasks in normal living environments.

For additional therapeutic approaches to visual impairments, the reader is referred to

Chapter 6 and Chapter 7.

Driving

Independence, in terms of driving skills, can be enhanced through visual therapy and

perceptual training. 90 Exercises to address visual attention and scanning, visuospatial

relationships, oculomotor skills, eye-hand-foot coordination, and response times are some

of the components required to safely drive a vehicle. Driving evaluation and retraining

should include behind-the-wheel time with a professionally-trained driving instructor, in

a dual-equipped vehicle.

Computer programs to address perceptual skills have become quite popular over the

past decade. Many rehabilitation programs have depended heavily upon this tool as a

therapeutic base. While “computer-assisted therapy” is a useful and motivating approach,

it does not provide stimulus to, or require responses from, other systems (e.g., vestibular,

motor, or other perceptual responses). 68 Any dysfunction in the perceptual realm may be

impacted by concomitant vestibular and/or cerebellar deficits. 54 Again, the importance of

hands-on therapy to reintegrate multiple systems into efficiently coordinated responses

requires more than one evaluative or therapeutic approach. If driving skills are not ade

quate at evaluation, it may well be possible to enhance skills via training. It may be

necessary to undertake drivers’ retraining with both classroom and behind-the-wheel

instruction in order to improve driving skills.

All therapeutic disciplines should be polled as to potential limitations which may be

experienced prior to the driving evaluation. This information should be reviewed by the

treating physician and a determination made about the propriety of the driving evaluation.

This information will be invaluable to the driving evaluator as the assessment is undertaken.

Cardiovascular Fitness

As major sensorimotor deficits are improved and general mobility advances to higher

levels, it may be appropriate to initiate an aerobic and conditioning program. These

programs can be developed to fit into the person’s lifestyle by gradually transferring the

exercise routine from the clinical setting to a community gym. The initial exercises must

be performed with the therapist’s close supervision and medical clearance.

An aerobic and conditioning program can be created for the people with and without

significant motor impairments. Stretching should also be taught to start any exercise

routine. An exercise program can be developed with stationary bicycles (standard or

recumbent), treadmills, and weights. Muscle conditioning may utilize isometric exercise

or full range exercise with weights, elastic exercise bands, free weights, or exercise

machines. Low-impact aerobic exercise routines can be developed with walking, swim

ming, bicycling, and aerobic classes.

As the person becomes more independent and community reentry is developed, the

therapist may assist in the choice of, and transfer to, a community-type exercise routine

(i.e., a local gym or fitness center). Independent aerobic exercise routines can be established

in walking, swimming, or bicycling as well as a maintenance stretching and muscle toning

exercise program (i.e., sit-ups, push-ups, etc.). In some instances, even “short form” Tai

Chi has been utilized.

As the benefits of conditioning renew the individual’s sense of well-being and enhance

the overall functional status, the continuation of exercise as an enjoyable routine may

allow a gradual reduction of supervision.

Motorically- and cognitively-impaired individuals also gain great benefit from a fitness

program. Aside from endurance and stamina, it has been demonstrated that thinking ability

and emotional status improve with physical fitness. 115,116 As a result, there are enhanced

levels of energy, feelings of well-being, and independence for most people with TBI.

Pool/Aquatic Therapy

Although the healing elements of water have been used for centuries, organized thera

peutic protocols for the neurologically impaired have emerged only during the past

decade. Current programs for musculoskeletal injuries (e.g., neck and back) are widely

accepted by therapists and well received by those being

treated. In this regard, the use of

a pool program is a positive aspect to the physical rehabilitation for the person with MTBI.

Aquatic therapy can address difficulties with balance and coordination, muscle weakness,

poor endurance, and sensory dysfunctions. The buoyancy and warmth of the water,

together with use of appliances to introduce resistive exercises, make a good combination

for therapeutic application. Subtle vestibular impairments may manifest in aquatic activ

ities, as water reduces proprioceptive feedback making balance functions more dependent

upon visual and vestibular feedback. Precautions for cardiac or other medical consider

ations should be taken prior to introduction of an aquatic program.

The more motorically-impaired person can have quite positive responses to a pool

program. Abnormal muscle tone, motor control, gait patterns, and range of motion deficits

can be addressed by utilizing the characteristics of water. This approach can add an

element of fun and should be relaxing. As usual, normal precautions must be taken for

cardiac, incontinence, and swallowing issues. 117,118

Summary

This chapter presents an historical review of the integration of physical rehabilitation

services into the developing field of head trauma rehabilitation. The chapter provides a

comprehensive review of evaluative and management protocols in areas which are most

commonly observed to be problematic on a long-term basis for the person with TBI. The

reader has been encouraged to adopt an expectation for continued improvement associ

ated with continued treatment beyond acute hospitalization. Physical and occupational

therapists should understand the tremendously complicated clinical presentation often

associated with TBI and become familiar with treatment strategies which can be used

either individually or in tandem to treat the physical residuals associated with TBI.

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16

Vocational Rehabilitation

Mark J. Ashley, Joe Ninomiya, Jr., Amy Berryman, and Karen Goodwin

CONTENTS

Introduction

Return to work following a traumatic brain injury (TBI) represents, perhaps, a pinnacle

achievement for both the injured individual and those professionals working with the

individual. If the ultimate measure of rehabilitative success is life satisfaction, vocational

success bears significantly on life satisfaction. Melamed, Groswasser and Stern 1 reviewed

gratification of basic needs, physical well-being, emotional security, and family, social,

economic, and vocational needs 1 to 2 years following discharge from rehabilitation for

78 people with TBI. Those individuals who were employed in the open labor market, lived

active lives, and had higher degrees of acceptance of disability reported the highest

satisfaction. Lower satisfaction was associated with unemployment, employment in pro

tected conditions, and with passive, uninvolved lifestyles. These findings are supported

by other authors who report life satisfaction associated with employment and degree of

social integration. 2,3 Self-directed vocational participation as an adult is promoted from a

very early age through young adulthood as a means of securing social and financial

stability. TBI frequently robs an individual of the ability to participate meaningfully in

life, through vocational and social involvement, in keeping with the rest of society.

Ironically, while rehabilitation endeavors to assist individuals to achieve maximal recov

ery so they will have the opportunity to participate fully in life, a societal predisposition

exists toward insufficient effort in returning people to the workforce. This is manifest by

restricted vocational rehabilitation benefits under various workers' compensation statutes

across the United States, as well as by lack of provision of benefits for vocational rehabil

itation services in any accident and health insurance coverage. Vocational rehabilitation

services provided by publicly funded sources such as state departments of vocational

rehabilitation are often ill-prepared to deal with the complexity of problems presented by

persons with traumatic brain injury. 4–6 The General Accounting Office (GAO) of the United

States reviewed differences in return to work strategies comparing the United States to

Germany and Sweden. 7 Public expenditures for vocational rehabilitation were 2 times

higher in Germany and 2.6 times higher in Sweden as a percentage of gross domestic

product. The GAO cited divergent goals of Social Security's eligibility and provision of

benefits and vocational rehabilitation agencies. It was concluded that differences also

existed in the availability of vocational rehabilitation services, timing of vocational referral

(later in the United States) and level of financial incentive involved in returning to work.

Heinemann et al. 8 completed a survey designed to measure the unmet needs of persons

with TBI. Responses from 895 respondents indicated that two of the three greatest needs

— improving memory or problem solving skills (51.9%), increasing income (50.5%), and

improving job skills (46.3%) — were vocationally related.

Vocational rehabilitation services have been available since the 1970s, 9 with funding

provided by the public sector in the form of state departments of vocational rehabilita

tion or the private sector as a benefit under workers' compensation. The primary thrust

of vocational rehabilitation (i.e., returning an individual to work) is accomplished by

careful evaluation of work responsibilities and comparison of the physical requirements

of those responsibilities to the individual's capabilities following injury. Very few con

ditions present the complexity of deficits seen with traumatic brain injury, however.

People with traumatic brain injury present with far more complicated problems, includ

ing behavioral, cognitive, communicative, psychological, emotional, social, and physical

disabilities.

Provision of vocational rehabilitation services is not uniformly applied to all individuals

who sustain traumatic brain injury. 10,11 Return to work following traumatic brain injury is

difficult for many individuals regardless of the level of severity of injury 10,12 and is made

more difficult by a lack of appropriate funding, 13 a lack of understanding as to the proper

undertaking of vocational rehabilitation services, 4–5 and a lack of awareness on the injured

person's part, or the care provider's, of the applicability of vocational rehabilitation ser

vices. 11 Reported rates of return to work vary considerably in the literature, depending

upon the population studied and limitations of individual study methodologies. 14 Return

to work is reported to range from 20 to 100%. 15–18

Vocation serves a tremendously important role in life, yet vocational rehabilitation is

one of the least understood and least delivered services for people with TBI. This chapter

will address the provision of vocational rehabilitation services to individuals with trau

matic brain injury.

Employment Trends Following TBI

Return to work following traumatic brain injury is not easily accomplished and may not

be accomplished at all by some individuals. Rates of return to work vary throughout the

literature and are impacted by both the definition of "work" and the nature of the popu

lation studied. Rao et al. 19 conducted a follow-up study on 79 consecutively admitted

patients over a 2-year period. At a mean of 16.5 months postdischarge, 66%, or 52 indi

viduals, had returned to work or school and 34% had not. In another study, McMordie et

al. 20 found only 19% of individuals out of 177 cases were competitively employed. In this

particular study, 45% of the sample was engaged in some work-related activity. Gonser 21

followed 122 people with severe head injury for 2 to 4 years postinjury. Of these, 43%

were found to be without “employment handicap.” At the other end of the chronicity and

severity spectrums, Englander et al. 22 followed 77 individuals with mild traumatic brain

injury (MTBI) as measured by Glasgow Coma Scale (GCS) scores of 13 to 15 and post

traumatic amnesia (PTA) of less than 48 hours. Subjects were contacted via telephone

between 1 and 3 months postinjury. Among these, 88% had returned to work or school

and 16% of those returning to work or school did so with some continuing symptoms.

Felmingham et al. 23 assessed 55 individuals with traumatic brain injury aged 16 and over.

Mean GCS and PTA were 7 and 33.5 days, respectively. Of these, 22% who were employed

at 6 months were unemployed at 24 months. Psychological impairments were reported

as the main reason for unemployment. Of those, 29% who were unemployed at 6 months

were employed at 24 months.

Van Der Naalt et al. 18 reported on 1-year follow-up for 70 people with TBI in the

Netherlands who originally sustained mild to moderate TBI. Mild head injury was

defined as an initial GCS of 13 to 14 and moderate head injury as an initial GCS of 9 to

12 and a duration of PTA of longer than 1 hour. Subjects with PTA longer than 28 days

were excluded. The entire group of subjects returned to work by 1 year postinjury, though

those with more severe injury did so on a more protracted basis over the course of time

from injury to the 1-year postinjury point. Average return to work time for mild head

injury was 2.7 months and for moderate head injury was 4.1 months. This did not

necessarily mean return to full capacity, however. Return to full capacity averaged 5.6

months for the mild head injury group and 7.8 months for the moderate head injury

group. Only 73% had resumed previous work and 84% complained of continuing prob

lems. The prevalence of complaints during follow-up was reported for 1, 3, 6, and 12

months. At 1 year, physical complaints consisted of headache, dizziness, balance disor

ders, tinnitus, hearing loss, drowsiness, and fatigue. Cognitive complaints included for

getfulness, poor concentration, and slowness. Affective complaints included irritability,

reduced tolerance for noise, and anxiety.

Return to work by an individual following TBI can also be complicated by difficulty in

maintaining employment. Studies above note a number of individuals who had returned

to work but did not disclose the nature of difficulties encountered while at work or in

maintaining the vocational placement. Sale et al. 24 followed 29 people with TBI and studied

reasons for job separations. This group experienced 38 individual job separations. The

mean length of employment noted before job separation was 5.8 months, with a range

observed of 0.2 months to 27.6 months. Fully 2 / 3 of all job separations came within the

first 6 months of employment. The most frequently cited reason for job separation was

interpersonal relationship difficulties. These included displays of anger, inappropriate

social interaction, and overfamiliarity. Additional reasons for job separation included

economic layoffs, substance abuse, criminal activity, and mental health problems.

Employment tends to decline over time as a consequence of these problems. Ben-Yishay

et al. 12 found a drop from 64% competitive employment immediately following program

completion to 50% at 3 years postdischarge. A similar decline was noted in noncompetitive

employment placements from 30% at discharge to 22% by year 3.

West 25 reviewed 37 individuals who were placed in supported employment. Only 19

(51%) of these individuals retained their jobs at 6 months. In comparison of those indi

viduals who remained employed to those who lost employment, there was no significant

difference found between the groups with reference to race, marital status, highest edu

cational level achieved, residential situation, community type, cause of injury, injury

severity, work status prior to injury, or work status prior to referral to the supported

employment project. While there was a difference in average age, with the younger group

tending toward employment retention, the difference was not

statistically significant.

Almost all the participants were employed in entry-level unskilled or semiskilled posi

tions. The study reviewed the integration of the individual into the jobsite, workforce

position, and monetary benefits associated with employment. Inequities of the workplace

and opportunities for monetary and nonmonetary benefits were found to be factors in job

retention of supported individuals. Job retention outcomes appeared to be better for those

individuals placed in positions offering fringe benefits, opportunities for raises and

advancement, formal and informal support, and opportunities for socialization.

Wall et al. 26 reviewed 31 clients with TBI and 7 with acquired brain injury (ABI) arising

from CVA (cardiovascular accident) or chronic neurological conditions who participated

in a community-base training program. Injury severity was not provided. Mean time since

injury was 10 years and since diagnosis was 8.91 years. Median number of years of

education was 12.0 and mean prework history was 31.44 months. Fifty-eight percent (58%)

received income from a federally-funded program averaging $439 monthly. Thirty-seven

percent (37%) were working at injury or onset of illness. The average program duration

was 10.54 weeks with 58% completing the program. Those who completed the program

differed only in that they had a longer duration of disability and longer preinjury work

histories. A total of 67% of persons who completed the program retained their job at 60

days and 59% at about 18 months out. Mean starting salary was $5.68 per hour. Approx

imately half of those who did not complete the program reported substance abuse.

As can be seen, difficulties with employment following TBI are a common finding in

both short- and long-term studies. The nature of the neurological injuries sustained,

inadequacies of vocational rehabilitation programming, and shortcomings of medical

rehabilitation programming resulting in failure to provide adequate assistance in recovery

from TBI are questionable factors relating to reemployment difficulties. It is safe to assume

that the neurological injuries sustained impacts the degree to which recovery can be

expected. Comparatively less research has focused on the latter two questions.

Prognosticating Return to Work

Recovery from traumatic brain injury can occur over protracted periods of time. 27–29 As a

consequence, no reliable means of determining exactly when vocational rehabilitation

services should be undertaken exists. Unfortunately, however, injured individuals, fami

lies, and professionals share a common concern for identifying the long-term, perhaps

ultimate, recovery potential following injury. These questions begin very soon after injury

and persist for many months, if not years. Return to work is impacted both by the nature

of the sequelae from the TBI as well as noninjury related factors.

A number of acute measures can aid in predicting return to work potential. An aware

ness of prognostic variables impacting individuals with TBI can help determine the

intensity and type of vocational rehabilitation services to be delivered. 30 Gonser 21 reviewed

both cognitive and physical disabilities as prognostic factors in vocational return and

suggested that neuropsychological impairment was the single most important factor in

the prognostication of the vocational return. Ruff et al. 31 also found neuropsychological

function to be important in return to work. They reviewed predictors of outcome follow

ing severe head injury and found age, WAIS-R vocabulary score, and selective attention

speed combined to correctly classify 88% of subjects in a category of either productive or

nonproductive.

Age at injury has been well documented as a prognostic variable in return to work. 23,30-34

Most studies support the idea that a direct correlation exists between age and return to

work. 23,30-34 Individuals who are younger at the time of injury are more likely to progress

to return to work than individuals who are older. 30 Preinjury employment status and

educational level have been demonstrated to be strong predictors of return to work. 30 That

is to say, individuals who were employed at the time of injury and individuals with higher

educational achievement were more likely to return to work than individuals who were

unemployed at the time of injury, had poor employment history, or had lesser educational

achievement. Keyser-Marcus et al. 30 found individuals who were employed at the time of

injury were three to five times more likely to be employed postinjury. A partial explanation

for this finding may be that, following brain injury, information that was well learned at

the time of injury is more readily called upon by the individual, in contrast to information

that must be acquired following injury and reliance upon new learning skills. This can be

of great assistance in returning an individual to work, in particular, in instances where

the work to be performed by the individual relies upon old information and has little

demand for new learning. As such, rote tasks will be largely more successful in return to

work scenarios than those tasks that require a high dependence on new learning. Con

versely, some positions require much greater reliance on new information processing and

will not benefit from dependence upon rote tasks. 35

Keyser-Marcus et al. 30 also reported that rehabilitation length of stay (LOS) predicted

return to work at 1 year postinjury. Shorter LOS was associated with return to work. While

it might be argued that LOS is an indirect measure of injury severity, more direct measures

of injury severity, such as Glasgow Coma Scale (GCS) score and duration of posttraumatic

amnesia (PTA), were not predictive of return to work. These findings support those of

Gollaher et al. 14 and Ip et al. 15 The GCS has not been found to be highly predictive of

outcome, in particular, for those individuals who are in the moderate range of severity of

injury. 36 The utility of posttraumatic amnesia for long-term functional prediction has also

been questioned. 37 Gollaher et al. 14 utilized a functional outcome measure, the Disability

Rating Scale (DRS), 38 which is based upon the GCS, but further discriminates higher

functional levels. Educational level, admission DRS, discharge DRS, and preinjury pro

ductivity allowed correct classification of 84% for employed subjects, 66% for unemployed

subjects, and 75% across both groups.

Coma duration has been documented as a prognostic variable for overall outcome

following TBI and for return to work. Shorter coma durations are associated with greater

likelihood of return to work. Similarly, duration of PTA has been correlated to return to

work, 39 as has duration of acute rehabilitation treatment. 30,40 Again, in both instances,

shorter periods are associated with a greater likelihood of return to work. Rao et al. 19 noted

that fewer positive findings on CT scan correlated with return to work.

The relationship between severity of injury and the vocational outcome is not linear. 41

Generally speaking, when impairment level at 24 hours postinjury is related to produc

tivity at follow-up, a relationship is noted that more severe impairment leads to less

productivity. Some notable exceptions exist, however, in that some individuals who are

severely impaired at 24 hours postinjury achieve good outcomes while comparatively less

severely impaired individuals suffer poorer outcomes. In a study by Sherer et al., 42 initial

severity of injury did not significantly predict postinjury productivity. Individuals in their

sample ranged from mild to severe traumatic brain injuries and all were involved in

postacute rehabilitation programs. Education level, preinjury substance abuse, need for

behavioral supervision, and need for physical supervision all correlated with productivity

status. Interestingly, when adjusting for the effects of all other predictors, preinjury sub

stance abuse emerged as the only significant predictor of productivity. Substance abuse

has emerged as a predictor in several other studies as well. 24,42–44 Sherer et al. cited possible

selection bias in the study compared to other studies where severity of injury was found

to be indicative of return to work. The fact remains, however, that many moderately to

severely injured individuals were found to be unable to successfully return to work when

evaluated some 2 years postinjury. 45 Felmingham et al. 23 agreed that severity of injury

impacted outcome, but only when paired with age.

The addition of variables identified following acute rehabilitation to prediction of the

return to work can enhance prognostic predictability. Felmingham et al. 23 found that adding

postdischarge predictors to acute variables improved the ability to predict work status 2

years after rehabilitation, particularly regarding psychological well-being. Those noted to

have better adjustment tended to perform better in the work force. In a similar vein, some

have noted that individuals who have difficulty with awareness and acceptance of deficits

associated with traumatic brain injury are less likely to experience vocational success. 46

Felmingham et al. concluded that severity of injury (only when paired with age), age at

the time of injury, premorbid employment status or work status at 6 months postinjury,

and level of psychological distress 6 months postdischarge from a rehabilitation hospital

setting were significant predictors of return to work. Rao and Kilgore 43 developed a regres

sion equation that predicted return to work with 73.5 to 84.4% accuracy. Social factors such

as substance abuse, family and community supports, and financial need to return to work

were factors in cases where inaccurate prediction of return to work status occurred.

The research literature implicates age, severity of injury, coma duration, duration of

acute rehabilitation, duration of posttraumatic amnesia, postacute adjustment, awareness

and acceptance of deficits, substance abuse, premorbid work status, educational attain

ment, and functional status in the prognostication of return to work. It is clear that no

single variable has predictive power sufficient to be used independently of the others.

Many of the above variables essentially implicate the overall severity of injury, though

not all. There are, nonetheless, notable exceptions in instances where persons with less

severe injuries face difficulty in return to work, and when psychosocial circumstances or

issues such as substance abuse and family and community supports, or financial need to

return to work, intervene.

Industry-Related Factors Influencing Return to Work

Traumatically brain-injured individuals may not be familiar with vocational rehabilitation

services, and vice versa. In a survey of 620 traumatically brain-injured individuals who

were 1 year postinjury, only 34% were aware of the existence of vocational rehabilitation

services. 11 Those involved in outpatient or postacute rehabilitation and those who were

employed preinjury were more likely to be aware of available services.

Ironically, vocational rehabilitation counselors appear to be similarly unaware of the

needs of people with TBI. Hallauer et al. 4 found substantial inexperience with TBI for

most vocational rehabilitation counselors. Most counselors surveyed had work experience

with fewer than ten TBI clients. Counselors tended to overattribute problems in memory

dysfunction, even in the absence of supportive test findings. In a survey that involved the

New York State Office of Vocational Rehabilitation, 5 the vocational rehabilitation program

success for 47 individuals with TBI was reviewed. Only 8.5% of the individuals who

received services were ultimately placed in jobs. The vocational rehabilitation counselors,

as a group, reported factual unawareness for the need for cognitive remedial services for

this population. These professionals were keenly aware that they did not have specific

programs developed to address the needs of the individual with TBI. The need to bring

vocational rehabilitation counselors and medical rehabilitation teams together has been

suggested by a number of authors. 47–49 Each of these groups points to substantial benefit

to be achieved by coordination of all parties in an interdisciplinary fashion. The knowledge

base of the vocational rehabilitation counselor can be materially increased in this manner. 49

An additional mismatch can be found between the perceptions of vocational rehabilitation

counselors and employers. 50 Employers' primary concerns had to do with whether the

individual could actually fulfill the job responsibilities. Concerns of vocational rehabilita

tion counselors, however, tended to focus on workplace accommodations. Lastly, one

study indicated failed vocational rehabilitation programs tended to be too short in dura

tion or too long postinjury to be effective. 51

Lack of availability of rehabilitation services, division of responsibility for rehabilitation

between several governmental and private sector agencies, economical decline, employer's

fitness requirements, disability discrimination, delayed or ineffectual management of treat

able diseases and conditions, and disability compensation benefits can all contribute to

failure to return to work. 52–58 Numerous articles have suggested the potential contribution

of compensation in failure to return to work in the general population. 7,55–58 While care

must be taken in interpretation of these ideas, there are clearly some discrepancies in return

to work that are difficult to explain, namely those found in return to work of people with

mild to moderate TBI. There are differences in return to work rates for those people

receiving disability and social security benefits and those who do not 55,57 and some find

vocational rehabilitation to be a potentially destabilizing threat to their financial status. 56

In summary, at the point of involvement of vocational rehabilitation, the individual with

TBI may, or may not, have participated in medical rehabilitation. Participation in medical

rehabilitation cannot be guaranteed, especially for those individuals who might be referred

to Departments of Vocational Rehabilitation without adequate documentation of the pre

vious TBI. Once involved in the vocational rehabilitation process, placement may not be

achieved or maintained due to (1) inadequate resolution of sequelae of the TBI, (2) aware

ness by individuals with TBI, their families, medical rehabilitation professionals, or voca

tional rehabilitation professionals of the need for vocational rehabilitation services, (3)

knowledge on the vocational rehabilitation counselor's part as to how to pursue job

placement for individuals with TBI, (4) failure of the job placement to meet the esteem

and financial needs of the injured worker, (5) socially inappropriate or unacceptable

behaviors, (6) a mismatch between the focus of the vocational rehabilitation counselor and

the needs of the employer, (7) financial disincentives to return to work, or (8) a societal

predisposition toward continued unemployment due to divergent agency goals or insuf

ficient public expenditures to support return to work efforts. This list is by no means

exhaustive or complete and, as such, points to the tremendous complexity of returning

an individual with TBI to work.

Vocational Rehabilitation Prerequisites

Readiness for vocational rehabilitation, of course, involves resolution of deficits following

traumatic brain injury — and more. In many jurisdictions, state legislatures have enacted

rules that must be followed, in particular, when individuals are injured in the course of

their employment. The vocational rehabilitation counselor and, in some instances, medical

rehabilitation providers should be familiar with reporting requirements and be able to

comply with the various filings that may be required.

Ideally, the vocational rehabilitation process begins

during the medical rehabilitation of

individuals with traumatic brain injury. The vocational rehabilitation counselor should be

familiar with the goals and plans of the medical rehabilitation team from an early point

in the rehabilitation process. Likewise, the medical rehabilitation team can obtain insight

from the vocational rehabilitation counselor into the injured individual's personality, social

status, educational attainment, socialization skills, and vocational aptitudes, all of which

may bear upon medical rehabilitation goal setting. Rehabilitation teams often focus on

"functional" capabilities, and achievement of a "functional" level of independence may

not be sufficient to allow successful return to work.

An early review of an individual's deficits may allow a vocational rehabilitation coun

selor timely recognition of those barriers to return to work which are likely to be overcome

and those which are less likely. In instances where the individual is unlikely to return to

a previous vocational setting, introduction of this idea to the injured individual and the

family may allow for professional assistance with adjustment and better financial planning

for the family. Adjustment to disability can be quite difficult and some people with TBI

are reluctant to accept that their level of functioning may not be sufficient to allow a return

to a previous level of employment. 23,46,59 Often, clients are unwilling to shift their expec

tations for return to work and can be resistant to

rehabilitation plans that move in a

direction other than return to previous employment. Medical rehabilitation providers can

be quite helpful in assisting with adjustment issues and creatively addressing barriers to

employment or development of vocational alternatives. The interplay between the voca

tional and medical rehabilitation professionals with the individual and his/her family can

best ensure that the highest level of independence and life satisfaction is respected during

goal setting.

The vocational rehabilitation counselor can work with medical rehabilitation profession

als to conduct prevocational testing. Prevocational testing can be invaluable in identifying

barriers to return to work for all parties. A host of standardized and subjective assessments

can be utilized in this pursuit and detailed information can be obtained which spells out

deficits that will impact return to work. The allied health disciplines of occupational

therapy, physical therapy, speech therapy, therapeutic recreation, educational therapy,

clinical psychology, and neuropsychology can also provide insight into likely problem

areas. Situational assessment to confirm test findings should be considered in this assess

ment. 60 Additionally, a review of a thorough job description, together with functional

observation and the comprehensive interview, should accompany neuropsychological

evaluation as the VRC (vocational rehabilitation counselor)

attempts to discern vocational

readiness and aptitude. 32 Care must be taken in evaluating people with traumatic brain

injury to avoid an overreliance on standardized testing. One study suggested that 38% of

vocational rehabilitation counselors surveyed relied, either moderately or very heavily,

on standardized testing. 5 A learning-style evaluation during prevocational testing may be

helpful in determining optimal and nonoptimal strategy development for presentation of

new learning. 32,61 To that end, the degree to which an intended vocational placement relies

upon rote activities vs. new learning should be considered.

Injury-Related Factors Influencing Return to Work

Introduction of vocational rehabilitation services typically occurs at a time determined by

medical rehabilitation professionals. While, on the surface, this may seem logical, the

approach is problematic in those instances where well-meaning, though poorly informed,

professionals believe that the medical rehabilitation has, in fact, resulted in a readiness

for vocational rehabilitation. Unfortunately, all too often, this is not the case and individ

uals with TBI are prematurely returned to work and subjected unnecessarily to failure.

The typical approach taken in vocational rehabilitation is to attempt to achieve medical

stability prior to undertaking vocational rehabilitation services. Recovery from traumatic

brain injury, however, seldom finds an individual at a point at which a clear demarcation

exists between the end of medical treatment and readiness for vocational rehabilitation.

The complexity of deficits seen following traumatic brain injury complicates the delinea

tion of the starting point for vocational rehabilitation.

The constellation of deficits seen following traumatic brain injury can include motor,

cognitive, communicative, psychosocial, psychological, and behavioral impairments. 3,62

Some of these deficits will persist in some fashion despite the best efforts at medical

rehabilitation. Of course, severity of injury may impact both the number of deficits and

their persistence, though there is not, necessarily, a direct relationship between severity

of injury and likelihood of return to work. 23,30,43

Cognitive deficits, physical deficits, and personality changes have been cited as contrib

utory to failure to return to work. 3,16,20,63–65 Greenspan et al. 10 indicated that motor and

cognitive impairments related to TBI significantly contributed to failure to return to work

after 1 year. McMordie et al., 20 who included learning, motor, and ambulation impairments,

support Greenspan’s findings. Leblanc, Hayden, and Paulman 60 agreed that cognitive

dysfunction played a major role in return to work among people with brain injury.

Physical Deficits

Given the shortened time frames in rehabilitation of people with TBI, 66–68 therapists are

forced to focus on functional capabilities for performance

of activities of daily living as a

primary goal. Rarely will goals beyond these be a consideration early in the rehabilitation

of a person with TBI, largely due to funding and utilization review constraints. Though

the world has become much more “accessible” for people with physical disabilities, opti

mization of physical functioning following TBI via extended therapy can be quite impor

tant in returning to work. Wehman et al. 34 discerned that an individual's level of functional

limitations impacted the likelihood of return to work. Just as physical and cognitive

limitations would impair functional capabilities with reference to activities of daily living,

these limitations appeared to ultimately culminate in difficulties in return to work as well.

Physical limitations can bring about significant challenge to self-concept, body image, and

social interactions, all of which are likely to impact return to work. 69 The VRC is in a

unique position to advocate for such additional interventions.

The VRC must consider mobility, balance, coordination, vestibular function, extremity

strength and range of motion, muscular and cardiorespiratory endurance, dexterity, vision,

audition, and smell. The individual must be able to move about the workplace freely and

safely. The highest level of ambulation with the least reliance upon aids should be sought.

Canes, walkers, and wheelchairs, though designed to enhance environmental access, unfor

tunately, may contribute to workplace biases about an individual’s inherent abilities. More

pragmatically, such devices can raise questions in an employer’s mind regarding safety.

Balance, coordination, and vestibular function must be such that the person is not

experiencing dizziness that could impede the ability to move about the workplace or

complete various job tasks. 70 Of course, such impairments may preclude return to certain

jobs, such as those that require climbing ladders or working at height. Physical therapy

and medical treatment can be quite beneficial in improving functional capacity for balance

disorders following TBI and can improve protective reactions. Care should be taken to

avoid reliance solely upon medications that reduce the experience of dizziness as these

medications act only to reduce the symptoms rather than improve the underlying condi

tion. Consequently, impaired protective reactions continue to be present, thereby increas

ing the likelihood of reinjury. Information about vestibular dysfunction can be found in

Chapter 5.

Perceptual deficits in either vision or hearing can also impact successful job task com

pletion, socialization, communication, and safety. (See Chapter 6 and Chapter 7 on vision

and Chapter 8 on audiology.) In some workplaces, the sense of smell is important to safety,

such as in working with combustible liquids or gases, and may be integral to actual job

task completion, for example, in food preparation or storage responsibilities.

Muscular and cardiorespiratory endurance will materially impact job performance and

mental acuity. Fatigue is a frequently reported component of TBI impairment. 3 Decondi

tioning following prolonged disability is common and should be assessed and addressed

prior to return to work. Most jobs require a fairly high level of manual dexterity. As such,

dexterity must be considered, as well as adaptations that may be appropriate to a specific

job description. (Further detailed information about treatment of physical deficits can be

found in Chapter 15.)

Psychological and Behavioral Issues

TBI can cause significant disruption of function in the psychological/psychiatric realm,

resulting in deficits in interpersonal, social, and occupational function. 71 Thorough reha

bilitation for people with TBI may include psychiatric, psychological, and neuropsycho

logical evaluation and interventions. Personality and neuropsychological testing that

utilizes input from the client, family, friends, and coworkers will provide the greatest level

of understanding for all rehabilitation professionals involved. Care should be taken, how

ever, to avoid overreliance on neuropsychological test results for the determination of

vocational aptitude or readiness. 60,72 Neuropsychological findings are best used in con

junction with observation of function in real-world

settings. It is not uncommon following

TBI to need to provide psychological interventions for awareness of, and adjustment to

disability, 73–75 motivation, sexuality, stress management, fear, interpersonal relationship

management, depression, 76,77 substance abuse, 76 lifestyle changes, irritability and loss of

temper, 3 family issues, parenting, 78 coping style, 79 spousal relationships, 80 anxiety, 76 and

goal setting. The VRC may play a role in many of these areas, either in providing some

of the counseling or provision of insight into some of these areas to other psychology staff.

Evaluative tools, such as the Minnesota Multiphasic Personality Inventory II, 81 the Tay

lor–Johnson Temperament Analysis, 82 the Fundamental Interpersonal Relations Orienta

tion–Behavior Scale, 83 and the Beck Depression Scale, 84 can be useful in understanding

variables that may be barriers to return to work. Care should be taken in interpretation of

the MMPI–II as deficits following TBI can, fairly predictably, elevate specific scales such

as depression, hypochondriasis/somatization, schizophrenia, and psychosis. 85 Some have

suggested that scoring of the MMPI for this population should be altered for this reason. 86–88

The tool can be useful, nonetheless, in a careful consideration of its findings coupled with

information from the clinical observations of allied health professionals and family.

TBI is overwhelming in its impact upon the individual and coping with the seemingly

total change in one’s abilities and lifestyle is arduous and grueling. Adaptation to such

profound changes in one’s life can take a lifetime, yet rehabilitation demands such accom

modation in months. The VRC should have sufficient background to be able to identify

when phases of the vocational rehabilitation process will be too challenging or likely to

elicit maladaptive responses or adjustment opportunities. For example, a person placed

in an employment position by a VRC who knows the placement will fail may yield either

an improved awareness of remaining areas of deficit to be worked on in therapy or a

humiliation that strips the individual of all motivation. The difference between these two

outcomes should be predicted by the VRC who is aware of the psychological status of the

injured worker. Prevocational counseling allows for such insight to be gained by the VRC.

The VRC may be in a position to recommend the involvement of a counselor or psychol

ogist for rigorous investigation and treatment of issues pertaining to attitudes toward

return to work, motivation, adjustment to disability, and so on. Given the pervasive and

all encompassing nature the impact of TBI has on one’s life, all but the rarest of individuals

will benefit from some assistance in handling the psychological burden.

Participation in therapy following TBI is difficult and some people suffer from motiva

tional challenges to continue therapeutic endeavors. The appropriately designed voca

tional rehabilitation plan can be helpful to some in coming to an understanding of why

seemingly useless therapy tasks will benefit them when they return to work. Conversely,

while the proper timing of return to work has been emphasized, there are some instances

where motivation to complete therapy tasks and goals can be enhanced by engaging the

person in some part-time, perhaps lower level, return to work that is meaningfully asso

ciated with or drawn from their intended final vocational placement. Participation in the

workplace exercises, in effect, all the skills that are the focus of therapeutic endeavors.

Such placements, conducted coincidentally with therapy, can allow the individual to

gradually realize limitations and the relationship between those limitations, successful

completion of therapy tasks to address those limitations, and success in the workplace.

The individual’s financial needs and status must be well understood prior to undertak

ing vocational rehabilitation. 54–58 This includes a review of all sources of income, including

income that may derive from pending legal proceedings. The individual’s financial well

being should be considered, together with the benefits that come from independence and

self-reliance. An ethical quagmire can readily emerge in these considerations and the VRC

should be well-versed in both legal requirements that may impact vocational planning

and ethical issues that ought to guide the VRC’s approach

to a case. An excellent review

of ethical issues can be found in Chapter 23.

Motivational concerns that may present as challenges to a successful vocational plan

can arise from both questionable and legitimate issues. Since job separations are common

following TBI, and return to work occurs for only a portion of those injured, care must

be taken not to jeopardize availability of financial support from such sources as Social

Security, disability insurance policies, or permanent disability payments from workers'

compensation claims. Ashley et al. 89 conducted a follow-up study of 332 people with TBI

who averaged 7.1 years postinjury and 5.3 years postdischarge. The group was heavily

biased in that all participants had access to treatment funding from workers' compensa

tion, accident and health, or liability insurance coverage. The study showed that only

83.9% of respondents reported they were financially "getting by or better." The estimated

mean of monthly income loss per family was $1,058.00, while the mean household earnings

was decreased by about $402.00, suggesting that others in the family had become

employed or changed employment to higher paying positions.

TBI regularly places families below the median income level and often into poverty

levels. In the study by Ashley et al., 89 16.1% of respondents reported increased indebted

ness and 7.4% required public assistance for medical costs. These numbers can be reason

ably assumed to be much higher for the TBI population in general.

Income stability can become an issue in the case of people who were employed in

seasonal positions. Those people who are covered by workers' compensation may acquire

a more stable income source following injury. In some cases, prolonged medical disability

translates to prolonged maintenance of immigration status. In still others, psychological

benefits accrue from being dependent upon a spouse or parent or, conversely, spouses or

other family members may derive some psychological or financial benefit from continued

levels of dependency, such as when family members are paid for care of an injured person.

Cognitive Deficits

Cognitive rehabilitation following TBI represents one of the greatest challenges facing

allied health professionals and people with TBI. Cognitive function cuts across all aspects

of daily living, social interaction, psychological function and adjustment, communication,

and, of course, work. Rehabilitative efforts in cognition can be both compensatory and

remediative. 90–92 Rehabilitation of cognitive function requires medical stability and a great

deal of therapeutic effort. The most successful cognitive rehabilitation takes place over

months, rather than weeks. Compensatory strategies may be developed, in some instances,

to support the injured worker in job performance; however, some levels of cognitive

dysfunction are less amenable to compensatory approaches. A realistic appraisal of the

likelihood of success is crucial.

Cognitive deficits, such as problems with attention, concentration, persistence, problem

solving, judgment, reasoning, memory, and self-regulation of behavior will all detrimen

tally affect the injured worker’s ability to perform on the job. Such deficits can be present

in people without any obvious physical impairments and can be camouflaged by intact

expressive language skills. Bjerke 93 found a lack of correspondence between neuropsy

chological tests results and levels of reported memory function for people with TBI.

Severity of injury did not correspond linearly to reported memory function. The VRC

must carefully investigate the allied health professionals’ assessment and documentation

of cognitive skills and determine the degree to which they will impact job performance.

Various jobs have different cognitive demands; for example, the cognitive requirements

for professional and technical positions are greater and will require more attention to

higher-level cognitive function. 35

A primary indicator of success may be found in the individual’s attention skills. The

person must be able to maintain a focus of attention without undue interference or loss

of information (vigilance). They must also be able to shift attention readily between two

or more activities and do so efficiently without undue delay or loss of information or

accuracy (cognitive shift). Melamed 94 found that attentional capacity for shifting between

dual task performance correlated with likelihood of return to work.

Many other aspects of cognitive dysfunction will impact job performance. Return to

work may be most successful in cases where job performance relies heavily upon

previously learned information and skills and where physical impairments are relatively

minor or can be minimized by adaptation of the workplace. Job performance that relies

heavily upon new learning or rapid information assimilation will pose far greater chal

lenges to the person with cognitive deficits following TBI. Planning disorders can also

manifest following TBI 95 with obvious detriment to vocational endeavors. The end product

of job performance may not be immediately apparent in many vocations where the work

of an individual contributes to a large process and delayed production or emergence of

a work product. In these instances, deficits in discriminating response-consequence

relations 96 may impact an injured person’s understanding of the impact of a failure to

properly execute his/her job responsibilities or his/her ability to identify social cues within

the workplace. (Further detail regarding cognitive function and rehabilitation can be found

in Chapter 12 and Chapter 13.)

Communicative Deficits

Some of the more common communicative deficits seen following TBI include oral dys

arthria, 97–99 impairments of voice production and volume, 100–104 impairments of the pro

sodic features of speech, 105 impairments in auditory processing speed and accuracy, 106 and

impairments in communicative pragmatics. 107–110

Oral dysarthria presents with a slurred, thickened speech and can imbue the speaker

with unflattering attributes to the uninformed listener. The speaker can appear to be under

the influence of alcohol or drugs or can appear less intelligent than is truly the case. Since

understanding dysarthric speech requires much more time and effort on the part of the

listener, communication on the job may be diminished to unacceptable levels. Couple this

with the logical impact on socialization and a formula for isolation is present. A negative

spiral beginning with difficult communication can progress to a reluctance to engage in

appropriate clarification of details for a job task, reluctance in allocation of job tasks to

the injured worker, frustration for the injured worker and supervisor at task failure, and

arrival at a conclusion that the injured worker cannot complete the necessary job tasks to

maintain employment.

Likewise, other communicative deficits can bring about deterioration of communicative

events within a workplace. Inability to engage in communicative pragmatics such as

appropriate conversational turn-taking or maintenance of the topic of conversation among

a group of coworkers will discourage others from approaching and engaging the injured

worker in either job-related or social discourse. People with TBI often have difficulty

getting the point from figurative or metaphoric expressions, knowing the alternate mean

ings of ambiguous words, deriving inference, conveying the communicative intent of a

speaker to another, and resolution of communicative ambiguity. 111 They will often produce

speech that is shorter in length, less complex, and with less cohesion than people without

TBI. 112 These tendencies will complicate communication on the job and require attention

prior to and after return to work. Understanding the communicative intent of a speaker

is heavily dependent upon interpretation of the prosodic nature of the communicative act

and accompanying cues can be found in facial expression and body language. Failure to

detect the facial and body language expressions of coworkers or employers often manifests

as failure to identify and respect social boundaries. This can have devastating impact on

communication and interpersonal relationships. Ability to perceive and remember facial

expression has been demonstrated to be impaired in some people with TBI. 113,114

Any communicative disorder must be considered for the potential to bring about effects

upon the workplace as described above. Disorders of

prosody, such as speaking with a

monotone voice or speaking too loudly or softly, can cause tremendous confusion of the

communicative intent. A person who speaks in a monotone voice can appear disinterested

or unmotivated. Speaking too loudly may make it difficult for coworkers or employers to

have confidence that the injured worker can handle sensitive issues in an appropriately

discreet fashion. The speaker may be confused to be angry or upset when speaking too

loudly. Dysfluency or stuttering sometimes occurs following TBI. 115,116 The general public

historically misunderstands the dysfluent person, thinking them shy, unconfident, or

difficult to listen to. Often the dysfluent person is reluctant to speak because of the effort

required and the embarrassment experienced.

The VRC may be able to impact the workplace by education of the nature of a particular

communicative disorder, by adaptation of the workplace, or by encouraging continued

remedial therapeutic efforts. Hearing problems may be addressed by medical intervention,

amplification, environmental noise reduction, or written communication. In some

instances, sign language may be used to some degree. Visual or language deficits may

preclude reliance upon written communication, however. As such, graphic skills must also

be evaluated for both their potential as a means of expressive communication and as a job

requirement for task documentation or interoffice

communication. Dexterity may impact

the person’s ability to write legibly or to use a keyboard for electronic communication.

Socialization Issues

As has been stated earlier, the primary reasons for job separation from the first and second

employment opportunities are related to interpersonal skills. Maintenance of personal

boundaries can be difficult for the person with TBI. This includes respecting personal

space, identifying body language which signals continued or waning interest in a conver

sational topic, respecting overt requests for changes in topic or cessation of a discussion,

engaging in appropriate social pleasantries, respecting professional relationships and

avoiding overly familiar behaviors, proper usage of manners, control of emotional lability,

and impulse control.

Social skills are acquired over a lifetime and are continuously updated. Social judgment

is crucial in the workplace as it represents a primary source of socialization for most

people. Social skills used on the job are considerably different than those used in the home

environment and there is a clear demarcation of expectations between these two environ

ments. TBI often impairs a person’s ability to pick up on social cues such as body language,

facial expression, and subtle linguistic cues that may be given. Failure to identify these

cues will readily result in social isolation and failure which obviously will impact both

the injured person’s ability to complete job tasks successfully and his/her derivation of

personal satisfaction and self-esteem from the workplace.

Differences in level of socialization have been identified with different types of sup

ported employment environment. 117 Individual, enclave, and work crew supported

employment environments were analyzed for the amount of contact between disabled

and nondisabled workers. Individual and enclave environments showed substantially

more interaction between coworkers than work crew environments. Individual and

enclave environments might be more conducive to social integration, a key component in

job retention and life satisfaction.

Return to Work Models

Several models for return to work after TBI evolved in the 1980s. These included the

cognitive remediation model, 75 the work hardening model, 118 and the supported employment

model. 119 Of these models, the most efficacious model appeared to be the supported

employment model. In the supported employment model, “job coaches” are assigned to

individuals to work alongside the injured worker in the workplace. Their primary func

tion is to teach the job, monitor performance, and provide feedback for the individual

and other rehabilitation professionals as to job completion and quality. 120,121 Compensa

tory strategies may be implemented on the job as identified

and designed by the job

coach. West et al. 121 describes the role of job coach as having an advocacy component

and an active role in job retention by provision of assessment of social skills and produc

tivity. These authors and others 35 suggest that job coaching be both intensive and of

sufficient duration so as to properly ensure both return to work and job retention.

Wehman et al. 122 reported that an average of 291 hours of job coaching was used to secure

and maintain job placement in a population of people with TBI who averaged 7 years

postinjury and 53 days of unconsciousness. Haffey and Abrams 123 reported a mean of

only 85 hours per client for job coaching; however, their population was much closer to

date of injury.

Utilization of job coaching, however, is not without its disadvantages. The injured

worker can be stigmatized by the presence of the job coach. It may be difficult to transition

the job coach out of the work environment. Lastly, the job coach may impact the manner

in which other employees behave and interact with the injured worker. 124 Consequently,

it may be advisable to look for opportunities to use coworkers in a supportive role with

the injured worker, though care must be taken to properly time the transition from a job

coach to a coworker when the relative workload warrants such a change.

Some authors suggest that supported employment may not be

the most efficient model

for successful vocational rehabilitation of people with TBI. 125 Models involving job coaches

can be costly, reportedly $9,000 to $10,000, 126 and, consequently, such services may not be

made available to people with less financial support for recovery. As a consequence, less

expensive models have been used with the TBI population. These models include the

clubhouse model, 127 community-based training model, 26 and the empowerment model. 125

- Clubhouse model uses community-based training and natural supports. “Clubhouses” are “work units” that provide various work samples for clients to identify their particular interests and relative strengths. Support, training, and employment opportunities drive this model. An estimated 18 to 23% of those involved in the clubhouse model ultimately participate in competitive employment. 127

- Community-based training model incorporates supported employment and work adjustment training to address economical disadvantages, job retention, and identification of meaningful and satisfying employment. This 16-week program allows for equal input from the client, program staff, and training/work site with a return to work plan developed. Clients obtain work skills in an unpaid work setting. When the employment opportunity begins, the job coach is introduced to assist the client during transition into competitive employment by providing suggestions for work modifications, assistive devices, and strategies for improved work performance. 26 Community-based training models greatly challenge strategy development and enhance the opportunity for generalized work skills. 26

- Empowerment model was designed to consist of several elements sequentially performed to include intake of personal information, vocational evaluation, work samples, work hardening, vocational counseling, job skills training, development of job skills, job training placement, and counseling for continued support. 125 Abrams et al. 125 followed 106 people involved with this type of vocational rehabilitation. Within 1 year, 92% were employed and 24% returned to the previous employment. The authors emphasized coordination of services based on individual need rather

than mandatory programmatic requirements for clients with TBI.

In summary, models of vocational rehabilitation currently in use for people with TBI

achieve the best outcomes when they consider the unique challenges of this population

and utilize integrative approaches over appropriate time durations and with appropriate

supports. As these models become more widely implemented, it will be possible to conduct

research to determine whether the programs are less expensive and involve more clients

in the vocational rehabilitation system and which approaches yield the best outcomes for

subgroups of the TBI population.

Formalized Vocational Rehabilitation in TBI

Prevocational Counseling

Prevocational counseling is a process whereby the client's readiness to return to work

becomes an active focus of treatment. The client's readiness and expectations must be

reviewed and, perhaps, adjusted. Adjustment to disability can stand as a significant barrier

to return to work, especially in instances where the individual may not be able to return

to preinjury employment. It may be necessary to return to a lesser position within an

employment setting, a part-time position, or a different position and employer altogether.

For some, return to competitive employment may be questionable and only obtainable

after an extended period of work hardening. Finally, some individuals may be unable to

return to work in any capacity or may have sheltered work placement as a long-term

outcome. Given the degree to which work impacts self-esteem and self-concept, 69 changes

in work status following injury can have tremendous impact upon the individual, his/

her family, and his/her social interaction.

In the prevocational counseling process, information is collected regarding historical

matters such as level of educational attainment and achievement. Previous work positions,

employers, pay scales, and relevant vocational information are collected. It can be helpful

to determine the nature of positions that exist with the employer of injury as well as

contacts that family and friends may have. Previous employers can be helpful in return

to work, especially in instances where the person was well regarded. As historical infor

mation is collected and considered, it must be combined with information of known or

anticipated limitations which may arise due to physical, cognitive, behavioral, psycholog

ical, social, communicative, or emotional factors. For example, an individual with an

extensive roofing installation background who has vestibular and visual deficits is unlikely

to return to roofing installation. However, the person’s extensive knowledge base may

facilitate work in the roofing field as an estimator, sales person, or supervisor.

Vocational Rehabilitation Plan Development

The vocational plan begins during the prevocational counseling process as the counselor

attempts to piece together options for the various phases of return to work that may be

necessary for the client. Requisite phases will vary from client to client and injury to injury.

In many instances, development of a formal vocational rehabilitation plan will be

required for submission to workers' compensation agencies for approval. In others, the

formal vocational rehabilitation plan and all the attendant filing of forms may not be

needed. Nonetheless, the formal vocational rehabilitation plan is integral to the process

of returning an injured worker to work. Plans developed for different individuals should

vary considerably in the amount of time needed, the cost, and the process owing to the

tremendous individuality of each person with TBI. The plan must be developed in con

gruence with the interests, goals, aptitudes, and abilities of the injured worker, as well as

consideration of the labor market and job availability.

Ninomiya et al. 128 developed a list of issues that should be considered during the

development of a rehabilitation plan. These items are:

- Actual vs. stated motivation for the client's return to work
- The client's cognitive abilities
- The client's emotional profile
- Physical deficits and limitations
- Family support and interactions

- Financial gain/need
- Litigation
- Self-esteem and self-concept
- Work ethic
- Work history
- Preinjury work characteristics
- Current and preinjury personality factors
- Adjustment to disability
- Transferable skills
- Age
- The general employment index in geographical area of the intended discharge
- Employer prejudices regarding brain injury and other disabilities
- General medical stability
- The presence or absence of a seizure disorder or other neurological deficits
- Potential areas of conflict arising from various secondary gain issues

Vocational outcomes are traditionally classified into seven categories. The outcomes

include return to work, modified work, alternative work, direct placement, on-the-job training,

formalized schooling or training, and self-employment. The order listed suggests a hierarchy

of desirability. The return to work outcome is achieved when the injured worker returns

to his former employment, in the same position, the same number of hours, and the same

workplace. A modified work outcome consists of a return to the former employer, though

modifications have been made to the work process or work station to accommodate for

physical, cognitive, or other limitations. An alternative work placement also occurs with

the former employer, though the injured worker is placed in a different position altogether.

The new position may have been identified via transferable skills analysis and is consistent

with any limitations. Direct placement consists of a new position with a new employer or

a similar position to the position of preinjury employment, again using transferable skills.

On-the-job training occurs with a new position and a new employer. The employer provides

a training environment and some or all of the training. Responsibility for compensation

can be shared between employer and a workers' compensation carrier. Continuation of

insurance or employer benefits may continue until a successful long-term placement is

assured. Formalized schooling or training plans involve enrollment in a vocational or aca

demic schooling setting for the purpose of achieving vocational placement upon comple

tion. The self-employment outcome is used when the plan is to establish a new, independent

business that the injured worker will operate. Each of these plans assumes a competitive

employment outcome. Occasionally, during execution of a plan, the VRC and injured

worker may determine that the plan is not going to be successful. They may opt to modify

the rehabilitation plan and establish a different outcome as the goal of the new plan.

The VRC will need to explore creative vocational options with the client, the employer,

and family and friends, as well as medical rehabilitation providers. The process can require

great diplomacy and careful planning. While many employers are eager to be helpful in

returning an individual to work, there may be other circumstances where the employer

is less willing. The individual may have had a poor work record or may have been injured

shortly after hiring. He/she may have been difficult to get along with. The employer may

be fearful of reinjury or customer reaction to the injured worker. Some employers are

angry with injured workers for either the damage done to themselves or others, or for the

financial losses incurred. On the other hand, employers can be unrealistically optimistic

about the person’s recovery and, in their efforts to be supportive and encouraging, promote

a return to work that is neither likely nor reasonable.

Care must be taken to avoid premature return to work or return to work that is ill-suited

to the person’s skills. A well-meaning family, employer, medical rehabilitation provider,

or client can bring about a return to work that is doomed to failure due to poor matching

of the job requirements and the person’s residual and recovered skills. Vocational failure

brings about embarrassment, humiliation, disappointment, and withdrawal of support.

The employer of injury may represent an excellent final job placement, but a poor initial

work hardening placement. The employer of injury and coworkers have intimate knowl

edge of the injured worker. Despite the best preparation, these parties will often be quite

surprised at the differences they find in the injured worker. Their reaction may be so

profound as to engender fear about safety, doubt about recovery, and reluctance to allow

sufficient time and opportunity for progression through an extended work hardening, on

the-job training, and job coaching process before arriving at a final job placement. The

injured worker, too, may be keenly aware of colleagues' watchfulness and the extra social

pressure can be unduly difficult.

Consequently, the prevocational counseling process should include an orientation for

the client and family as to these potential pitfalls. The plan should evolve to identify and

avoid as many of them as possible. Education regarding the prolonged nature of vocational

intervention and description of the process as a "therapy" rather than job placement can

be helpful in arriving at a good understanding of the need to effect appropriate opportu

nities for transition into the return to work process.

It is often necessary to educate financially-interested parties as to the need to follow a

protracted vocational rehabilitation course for people with TBI since most claims adjusters

and case managers will have little experience with TBI. Their usual experience with

vocational rehabilitation will be such that they will expect a comparatively short and

simple process. They may expect that the medical file be closed and the client determined

to be “permanent and stationary” (P&S) or at “maximum medical improvement” (MMI)

before allowing formal vocational rehabilitation involvement. As has been discussed

above, it is imperative in TBI that vocational and medical rehabilitation be better coordi

nated early in the recovery process. Determination of P&S or MMI status can be made

shortly before final job placement and need not precede the commencement of vocational

rehabilitation.

The VRC must evaluate the degree of awareness the medical rehabilitation professionals

have regarding the likely job requirements for which they must attempt to prepare the

injured person. The VRC may choose to develop job requirements for several possible job

descriptions and meet with medical rehabilitation staff to review the position demands.

Medical and therapeutic planning can be quite different when knowledge of such require

ments is introduced. These differences can range from alteration of timing for various

elective or planned surgical interventions to whether or how long therapy continues and

to what goals.

Vocational Counseling

The VRC should begin vocational rehabilitation counseling with adequate disclosure of

each party’s roles and responsibilities. Expectations for the vocational process should be

evaluated and clarified. Most people do not have a clear idea as to what vocational

rehabilitation entails and so it is quite important to undertake a clear discussion of what

is expected of the injured worker, an employer, and the VRC.

Most states have requirements for provision of vocational rehabilitation benefits. Some

insurance carriers and some states have published materials that explain available benefits

to the injured worker. Since memory function may be impaired, it may be advisable to

include a family member in the discussion of benefits to be sure that all their questions

are answered and that the information can be reliably presented to the injured worker, in

case aspects of the discussions are forgotten. Provision of available benefits in writing can

facilitate this process.

The VRC may face obstacles posed by misinformation that an injured worker or his/her

family has obtained from friends or family who had experience with vocational rehabilita

tion for a different injury or in a different state. The existence of such experience should be

actively investigated as it will most likely influence receptivity to vocational rehabilitation.

The VRC must learn the vocational goals and expectations the injured worker and his/

her family have. There may be discordance within a family or between the injured worker’s

desires and his/her abilities. Vocational counseling should undertake a supportive and

coordinated educational process to attempt to align expectations and goal setting from

the outset and before progression on the plan. The VRC will need to include medical

rehabilitation professionals, case managers, claims adjusters, attorneys, and staff of state

departments of vocational rehabilitation in these discussions to arrive at a vocational

rehabilitation plan that has attainable goals that are agreed upon by all interested parties.

Given the large number of interested parties and their respective roles, reaching concor

dance is crucial, though difficult.

Assessment of dependency must be undertaken in the vocational counseling process.

Dependency can take many forms and is fostered, to some degree, through the medical

rehabilitation process. The injured worker may need some assistance in overcoming

learned dependence and moving toward independence and self-reliance once again.

Dependency can be psychological, financial, social, or medical in nature. Psychological

dependencies include having learned to be more comfortable having things done for,

rather than doing for oneself, having developed a dislike of a particular job or distrust of

an employer, deriving some emotional benefit from medical treatment or the disabled

status, or having developed a fear of failure that precludes consideration of reentry into

the workplace as an independent person. Financial dependence can include the idea that

it is easier not to work than to work for a minor discrepancy in income, income stability

due to regular income payments rather than income derived from seasonal work, or

acceptance of the idea that injury deserves compensation even though a Social Security

or workers' compensation payment is not designed as such. Social dependency can occur

when immigration status is dependent upon medical status or when cultural mores are

such that injury is viewed as permanent and, consequently, as an entitlement rather than

as something which is temporary and amenable to change. Medical dependency can

include substance abuse that may or may not have preceded the injury. 129,130 Once depen

dencies and their etiology are identified, the VRC can work with a counselor or psychol

ogist to address the dependencies and attempt to reverse them. Some dependencies,

however, will not be amenable to reversal and vocational rehabilitation plan success will

be negatively affected.

Vocational Testing/Work Evaluation/Work Hardening

Vocational testing can include interest inventory testing, vocational aptitude testing, uti

lization of standardized work samples, and utilization of work samples to assess specific

skills. Many interest inventory and vocational aptitude

tests are commercially avail

able. 131–134 These tools are often helpful in identifying alternative employment options that

may be of interest and within the capabilities of an injured worker who cannot return to

the preinjury employment. Results of these tests facilitate discussion and exploration of

vocational options, though some care must be taken in that the universe of options is

opened to the individual. This can be problematic, as some options may require an

extended vocational or educational training that is not practical. Similarly, some options

may entail self-employment. Given the nature of limitations experienced following TBI,

formalized schooling and self-employment plans are less likely to be successful. In fact,

it has been demonstrated that formalized schooling plans in vocational rehabilitation with

other populations are less successful than nonschooling plans. 135

Vocational evaluation may require a protracted timeline to properly complete. 136 Work

evaluation consisting of situational 60,136 or community based assessments, functional eval

uation, simulated work, and work samples 137 might be included to identify potential

barriers to employment that may not have been identified. Work evaluation can be helpful

in determining whether a work adjustment or work hardening experience is warranted.

Standardized work samples can be used which allow comparison of the person’s function

with a normal population. These work samples can be used to evaluate ability to use small

tools, 138 size discrimination, 139 numerical sorting, 140 upper extremity range of motion, 141

clerical comprehension and aptitude, 142 independent problem solving, 143 multilevel sort

ing, 144 simulated assembly, 145 whole body range of motion, 146 trilevel measurement, 147

eye-hand-foot coordination, 148 and soldering and inspection. 149 Work samples designed

to assess specific work skills can also be derived from an employment setting. Information

is collected about the usual method of completion, time to complete, and job outcome,

which is then compared to the skills demonstrated by the injured worker.

Work hardening placement is used to develop physical, cognitive, social, and job skills

for a specific position, though the plan might intend that those skills will ultimately

transfer to other job placements. Strength and endurance can be gradually improved by

using a graded number of hours per day for the work schedule. An advantage to a work

hardening placement is that it is disposable. That is, mistakes made on this type of

placement can be used as learning experiences and are not likely to be noted by friends

and coworkers. Gradual improvement in work productivity is the key to work hardening

placement. It is sometimes useful to utilize more than one work hardening placement due

to information gleaned from the first. The individual may demonstrate skills, or a lack

thereof, that were not identified during testing. Accommodation to the work place and

all its demands can be accomplished by transition built into the work schedule and work

responsibilities. Development of positive worker characteristics is an early focus. Contin

ued monitoring by the VRC or job coach can provide excellent information to therapists

for additional emphasis on identified areas or for compensatory approaches to be devel

oped. The VRC must ensure that the work hardening experience provides good feedback

to the injured worker and work to maintain an employer's willingness to continue to

provide access to the work hardening setting. Work hardening experiences need not be

paid positions in order to be valuable. Some people benefit from protracted volunteer

experiences, gradually improving endurance, positive worker characteristics, and job

skills. On the other hand, work hardening experiences may progress within an employer's

setting and culminate in an actual job placement. Obtaining a job placement from an initial

work hardening experience may be as dependent upon the VRC's management of the

entire process as it is upon the injured worker's skills and progress. 24

To summarize, in the general course of vocational rehabilitation for TBI, the VRC enters

the process by monitoring the medical rehabilitation status and progress. A job analysis

and description of the employment at the time of injury

should be obtained and shared

with the medical rehabilitation team. Likewise, a work history that reviews all past

employment should be collected and shared. As this information is considered, the VRC

and medical rehabilitation team can begin to discuss the return to work process and bring

about the establishment of appropriate expectations for return to work amongst them

selves and with the injured worker and family, review prognostic variables which may

impact return to work, and review funding options and programs that will be available.

The VRC must be certain to file all appropriate paperwork on behalf of the injured

worker, insurer, or employer, as required by law. Continued monitoring of progress in the

medical rehabilitation occurs until the proper time for administration of prevocational

counseling and vocational testing is identified. As the injured worker nears completion

of the medical rehabilitation plan, vocational evaluation begins.

As the medical rehabilitation process winds down, part-time work hardening placement

can be used to reintroduce the injured worker to the workplace, and assess and reestablish

good basic worker characteristics, such as appropriate dress, punctuality, and job task

completion. Work hardening placement may be progressive either in the amount of time

spent on the job, in the nature of the work undertaken on a given job, or in changing from

one job description to a more demanding one. Extensive job coaching should be used in

the work evaluation and work hardening processes.

Success in work hardening placement(s) leads to job placement in what may become

the final placement for the injured worker. Job coaching should continue as needed and

be transitioned out of the job site according to success. Continued monitoring should be

undertaken for 6 to 12 months before case closure is achieved. Sale et al. 24 reported that

placements often failed due to a number of events occurring on the job rather than a single

event, suggesting a role for VRC intervention. Finally, the VRC should always compare

the original vocational goals and predicted vocational outcome with the final achievement

to attempt to derive ways of improving personal effectiveness.

Follow-Up

The role of follow-up cannot be overstated. Given the instability in job maintenance

following TBI, planned follow-up conducted over a lengthy period of time is only logical. 12

Unfortunately, though, completion of follow-up activities requires the approval of the

client, the employer, possibly an insurance carrier, in addition to the willingness of the

VRC. Objectives for the follow-up visits should be clearly delineated in advance with all

interested parties.

The primary purpose of follow-up is to determine whether the individual is experiencing

any problems on the job site that can be rectified before they culminate in job separation.

The injured worker may be aware and forthcoming about problems, as may be the

employer. However, either party may be unaware of difficulties, as well. Consider tardi

ness, absenteeism, social interaction, and task completion at a minimum. Careful interview

with the injured worker, family, coworkers, and the employer may reveal small or emerg

ing problems that can be addressed. The VRC should review current job duties and

compare with original responsibilities. Any changes that are noted should be reviewed to

determine if they are compatible with known skills and aptitudes of the injured worker.

The VRC must also investigate whether events have transpired which might jeopardize

placement that may not be work-site related. These include motor vehicle infractions or

accidents, hospitalization, substance abuse, family or marital discord, or failure to comply

with prescribed medical or therapeutic treatment plans. It may be advisable to contact

the local department of motor vehicles (DMV) to check for infractions, accidents, or

substance abuse.

The VRC must collate the collected information at follow-up and determine the manner

to best approach addressing identified areas of concern. The goal must be to conduct

follow-up frequently enough so as to allow early identification and resolution of problems,

thereby ensuring job retention.

Summary

Successful vocational rehabilitation represents, perhaps, the highest achievement of return

to life to be achieved after TBI. Formal vocational rehabilitation is challenged by societal

predispositions that often preclude the initiation or successful completion of such efforts.

The process is extremely complicated and requires a thoughtful, adaptable, and progres

sive approach to restoration of the ability to work. Stability of achieved medical rehabil

itation outcomes and overall life satisfaction can be positively impacted by undertaking

the hard work involved in returning a person with TBI to work.

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17

Therapeutic Recreation in Traumatic Brain Injury Rehabilitation

Sam S. Andrews, Kenneth A. Gerhart, and Kenneth R. Hosack

CONTENTS

Brief History of Therapeutic Recreation

Therapeutic Recreation traces its beginnings to 400 B.C. when Socrates and Plato first

considered the relationship between physical health and mental health. Centuries later,

one of the signers of the United States Declaration of Independence, Benjamin Rush, M.D.,

advocated for recreation in the Pennsylvania Hospital, a

psychiatric facility in Philadel

phia. In 1810, Rush said of the individuals hospitalized there, “certain kinds of labor,

exercise, and amusements should be contrived for them, which should act, at the same

time, upon their bodies and minds.” 1 As such, recreational therapy had its roots in

vocational and occupational therapy in psychiatric facilities for about the next 100 years,

during which time crafts, amusements, drama, and hospital occupations were believed

to be valuable for those involved in such typically long hospitalizations. Even as late as

the beginning of the 20th century, the terms occupational and recreational were virtually

synonymous.

It was in the early 1900s, however, that occupational and recreational therapies began

to slowly separate and differentiate themselves. In 1908, in Chicago’s Hull House, classes

were offered in occupations and amusements for hospital attendants. In 1911, William

Dunton, the “father of occupational therapy” and a staff psychiatrist at Sheppard Enoch

Pratt Asylum (SEPA) in Baltimore, taught a series of classes on occupation and recreation

for nurses at SEPA and, soon after, created a new department by the same name. 1 The

first National Recreation Congress was conducted in 1918, and Recreation Therapy became

more widespread in general hospitals and centers for people with visual impairments.

Around that same time, the federal government first began

to recognize and support

Therapeutic Recreation. The first federal Recreation Act was passed in 1926 (443ss869-869

3) and the United States Works Progress Administration began to distribute Recreation

Division funds to recreational leaders at various institutions in 1934.

Therapeutic Recreation expanded to serve various disability groups, including persons

with developmental disabilities, visual impairments, and amputations, as well as geriatric

populations. Therapeutic Recreation continued to be codified as a discrete discipline, and

in 1935, Dr. John Davis wrote a text entitled Recreational Therapy, Play, and Mental Health. 1

A year later, he and Dunton coauthored another text called Principles and Practice of

Recreational Therapy. 1

Therapeutic Recreation continued to develop during World War II when there was height

ened interest in mobilizing and restoring soldiers to maximum health and productivity. The

Federal Vocational Act was passed in 1943 and the VA Recreation Service was established

in 1945. Three years later, the American Recreation Society created a Hospital Recreation

Section. In the early 1950s, colleges and universities began to offer bachelor’s and master’s

programs in physical education and recreation in rehabilitation. By 1955, the first hospital

recreation personnel standards were published, dividing personnel into three titles: Hospital

Recreation Director, Hospital Recreation Leader, and

Hospital Recreation Aide.

During the decades of the 1950s and 1960s, the profession of Therapeutic Recreation

experienced significant growth as three separate phenomena within health care were

integrated. First, hospitals and other service providers furthered their treatment efforts by

grouping individuals according to specific diagnoses or etiologies, such as those with

spinal cord injury, developmental disabilities, and amputations, in order to offer more

specialized rehabilitation services. Second, efforts to humanize institutions were underway

and became part of the societal movement to “habilitate” people with disabilities and to

enhance their functional skills. The third phenomenon, which was closely related to the

second, was the societal movement toward deinstitutionalization, normalization of living,

and community integration. Those who were still institutionalized, or those who needed

to be so, gradually became recipients of more respectful and considerate treatment. This

movement toward “normalization” continued to increase emphasis on progressively

restoring functional activities of common daily life. Recreation personnel played a key

role in providing those normal life activities.

Over the past 40 years, Therapeutic Recreation has continued to grow and develop as

a profession. One of the first formal definitions of Therapeutic Recreation, offered by

Dunton, described Therapeutic Recreation as: any free,

voluntary, and expressive activity, motor, sensory, or mental, vitalized by the expansive play spirit, sustained by deep-rooted pleasurable attitudes and evoked by wholesome emotional release, prescribed by medical authority as an adjuvant in treatment. 1

That definition, along with the profession it describes, has continued to evolve. Today, the

National Council for Therapeutic Recreation Certification (NCTRC) provides the profes

sional designation and titles of Certified Therapeutic Recreation Specialist (CTRS) and

Certified Therapeutic Recreation Assistant (CTRA). The O*Net, which has recently

replaced the Dictionary of Occupational Titles, now defines recreation therapists as individ

uals who “plan, direct, or coordinate medically approved recreation programs for patients

in hospitals, nursing homes, or other institutions. Activities include sports, trips, dramat

ics, social activities, and arts and crafts. May assess a patient condition and recommend

appropriate recreational activity.” 2

Therapeutic Recreation for Persons with Traumatic Brain Injury

Therapeutic Recreation programs specifically for individuals with severe traumatic brain

injury (TBI) were further developed in the 1960s and 1970s as specialty-diagnosis reha

bilitation programs continued to evolve. The Vietnam War brought on rapid advances in

emergency trauma systems and neuroradiological and neurosurgical advances that

resulted in a dramatic increase in the number of survivors of TBI. In 1981, the newly

formed National Head Injury Foundation coined the phrase “silent epidemic” to describe

this rapid increase in the number of TBI survivors. 3 Categorical brain injury rehabilitation

programs grew dramatically in the 1980s, and Therapeutic Recreation became a part of

the interdisciplinary teams with those programs. In 1985, Therapeutic Recreation for

persons with brain injury was first included in the Standards Manual for Facilities Serving

People with Disabilities by the Commission on Accreditation of Rehabilitation Facilities

(CARF). This established the recreation therapist as a member of the primary core team

of allied health professionals. 4 Between 1985 and 2002, CARF continually refined its

standards to include additional components through the continuum of care from acute

through community integration, and Therapeutic Recreation continued to be one of the

disciplines recommended for traumatic brain injury, as determined by individual patient

assessment and progress. 5

Effectiveness of Therapeutic Recreation for Persons with Disabilities

Research specifically with survivors of traumatic brain injury is sparse; therefore, what

follows is a review of studies that discuss the effectiveness of Therapeutic Recreation with

various disability groups that are the most relevant to individuals with traumatic brain

injury. One of the most significant efforts was made in 1991 by Coyle, Kinney, Riley, and

Shank. 6 Through the support of a grant from the U.S. Department of Education’s National

Institute on Disability Rehabilitation and Research (NIDRR), Coyle, Kinney, Riley, and

Shank convened panels of expert Therapeutic Recreation practitioners and educators with

extensive experience and skill in treating a wide array of people with disabilities and

compiled the results of research, interventions, and outcomes. This panel, called the

National Consensus Conference on the Benefits of Therapeutic Recreation in Rehabilita

tion, concluded that Therapeutic Recreation does hold substantial value for people with

disabilities. Areas of benefit that have been identified by this panel, 6 and others, include:

- Physical health and health maintenance (e.g., improvement in general physical and perceptual motor functioning in individuals with disabilities)

- Cognitive functioning (e.g., improved short- and long-term memory)

- Mental and psychosocial health (e.g., improved coping skills, self-control, sense of self, social skills, cooperation, growth and personal development, reduction of inappropriate behavior, and increased acquisition of developmental milestones)

- Personal and life satisfaction (e.g., community integration, productivity, and increased life and leisure satisfaction)

Physical Health

Improving and maintaining physical health and functioning is a goal of all rehabilitation,

and Therapeutic Recreation is extremely valuable in this area. Connolly and Garbarini

report that Therapeutic Recreation reduces the risk of

physical complications secondary

to disability. 7 One of the primary ways Therapeutic Recreation does this is by promoting

participation in leisure activities that foster physical activity and exercise. Santiago, Coyle,

and Kinney report that recreation programs that improve aerobic fitness, for example, do

enhance health. 8 While the effect of exercise on health in nondisabled people is well

documented and does not need to be reviewed, a review of a few disability-specific and

Therapeutic Recreation-specific findings may prove useful. Exercise and physical activity

in disabled persons have direct effects on muscle strength, endurance, flexibility, and

balance. They also reportedly reduce health risk factors 9 and help prevent secondary

complications for people with disabilities. 8,10 Exercise can prevent or forestall such sec

ondary complications as contractures, bladder complications, decubitus ulcers, cardiovas

cular disease, osteoporosis, and obesity. 11,12 Stotts found that a group of spinal cord injured

persons who participated in wheelchair athletics had three times fewer hospital admis

sions than comparable nonparticipants. 11 Indeed, among disabled persons who participate

in sports, lower levels of obesity have already been reported, along with decreased inci

dences of skin breakdowns, greater levels of respiratory endurance, higher levels of health

maintenance, and a reduced frequency of rehospitalization overall. 9,11,12 Conversely, others

have reported that physical inactivity can contribute to progressively decreasing health

in adults with physical disabilities. 13 In perhaps the most significant finding, activity level

was one of the most prominent predictors of survival itself among people with spinal

cord injury. 14

For many individuals — and, certainly, for people with TBI — recreational activities

may be more motivating, more desirable, and more tolerable than mere exercise. As such,

Therapeutic Recreation has been shown to be an extremely effective means of addressing

the above health issues and goals. Moreover, it is frequently a valuable adjunct to physical

therapy, bringing many of physical therapy's goals and skills into "real world" applica

tion. 15 For example, wheelchair handling skills taught in the hospital's physical therapy

department can be put to use in a wheelchair basketball tournament or tennis game.

Strengthening exercises or balance activities, practiced with the physical therapist, can

translate to rowing, sailing, skiing, or jogging. Therapeutic Recreation activities can often

go beyond what physical therapy has to offer with respect to fitness and endurance

building. Individuals struggling through initial rehabilitation have sometimes argued that

the routines of activities of daily living (ADL) were all the exercise they needed, but

research has shown that this is not the case. In a group of individuals with paraplegia,

researchers found that performance of ADL and self-care activities alone were not enough

to maintain fitness. 16,17 Conversely, fitness through Therapeutic Recreation can enhance

the performance of ADL. Exercise and leisure activities which increase fitness levels can

also lead to increases in the ability to do work and to meet the demands of every day

life. 16,19 In other words, fitness can lead to increased productivity.

Cognitive Functioning

Relevant to those with severe TBI are reports that Therapeutic Recreation has positive

effects on cognitive functioning and decreases confusion and disorientation. 7 It can engage

individuals with TBI in interesting but simplified activities that place few functional

demands upon them. 15 This is particularly important early in the rehabilitation process as

it allows the Therapeutic Recreation specialist to address such areas as attention span,

selective attention, recognition of things and events, and figure-ground discrimination.

Additionally, Therapeutic Recreation can be an important way of engaging individuals

with TBI in cognitive and physical rehabilitation within an activity they enjoy, particularly

when they have deficits in self-awareness and may not be able to understand or comply

with traditional therapy.

Many of the mental and cognitive benefits of Therapeutic Recreation also appear to be

related to the positive effects of the physical activity

and exercise which it promotes. In a

study of people with severe mobility impairments, investigators found that mental alert

ness and cognitive activity increased following exercise. 20 Cognitive function was also

found to improve when elderly people with mental illnesses underwent fitness training. 21

Activity may also strengthen the ability to cope. Example: Several years ago, an individual who had been an aircraft mechanic was hospitalized in a low level of responsiveness following a traumatic brain injury. After attempting several strategies to improve arousal, he was taken to an aircraft maintenance facility to be exposed to the familiar environment of the people, aircraft, sights, smells, and sounds of the facility. The experience was successful and he returned to the hospital substantially more responsive than when he left. Although the experience was not strictly recreational in nature, Therapeutic Recreation resources were utilized to facilitate the trip. The increased responsiveness might have occurred anyway, but the experience seemed to accelerate the rate of improvement.

Mental Health

Therapeutic Recreation also has a positive effect on mental health. Researchers report that

depression and depressive symptomatology decrease with exercise and activity, 7,9,10 and

that depression may actually be caused by lack of activity. 13 Moreover, the overall mental

health of adults has been reported to be dramatically influenced by their satisfaction with

their leisure activities — often more so than by their satisfaction with work and health itself. 22

Depression, stress, and other negative mental states adversely affect quality of life. 23

However, Therapeutic Recreation has the potential to impact these. Depressive symptoms

are less in people who exercise, including people with

disabilities. 10,24,25 Others have also

reported that, following recreation, participants have less tension, better temperament,

more energy, less confusion, better coping, and less anxiety, fatigue, confusion, and anger,

as well as lower levels of stress. 7,24,26,27 All of these are particularly relevant to those with

traumatic brain injuries.

In addition to the areas described above, all of which relate to psychosocial health, a

key area for people with TBI is restoration of their self-image and sense of self. Many

different elements contribute to an individual's sense of self. A few of them include:

developing a sense of mastery, controlling stress, seeing one's life as productive and

meaningful, developing a positive body image, and having a positive attitude toward

one's (and others') disabilities. 15 While most of these will be discussed in detail in later

sections, one particular element that has been shown to be vital for a positive sense of self

— the development of a sense of mastery — merits consideration here.

A sense of mastery often results when the individual experiences the feeling of having

performed successfully and effectively. Many Therapeutic Recreation activities can lead

to a sense of mastery. Sports, athletics, outdoor activities, and even creative endeavors all

can have an impact. However, the mastery experience is particularly enhanced when the

risk or difficulty of the activity continually increases so

that the individual faces ongoing

and increasing challenges. 28 Actual increases in self-efficacy have been demonstrated fol

lowing disabled individuals' participation in two different outdoor activities — rugged

terrain hiking and camping. 29,30

The implications for the individual with the TBI are profound. Mastery of old activities

(that now may be difficult and, perhaps, overwhelming) can potentially lead to a sense

of mastery. Winning a ping pong game, mastering a computer game, successfully using

public transportation, or going to a public sporting event can represent "risk" to the TBI

survivor and, as such, can create opportunities for mastery. More importantly, such mas

tery generalizes to other life areas. Hedrick found that wheelchair tennis skills significantly

increased disabled teens' perceptions of their physical competence. 31 Similarly, others

report that skills taught and activities experienced in rehabilitation generalize into indi

viduals' postrehabilitation life (e.g., people with spinal cord injuries who participated in

a camping experience prior to discharge were likely to continue with outdoor activities

in the community). 32

Psychosocial Health

Leisure activities, by their very nature, encourage socialization and interaction with oth

ers. 33 They are a vehicle for getting involved in the community and for achieving com

munity integration. 34 The effective use of leisure is what Therapeutic Recreation is about;

the impact of Therapeutic Recreation on community integration is clear, and the role of

the Therapeutic Recreation specialist in enhancing community integration seems obvious.

Frequently, leisure is an effective vehicle for community involvement, and those who are

engaged in leisure activities view themselves as productive and having purpose. Thera

peutic Recreation helps prevent social isolation and may prevent the individual from

becoming withdrawn. It may increase the hospitalized individual's will to survive and

help him or her embrace the rehabilitation program. 15 Later on, the skills Therapeutic

Recreation teaches continue to counteract the tendency for isolation. Activities, sports, and

leisure pursuits all decrease isolation by increasing interaction with others in groups, on

teams, and in the community. Therapeutic Recreation experiences can enhance not only

social interaction but also the desire for social interaction as well. 15 A particular therapeutic

exercise program actually increased the participants' social contacts outside the program

by 25% in one study of nonbrain-injured adults. 25 Finally, there is also evidence that

socialization and community integration affect health. Disabled people who are inactive

and socially isolated (as evidenced by increased TV watching) have more medical com

plications and less leisure satisfaction. 35

Sports activities, in particular, may foster community integration. Disabled athletes are

perceived by the general population as having higher social status and integration. For

the participant, sports decrease isolation, while for those who observe them — particularly

nondisabled people — they provide education, positive profiles of athletes, and ultimately

may promote healthier attitudes toward disability and individuals with disabilities. 36 Sir

Ludwig Guttman is generally credited with utilizing sports as a fundamental component

of the rehabilitation process for physically disabled World War II veterans in the United

Kingdom. 37 Although Sir Ludwig's role at Stoke Mandeville was as a neurosurgeon and

the master influence of the facility, he insisted that those he cared for actively participate

in sports because of his strong belief in their physical and psychosocial benefit. Modern

Therapeutic Recreation, in many ways, reflects those same principles today, but it does

so for a broader spectrum of people and with a scope that extends far beyond sports.

In addition to sports activities, social interaction and community integration can occur

through arts, music, horticulture, and volunteerism of many kinds. Therapeutic outings,

as part of the rehabilitation experience, provide individuals and their families with expo

sure to familiar community venues and potential future activities. They also provide an

opportunity to experience possible attitudinal and physical barriers in a supportive milieu.

In one study of 200 people with spinal cord injuries who participated in outings, all but

four reported that outings gave them the confidence they needed to get out in the com

munity more often and more easily once they were discharged. 38

Personal Satisfaction and Satisfaction with Life

Out of the sense of mastery described above grows a feeling of purposefulness and

productivity. Both are key elements in a satisfying life. Though we typically associate

productivity with productive work or employment, this is a very limited view of a concept

that should also include productive avocational activities and leisure, family role and

productive relationships, community service, and learning and education. 39 Moreover, a

limited, employment-focused view of productivity too often can relegate rehabilitation

consumers, particularly TBI survivors, to hopeless "un-productivity." Physical limitations,

reduced endurance, and cognitive disabilities, as well as a highly competitive workplace

and numerous work disincentives that exist on a societal level, may make returning to

work an unrealistic, impractical, and unlikely outcome.

People with disabilities seem to know this and have taken a different look at "work."

Those with spinal cord injuries, for example, have been shown to reassess their values

and reorder their priorities in order to increase the importance and value of those activities

in which they can be successful. Frequently, work moves down on the list. Often, leisure,

recreation, and relationships with others take on greater importance. 40 Others have

reported similar findings. Riddick, for example, reports that satisfaction with leisure is

frequently more important than satisfaction with work — and even with health — in

determining well-being. 22 Godbey writes that it is the ability of people with disabilities

“to use leisure in satisfying and appropriate ways which determines their fate as surely

as their ability to do useful work.” 41

Clearly, Therapeutic Recreation interventions frequently impact productivity in all of its

conceptualizations. The benefits already mentioned (i.e., the ability of meaningful activity

to improve physical and mental health, cognitive functioning, and functional carryover,

and the successful mastery of new challenges) all carry over to other potentially productive

life areas. For those who are able to work, the benefits are obvious; for those who are not,

leisure is often thought of as a replacement for work. 15 Moreover, even among those who

do work, leisure has been shown to compensate, at least partially, for lacking job satisfac

tion. 42 Others have found that work is not a factor in successful community reintegration,

while leisure and recreation are factors. 43 Thus, Therapeutic Recreation teaches skills and

builds the confidence and successes necessary to be productive in a variety of life areas.

Finally, participation in leisure and leisure satisfaction has been more directly linked to

quality of life. 9,17,41 Both have been found to correlate with higher life satisfaction. 17,44

Of direct application to brain injury is the work of Niemi and his colleagues. 45 They

studied a group of individuals who had survived strokes 4 years earlier and found that

poorer leisure functioning was a major factor preventing them from returning to their

prestroke quality of life. Similarly, in another study of 700 adults with physical disabilities,

researchers found that the participants' satisfaction with their leisure activities was one

of the strongest predictors of overall life satisfaction. This prompted the researchers to

recommend that time be allotted during rehabilitation to help hospitalized persons under

stand how their disabilities impacted their leisure involvement. 42 That this same study

found leisure satisfaction to be lowest among those with newly acquired disabilities further

suggested that leisure adjustment and education could not only enhance the rehabilitation

process but might improve future life satisfaction as well.

In summary, Therapeutic Recreation improves physical and mental health, cognitive

functioning, psychosocial functioning, and life satisfaction. Being active and engaged in

the community through strategic and appropriate recreational interventions can result in

better self-esteem, less depression, less stress, greater productivity, and better overall

health. All of these result in decreased health care utilization and less subjective burden

and expense for survivors, their families, and those who pay their medical bills.

Models of Service Delivery

The following section describes a model of Therapeutic Recreation service delivery within

a categorical brain-injury rehabilitation program at Craig Hospital that has proven to be

effective for more than 30 years for people with traumatic brain injuries and their families.

First, any model of Therapeutic Recreation must emphasize movement from a high level

of dependence along a continuum toward a reduced level of dependence or independence.

At the far end of the continuum of service delivery and outcome, the therapist should

provide as little intervention and control as possible. This conceptual framework is sup

ported by Gunn and Peterson 46 who divide Therapeutic Recreation service into three

general phases. The first phase of intervention on the continuum involves a high degree

of control by the Therapeutic Recreation specialist and constrained obligatory behavior

of the participant. The second phase is characterized by skill building in a variety of areas.

The final phase is achieved when participation in recreation becomes a reality lifestyle

and there is little or no control by the therapist except for provision of opportunity. The

individual is independent, self-regulated, and his or her behaviors are intrinsically reward

ing. 46 The health promotion model, constructed by Austin and Crawford, depicts a similar

movement by the individual through a continuum starting with poor health in an unfa

vorable environment and culminating in optimal health in a favorable environment. 47

Although total success is not always possible, some movement through the continuum as

described above is almost always possible.

Common concepts in most models of Therapeutic Recreation service delivery and inter

vention are:

- A continuum of growth and intervention
- Belief in the strengths and abilities of the individual
- Increasing freedom and self-determination
- Decreasing therapist control
- Increasing involvement and participation or inclusion in the “natural” community 37

Exposing individuals with TBI to familiar, practical, and measured activity is an effective

tool in early intervention. As they move through the continuum, gradual and strategic

exposure provides the opportunity to measure progress, evaluate the effectiveness of

interventions, and prepare them to actualize life skills, functionality, social connection,

and quality of life.

Therapeutic Recreation for people with TBI should be delivered within the context of

an interdisciplinary team, and collaborative activities should be created that maximize

functional independence, provide education, and help educate and enhance involvement

with family and friends.

Therapeutic Recreation provides ecological validity to the findings and recommenda

tions of other team members. Therapy in a protected hospital setting often requires ther

apists to make inferential assumptions about how an individual will function outside the

hospital. Therapeutic Recreation is the discipline specifically charged with verifying the

validity of such assumptions. Therapeutic Recreation is the functional integration of phys

ical, cognitive, emotional, and psychosocial skills in real world settings and is invaluable

to a valid rehabilitation process.

Assessment

Assessment should occur early following injury with the individual, family, and significant

others, and should include a thorough history. Although the individual may change

drastically in a very short time, early and accurate information about his or her preinjury

life is essential in developing a treatment plan. Information regarding social, educational,

vocational, and recreational history is the cornerstone for development of Therapeutic

Recreation treatment strategies. The value of recreation prior to injury should serve as a

reference for the Therapeutic Recreation specialist as he or she implements “already

familiar” activities early in the rehabilitation program. Communication with family and

members of other clinical disciplines with respect to early treatment goals helps the

Therapeutic Recreation specialist formulate a collaborative intervention strategy with

other treating disciplines so that appropriate therapeutic intervention in the most appro

priate therapeutic environment can be established from the beginning.

A critical part of assessment of the person with TBI is the therapists' understanding of

the brain, brain anatomy and physiology, types of brain injury, and common functional

sequelae of brain injury. For each individual, therapists must understand the key roles of

initiation, planning, problem solving, self-awareness, etc., and how these cognitive skills

and deficits may impact the individual's recreational treatment plan. The Therapeutic

Recreation specialist can establish goals and intermediate objectives that illuminate these

aspects of behavior, set milestones for measurement of progress, and offer the opportunity

for creation of activity which provides optimal condition for the individual's advancement.

One formal instrument that is particularly useful to the Therapeutic Recreation specialist

is the Leisure Competence Measure (LCM). 48 This standardized tool is similar in function,

validation, and application to the Functional Independence Measure (FIM) 49 and is used

widely throughout the rehabilitation field to measure functioning over time, to guide

goal-setting and intervention, and to assess progress and

measure recreational therapy

outcomes. 48,50 As such, the LCM is readily understood by all other members of the mul

tidisciplinary rehabilitation team as well as payers, researchers, and others, and meets

accountability standards of such organizations as the Joint Commission on Accreditation

of Healthcare Organization (JACHO) and the Commission of Accreditation of Rehabili

tation Facilities (CARF). 50 The LCM uses eight subscales: (1) leisure awareness, (2) leisure

attitude, (3) leisure skills, (4) cultural/social behaviors, (5) interpersonal skills, (6)

community integration skills, (7) social contact, and (8) community participation. It has

been shown to be both valid and reliable. 50 As a part of that continuum, the LCM can

also be used to provide valuable information — in concrete and universal terms — to

community entities (e.g., adaptive recreation community programs, independent living

skills trainers [ILSTs], or home care providers) which may ultimately become involved

in treating and accommodating the individual.

Another instrument that can be of great use is some form of leisure interest survey to

gain vital information regarding individuals' values and interests. From this information,

the Therapeutic Recreation specialist can determine needs based on interest and values

and then formulate a plan of intervention that will address and, as completely as possible,

meet those needs. An example of a leisure interest survey

is included in Appendix 17A.

Treatment

Information is compiled and presented at the first patient/family conference, along with

other information the treating team has to share. This conference typically occurs within

the first 2 weeks following admission and is designed to provide information and align

expectations regarding diagnosis, condition, and short-term rehabilitation goals. The first

conference is ideal for explaining the planned Therapeutic Recreation intervention and

rationale and for emphasizing the importance of continuing active recreation and leisure

activity after discharge. This is also an excellent time to formally establish a therapeutic

alliance and a relationship based on collaboration with the individual with the TBI (if

possible) and family, and to obtain their input into the care plan. Communication with

family, staff, and case managers, when appropriate, continues on an ongoing basis, both

formally and informally.

The most effective approach to providing Therapeutic Recreation service is to bring it

to the individual as an integral part of the interdisciplinary team intervention. In collab

oration with the individual, his or her family, and members of other treating disciplines,

the Therapeutic Recreation specialist can, more effectively, create and schedule therapeutic

activities which:

• Augment the therapeutic activities other members of the treating team have initiated

• Extend the individual's exposure to opportunity for therapeutic intervention

• Appropriately intensify specific therapeutic exercises and skill training activities

• Increase the individual's opportunity to operate in a more familiar environment

• Increase the opportunity to operate in a more realistic setting

• Give family an appropriate venue for involvement in the treatment process

Involving the entire family in the recreational goals and activities often is a very effective

way for them to participate in the rehabilitation process when other opportunities may

be few. However, caution must be taken to avoid over involvement of family. Family

members, in their understandably heightened emotional state, may over-react or under

react to the medical condition of their loved one. There is often fear, confusion, and

misunderstanding of the individual's condition. Realistic activity involvement with the

TBI survivor and family together gives family the opportunity to be actively involved in

a more appropriate environment, one that the Therapeutic Recreation specialist can mon

itor and moderate. Thus, the family member (or friend) who tends to be overly involved

can be guided into a more subdued level of interaction. At the other end of the spectrum,

under-involved families, in the comfort of familiar activity and surroundings, can be

encouraged, and any concerns they might have about how their efforts might place their

loved one in jeopardy can be alleviated. In either case, appropriate involvement can give

the family a more realistic perspective and can more accurately illustrate the abilities and

limitations of the person with TBI.

Indeed, as often occurs after TBI, when the perceptions of limitations held by the injured

person and the staff differ, family insight and involvement may be crucial. In particular,

when the individual with the TBI is unable to make legally-competent decisions about

therapeutic activities, some of which may involve risk, the family will need to increase

its understanding of capabilities, risks, and potential benefits. With the Therapeutic Rec

reation specialist’s guidance and input, they are better able to decide when to hang on

and when to let go.

Co-Treatment with Other Members of the Rehabilitation Team

Co-treating is a very effective tool for treatment. It allows the physical or occupational

therapist, for example, and the Therapeutic Recreation specialist to address multiple

therapeutic issues, often with more than just one or two persons in a group. Recreation

activity is frequently an excellent opportunity to evaluate the individual’s progress when

all the clinical efforts of the treating team are incorporated into activity.

Examples of productive cotreatment goals and activities

include balance and coordina

tion, attentional/distractibility groups, sensory integration, sequential memory exercise,

and rekindling of skills and abilities. Commonly used activities are frequently drawn from

those the individual participated in prior to injury — shooting baskets, jogging, swimming,

shopping, going out to eat or to concerts, and the like. Often, life-skill activities such as

cooking, community integration outings, social skills groups, scavenger hunts, music

activities, use of animals, exercise, and horticulture activities are also conducted with

therapists from multiple disciplines. Interventions like these provide mutual validation

of the therapists, enhanced recognition of the therapists by the individual with TBI,

consistency in treatment techniques, and greater application of expertise toward the indi

vidual’s progress. Even more importantly, such activities give a taste of life in the postre

habilitation world. The list of possible activities that can translate to real-life skills is

endless and, in a good rehabilitation program that focuses on community reintegration,

that list is, in fact, comprised of real-life activities. Anything that individual might have

done, or might do in the future, whether adapted or not is fair game for a therapeutic

intervention, functional activity, and skill-building experience. The bottom line: only the

potential therapeutic value should be considered in selecting an activity. This is a tried

and-true Therapeutic Recreation concept that dates back more than 150 years. Introduced

by Amariah Brigham, then Superintendent of the Utica State Hospital in New York, it

remains a guiding principal even today. 1

Additionally, in the hospital setting, it is often Therapeutic Recreation that offers the

other disciplines a more accurate picture of “real world” behaviors, performance, and

capabilities. In a notable example, one individual’s discharge goals were totally revamped

when treatment in the greenhouse and recreation room yielded a totally different level of

cooperation and motivation than the physical and occupational therapists were able to

obtain in their more clinical, and seemingly more threatening and controlled, settings. In

fact, what the individual was truly capable of in a more informal setting was so clearly

and dramatically demonstrated to the entire team that a discharge to the home occurred

rather than institutionalization. Unquestionably, a monumental difference was made in

long-term care costs and personal quality of life in this instance.

This example illustrates another important point: without meaningful activities that

incorporate all of the myriad clinical goals (i.e., behavior, cognitive function, perception,

executive function, gross and fine motor skills, speech, attention span), the treating team

has to guess how effective its combined therapeutic efforts have been. A more realistic

and accurate evaluation can be made following the application of real-life skill exposure,

social activity, proper stimulation, and, in some cases, appropriate use of diversion. Clearly,

recreation in the rehabilitation setting is far more than "entertainment." Though a big

"menu" of activities is helpful, the goals and context of those activities are more important.

Therapeutic Recreation should never be thought of as something that merely keeps people

with disabilities from being bored, nor should it be presented as "stuff" to fill up their

evenings and weekends.

Translating Therapeutic Recreation to the Real World: Community Integration

Therapeutic Recreation must "set the table" for the individual to access the community

or, more likely, the community to reach out to the individual. Exposure to equipment and

materials during rehabilitation greatly enhances the probability that individuals and fam

ilies will access resources subsequent to discharge. Advocacy, practical assertiveness train

ing, education leading to reasonable accommodation, and education on seeking and

accessing resources in the community are vital subjects to be addressed. These topics must

be covered thoroughly and accurately if individuals with TBI or their family members are

to have any semblance of success in accomplishing social integration. Understanding of

these areas is equally important for families who hope to gain any effective form of respite

from the sometimes overwhelming day-to-day maintenance and essential survival tasks.

Despite the best efforts of the entire interdisciplinary staff, major barriers to social and

community integration exist. One such barrier is merely making the transition from safety

and security to uncertainty. While many therapeutic activities within the healthcare insti

tution provide opportunity, they are initially unfamiliar to the consumer and, therefore,

may not be as initially effective as they could. However, as time goes by, it is the rehabil

itation setting itself that becomes secure and familiar, and the outside world becomes

threatening. Thus, the Therapeutic Recreation specialist must work with the individual to

again make that world familiar. Transitional events or settings must be used to provide

exposure to the real-life venues that are likely to be encountered after discharge from the

healthcare facility.

Transportation is generally another barrier that presents major challenges, especially

because so many individuals with TBI have serious difficulty utilizing transportation on

an independent basis. They either have enough difficulty with orientation that they are

unable to travel throughout the community or they are legitimately fearful of using public

transportation. Consequently, transportation is an issue the Therapeutic Recreation spe

cialist needs to address thoroughly. Moreover, it is an issue that may need to be readdressed

over time as the needs, interests, and abilities of the person with a disability change.

A third barrier is social isolation. Among those TBI survivors who are able to move

about the community, some may, nonetheless, reject the idea of participation in specialized

community programs provided for people with similar disabilities. Others may be reluc

tant to participate in regular events and activities because of inabilities they may have, or

perceive themselves as having, in social functioning. They may encounter so many neg

ative experiences that they give up attempts to access their community and become

isolated and socially deprived. Often, the social deprivation is even more exasperating

due to the individual’s strong desire for intimate relationships, which, for many, are very

difficult to achieve. Those who make effective social connections usually do so as the result

of the efforts of a significant other. This can be an independent living skills trainer,

advocate, or any other dedicated individual who consistently intervenes on the individ

ual’s behalf.

Clearly, the possibility of isolation after discharge must be anticipated and addressed.

Every possible effort must be made to prevent social isolation. A progressive approach of

exposure to achievable and realistic situations is a must. Connecting the individuals and

their families with activities that augment, if not replicate, other therapeutic activities by

other disciplines brings about better understanding and enhanced self-esteem even when

only a small amount of success can be achieved. It has been frequently observed that

almost everyone functions more effectively in an environment in which they perceive a

greater level of comfort. This is doubly true of the person with TBI, and the role of the

Therapeutic Recreation specialist in facilitating a clear transition to home and community

is an obvious and vital one.

The Therapeutic Recreation specialist’s involvement with other key friends, family mem

bers, and facilitators is necessary for a smooth return to the community. Indeed, the

Therapeutic Recreation specialist must pay attention not only to the individual with TBI

but also to the person or persons who can be there to facilitate social interaction on a

consistent and long-term basis. Independent living skills trainers, recreation center staff

members, teachers, team members, and others can be effective resources to assist the

individual toward improved function. Others may need to be sought out as the individual

situation and needs dictate. It is likely that the Therapeutic Recreation specialist and the

discharging healthcare institution will need to orchestrate and channel individuals and

their families to community activities and events that they can participate in. At the very

least, this will be necessary during the transitional period as they begin their exploration

of other activities that are available beyond the rehabilitation setting. This task becomes

more challenging if the individual is being discharged to a community distant from where

the rehabilitation program takes place. The Therapeutic Recreation specialist then must

give increased effort to identifying and simulating activities available in the community

to which the individual will return and to identifying local experts and mentors. Clearly,

additional effort must be made to make contact with resource entities in that community.

Despite the goal of autonomy and self-determination for many individuals, some per

sons may require continuous connection with support systems, be they individuals or

organizations. In some cases, family members of the individual may have to continually

support and help initiate community activity for the major part of the individual's life.

The Therapeutic Recreation specialist should educate family as to the scope of the family

member's own abilities to cope with the demanding support role they will face. Coping

mechanisms and resource exploration on their behalf are very important as well.

There is almost always a need for a significant other to encourage, to help with initiation,

to moderate the individual's emotional reactions, to arrange for transportation, to inter

vene when a given situation becomes untenable, and to continually search out new and

appropriate resources. In many cases, this effort takes a tremendous physical and emo

tional toll on family. Consequently, family members must have the skills and resources

necessary to protect themselves, to the best extent possible, from exhaustion and exasper

ation which may diminish or curtail their ability to intervene effectively. It is important

that family members or significant others have skill in caring for themselves. They should

be encouraged and enabled to do so and to attend to their own needs, as well as their loved

one’s, so that they can maintain their efforts over a prolonged period, possibly even an

entire lifetime. Respite, delegation of responsibilities, and measured effort across the entire

lives of the person with the disability and his or her family must be common and frequently

utilized tools.

Anticipation of Noncompliance with Medical Advice

Practicality of actual experience can be of value, especially when it can be reasonably

expected that the individuals may not always follow directives or advice of staff or

physicians. There is frequently a perception that individuals with TBI have lost a great

deal of freedom and self-determination. Often, they may not have a realistic view of what

abilities or limitations they may have. They perceive some restrictions as unnecessary,

especially in light of how much they feel medical personnel and family have already taken

away. A common comment may be, “I have no idea why they are making me do things

this way," or "I do not see why I have to be here; I am just fine!" They, at the same time,

may not be able to find the nearest restroom, even with directions. Restrictions are often

documented in the medical record or mandated by law. Clearly, the physician can write

into the chart at the time of discharge that the individual is not cognitively and/or

physically capable of driving safely. In most states, this is sufficient to preclude most

individuals from driving or attempting to obtain a license to drive. However, as an

example, many of those same individuals face no government restriction in the use of

firearms and can be out in a field with a loaded gun, completely unaware of the seemingly

obvious safety issues or consequences. Even with a physician's strongly documented

opinion that the individual must not take up hunting activities, the common mentality of

many is, "They can take away a lot of things from me but they are not taking away my

hunting." The recreation assessment is absolutely critical in establishing if an issue such

as this might arise. If there is the slightest suspicion by staff that the individual might

return to hunting, it might make a great deal of sense to put the individual and a family

member through progressive competency exercises. Only then can deficiencies in the

ability to safely enter into a hunting situation become clear to all concerned. "Not going

there," more often than not, is seen as tacit approval, and of course, could produce a

deadly outcome. Therapeutic Recreation specialists should take their intervening roles

very seriously in cases like this. They must ensure that proper exploration of any issues

of this nature takes place. If the therapist does not have the desire or expertise to do so,

appropriate referral should be made.

The same issues and consequences can apply to skiing, driving a boat, operating farm

equipment, fishing along a stream, or other adventure activities. If the Therapeutic Rec

reation specialist does not have the expertise or resources to provide competency evalu

ation in any such activity, appropriate referral should be made.

Conclusion

Independence and success are relative and dynamic throughout the life of an individual

who has sustained a traumatic brain injury. Therapeutic Recreation is a vital piece of that

success, and it is a piece that has been shown to be effective in maintaining physical health,

improving mental health and cognitive functioning, increasing community integration

and productivity, and enhancing life satisfaction. As such, the Therapeutic Recreation

specialist is in an enviable position to impact the postrehabilitation outcomes of a survivor

of traumatic brain injury.

Along with other members of the other clinical disciplines, he or she must make a

concerted effort to educate the individual and any

significant persons in that individual’s

life about the importance of preparation for the real-life issues the TBI will force them to

face. A guided, gradual exposure to all that recreation and leisure have to offer will help

all those dealing with a traumatic brain injury to move from a position of dependence

and isolation to one of increased independence and autonomy. The temptation to ignore

quality of life issues is very great when there is so much to be done medically and

functionally. However, if quality of life is not addressed, one might legitimately ask, “What

was the purpose of going through the medical motions?” Therapeutic Recreation profes

sionals gain satisfaction from helping people with disabilities progress to the point that

they can experience success in regaining functionality and in restoring purpose, self

esteem, and joy to their lives. In these modern, technology-saturated times, there is an

unlimited amount of stuff available, but the lack of expertise on how to utilize that “stuff”

as a viable resource remains problematic. The role of the Therapeutic Recreation specialist

is to fill that gap in expertise in order to give the people with disabilities a much better

chance at maximizing the rehabilitation experience and returning to as high a quality of

life as is possible.

The Future of Therapeutic Recreation and TBI

The field of Therapeutic Recreation faces several serious issues in the future. The first is

that the field has not sufficiently convinced the medical and insurance communities that

Therapeutic Recreation is “medically necessary,” and, therefore, is not a covered benefit

in many insurance policies. This is, in part, due to a failure to view recreation as part of

a holistic health and wellness model. Therapeutic Recreation, historically, has not taken

the time and resources to conduct and disseminate respected scientific research addressing

its efficacy and cost-saving potential. The fact that Therapeutic Recreation is not included

as a benefit in insurance policies creates a dilemma for rehabilitation providers. Even

though hospital and rehabilitation administrators may recognize the value of Therapeutic

Recreation, difficult economic times often make them unable to offer such services or force

them to cut back on them, unless they have some philanthropic resource to fund recreation

staff and programs. In the recent past, the number of Therapeutic Recreation specialists in

rehabilitation facilities has declined due to economic pressures on institutional budgets.

This action is seen as a measure to reduce operating expenses while exacting little perceived

negative effect on the rehabilitation outcomes of individual consumers. Ideally, a case load

in an inpatient rehabilitation setting caring for those with new catastrophic injuries would

be five to six individuals, which is similar to a typical case load of a physical or occupational

therapist. A caseload of ten to twelve per therapist is

possibly manageable, but not ideal.

These ratios are predicated on the consideration that the Therapeutic Recreation specialist

is experienced and a functional part of an interdisciplinary treatment team. Unfortunately,

these ratios are generally not the case today as many rehabilitation programs have signif

icantly reduced their recreation departments or eliminated the departments entirely.

However, it is strongly argued that eliminating or cutting recreation resources may, in

fact, add expenses and create more burden on rehabilitation programs. First, the physical,

cognitive, psychosocial, and life satisfaction needs of people with disabilities and their

families will continue to exist in the absence of Therapeutic Recreation. Without recreation

resources, those needs simply spill over to physicians, nurses, psychologists, therapists,

and other members of rehabilitation teams. Recent observations in one institution were

that the absence of Therapeutic Recreation resulted in a significant increase in nurse call

light activity. Counselors, nurses, and psychologists experienced substantial increases in

patient and family needs, increased incidents of customer dissatisfaction, and staff stress.

This ultimately forced the institution to hire more staff and take steps to repair damage

to its marketing efforts. Therefore, the absence of recreational options and time in reha

bilitation programs creates a higher consumer and family demand, and appears to offer

little or no financial relief to the institution in the long run.

Beyond the rehabilitation hospital, the greater concern is the deterioration of postreha

bilitation outcomes without recreation. In the absence of a Therapeutic Recreation program,

persons with TBI may be discharged with significant unresolved issues and unmet needs

and face a community without the skills and knowledge to master their future. These

unmet needs almost certainly arise as serious barriers that prevent or impede a return to

as functional a lifestyle as can be reasonably expected. Rehabilitation, without Therapeutic

Recreation intervention, of a person who has sustained a traumatic brain injury is incom

plete and sometimes risky. The most important component of the rehabilitation process,

next to medical improvement for which physicians, counselors, and therapists strive, is

functionality. Competent Therapeutic Recreation service is a vital component to restoring

that functionality and the greatest possible lifestyle quality that can be reasonably expected.

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Appendix 17A: Leisure Interest Survey Date

Therapeutic Recreation: Leisure Interests Survey

Check ALL areas of interest that apply:

[ ] Horseback riding

[ ] Fishing

[ ] Hunting

[ ] Rafting

[ ] Snow skiing

[ ] Cross-country skiing

[ ] Snowboarding

[ ] Snowshoeing

[ ] Snowmobiling

[ ] Skateboarding

[ ] Rollerblading

[ ] ATV

[ ] Motorcycling

[ ] Rock climbing

[ ] Kite flying

[ ] Horseshoes

[ ] Yard games

[ ] Archery

[ ] Badminton

[ ] Frisbee

[ ] Camping

[ ] Hiking

[ ] Travel

[ ] Flying/gliding

[ ] Hot air ballooning

[ ] Weight training

[ ] Volleyball

[ ] Tennis

[ ] Basketball

[ ] Football

[ ] Racquetball

[ ] Table tennis

[ ] Darts

[ ] Rugby

[ ] Track/field

[ ] Running/jogging [ ] Hockey [ ] Bowling [ ] Aerobics [ ] Golf [ ] Soccer [ ] Cycling [ ] Fitness/exercise [ ] Trap shooting [ ] Target shooting [ ] Wrestling [ ] Martial arts [ ] Canoeing [ ] Sailing [ ] SCUBA diving [ ] Water skiing [ ] Kayaking [ ] Swimming [ ] Boating [ ] Ceramics [ ] Leatherwork [ ] Stained glass [ ] Pottery [ ] Model building [ ] Drawing [ ] Painting [ ] T-shirt painting [ ] Tye-dying [ ] Cooking [ ] Needle crafts [ ] Wood crafts [ ] Jewelry [ ] Sewing [ ] Stamping [ ] Table/card games [ ] Foosball [ ] Computer [ ] Video games [ ] Billiards [ ] Photography [ ] Writing [ ] Pets [ ] Hobbies [ ] Volunteering [ ] Puzzles [ ] Reading [ ] Singing [ ] Musical instruments [ ] RC models [ ] Farming/ranching [ ] Gardening: indoor [ ] Gardening: outdoor [ ] Horticultural craft [ ] Movies [ ] Mountain drives [ ] Concerts/symphony [ ] Restaurants [ ] Shopping [ ] Parks/dancing [ ] Cultural events [ ] Zoos [ ] Museums [ ] Air/boat/auto shows [ ] Auto racing [ ] Rodeo/stock shows [ ] Bingo [ ] Gambling [ ] Dog/horse races [ ] Spectator sports [ ] Comedy clubs [ ] Botanic gardens [ ] IMAX [ ] Special events

Comments, including any NEW interests patient expresses:

Signature: _____

Typed Name: Date: 559

0-8493-1362-7/04/$0.00+$1.50

Children and Adolescents: Practical Strategies for

School Participation and Transition

Roberta DePompei and Janet Tyler

CONTENTS

Introduction

Children and adolescents sustain traumatic brain injuries (TBI) of many types and sever

ities. Regardless of the etiology, severity level, or progress made in acute care, the chal

lenges of returning to home, school, and community are reported to be some of the least

organized and poorly supported experiences for the child/adolescent and family. 1-3

DiScala, Osberg, and Savage 4 and DiScala 5 found that many children and adolescents who

are hospitalized at the time of injury are not referred to

in-patient rehabilitation. When

children and adolescents are reported to have three or less disabilities (problems with

walking, eating, talking, dressing, etc.), 80% are discharged to home and community and,

when there are four disabilities or more reported, 60% are discharged to home and com

munity. The result is that the majority of rehabilitation for children and adolescents is

completed within the community and the school is often the primary provider of services.

We have traditionally approached the medical, educational, and community living

aspects of service provision by referring to a continuum of care. DePompei 6 suggested

that viewing treatment and rehabilitation from a traditional continuum of care (Figure

18.1) that says that treatment begins in the hospital and ends in the community may not

be the most beneficial perspective and may, itself, be responsible for the lack of smooth

transition among hospital, school, family, and community. This traditional continuum of

care begins with emergency medical services caring for the injured child and transporting

him/her to a hospital where trauma teams and medical teams in the acute care hospital

provide specialized medical interventions. When stabilized, rehabilitation teams are

involved in the process of treatment. At a point where the child/adolescent is showing

progress and is medically able to return home, the medical team discharges the child to

home, school, and community. The responsibility then rests with community resources

and parents to provide additional rehabilitation and education services and to prepare

the child/adolescent for transition to community living.

DePompei believes that the continuum of care is insufficient to explain the concepts

surrounding the injury and reintegration to community. It is, in and of itself, responsible

for the false dichotomy of medical-educational systems treating these children. An alter

native to thinking about a continuum of care can be found in Condalucci's 7-9 model of

Community Interdependence. The interdependence concept suggests that there must be

an interconnection or interrelationship among two or more entities. In our case, medical,

family, educational, and community entities should be responsible to one another as points

of contact on the circle. The Circle of Community Interdependence (Figure 18.2) is not a

linear model as is suggested by the continuum of care, but a circular concept that begins

and ends in the community.

In this concept, the beginning point is not emergency medical service. The injury or

illness begins in the community where the child/adolescent is a living, contributing

member. Treatment of the child's brain injury then engages experts in medicine, education,

community, and the family who collaborate with the same goal: to return the child to

where he/she began — the community. As this concept is

based on a circle, any point on

the circle may be the beginning point of care. For example, the child with a mild brain

injury may not be seen first in the medical community, but may remain in the educational

community for several months or years until the problem is recognized. It is at this later

point that the child may be referred to the medical community for services. The Circle of

Interdependence, therefore, accounts for all aspects of service equally within the commu

nity. This concept is supported heavily in the literature. 10-15

If we provide services from a community of interdependence concept, we should assume

responsibility for the entire circle of care regardless of which part we play in the circle.

Thus, we, in the medical community, provide the treatment we are trained to provide.

But treatment is provided with consideration of the eventual return of this child to the

community; and we, in the educational and life-long living community, receive the child/

FIGURE 18.1

Continum of care for youth with ABI. (From Blosser, J. and DePompei, R., Pediatric Traumatic Brain Injury: Proactive

Interventions, 2nd ed., Delmar, New York, 2002, chap. 2. With permission.)

FIGURE 18.2

Circle of Community Interdependence. (From Blosser, J. and DePompei, R., Pediatric Traumatic Brain Injury:

Proactive Interventions, 2nd ed., Delmar, New York, 2002, chap. 2. With permission.)

adolescent with an appreciation of the complex and unique medical and behavioral aspects

that will affect learning by this child. Using this thought process, we are better able to

focus on the total needs of the child/adolescent to function within the community. 2

In this chapter, we operate from two perspectives — that the majority of rehabilitation

for children and adolescents occurs at school and in the community and that there is a

circle of community care that should guide the interventions. If these perspectives are

accepted, we can begin to plan, interactively and proactively, for this population. This

chapter will focus on the following:

• Describing the cognitive-communicative behaviors a student may exhibit after traumatic brain injury.

• Suggesting how the cognitive-communicative challenges will affect learning and behaving in the classroom.

• Outlining strategies for learning in school.

• Discussing laws and regulations that affect education, provision of services, and transition issues.

• Providing methods to affect seamless transitions throughout the educational lifetime of the student.

Cognitive-Communicative Challenges after Traumatic Brain Injury

Many cognitive processes can be affected after sustaining a traumatic brain injury. These

processes can impact learning and behaving in the classroom. The processes of attention,

processing speed, short- and long-term memory, organization, and problem solving are

often challenged. Additionally, impulsive behaviors and receptive, expressive, and prag

matic language skills are potentially problematic. When developmental issues are also

considered, challenges to learning are further confounded.

Classroom behaviors often reflect problems the student is experiencing with the above

mentioned cognitive-communicative processes. Unfortunately, many teachers attempt to

alter the behaviors without considering the underlying processes that are affecting the

behaviors. If these underlying processes are considered in the educational process, class

room behaviors and learning can be modified. Table 18.1 outlines the cognitive processes,

describes how a process can be challenged in a student with traumatic brain injury, and

gives examples of how these behaviors may appear in the classroom and may be affecting

classroom participation. The behaviors are simply examples of what can occur in the

classroom, but should serve to stimulate discussion about processes that may be affecting

the capacity for learning in a specific student and what behaviors might occur in a

particular classroom.

When transition from hospital or rehabilitation facility to school is planned, reports are

generated that usually describe challenges to the cognitive-communicative processes.

Additional information should be provided in the report about what the behaviors that

reflect the problem areas might look like in the classroom. Provision of such information

would be most beneficial to teachers prior to a school reintegration when preplanning

adequate structure and academic outcomes for the student is the most beneficial.

Table 18.1

Cognitive Processes, Challenges to a Student with TBI, and Possible Classroom Behaviors

Underlying

Cognitive Process How Process Can Be Affected after TBI Possible Classroom Behaviors

Attention Unable to sustain or maintain attention to complete tasks or activities. Fussing with books, papers, pencils; looking out a window; bothering a neighbor; daydreaming; moving about the classroom; calling for teacher's attention about a different matter.

Delayed processing

speed Much slower to respond to written or verbal directions, questions, requests. Difficulty with rate, amount of complexity of information presented. Unable to formulate a response to a question in usual time allotted for students to respond, even though he may know the correct response or behavior. Speaking out; throwing paper or pencil; ceasing attempt to participate; bolting from classroom.

Short-term memory Information is not held long enough to respond to it. Unable to follow directions to locate certain page in text, sequence several requests at once, or respond to request to spontaneously change an activity.

Long-term memory Information is unable to be stored for retrieval when needed; information that is stored cannot be accessed when required. Recognizes memory strategies, such as rehearsal, but cannot use spontaneously; vocabulary learned for health on one day is not recalled the next; poor test-taking skills.

Organization Unable to move through the day in a logical manner; planning for events or tasks is sporadic and

uneven, lacking a methodological means to achieve an end; inability to plan how to attack a job or assignment in a logical order. Does not recall order of the classroom day and is unprepared for class assignments or locations; begins an assignment but does not finish; offers to do a task, such as collect and sort classroom papers, but becomes lost in the details before completing the task.

Problem solving Often cannot locate alternative methods to solve a problem — believes there is only one way to approach a dilemma; disorganized in planning how to solve a problem; unable to sequence behaviors in order to resolve a challenge. Insists there is no solution to a problem; tries to solve a problem in exactly the same way for long periods of time; does not recognize suggestions of the teacher for changing a way to work a problem.

Impulsivity Speaks or acts out immediately without evidence of "thinking through" the situation. Leaves seat to sharpen a pencil when teacher is talking; tells teacher her hair is dirty and looks bad; employs socially unacceptable language or gestures.

Expressive language Difficulty with word recall; poor organization of conversation; speaks off topic; rambles. Written work is equally tangential and disorganized. Uses "thing," "you know" rather than the noun or verb; tells long, unrelated story to the class; telling or writing about how to complete a science experiment is out of order and disorganized.

Receptive language Poor comprehension of vocabulary; inability to sequence or follow multiple directions. Even though able to talk all the time, unable to follow through on what he/she is told to do; appears not to hear what teacher says and asks for multiple repeats.

Pragmatic language Difficulty with turn-taking, maintaining, and requesting in conversations; inability to monitor quality of conversation; poor comprehension of humor and puns; use of socially unacceptable words. Unable to maintain adequate social space with other students; touches the teacher to gain attention; calls out to the teacher numerous times when told to wait; keeps talking when others indicate they are disinterested; does not laugh at other students' jokes; can not use slang that others would accept; curses at the teacher or at peers.

Another challenge when planning proactively for the student is to consider the devel

opmental changes that may affect future growth and learning. Lash 14 stated that, in the

case of children and adolescents, the saying “time heals all wounds” should be “time

reveals all wounds.” Blosser and DePompei 16 also suggested that the child may not grow

out of the disability, but rather may grow into it. There are three developmental perspec

tives to keep in mind with this population.

• A previous base of knowledge may allow the student to score within normal limits on standardized tests immediately after the injury. Over time, as new learning should happen, the student is unable to keep up with curricular demands and begins to fail. Often, parents are not aware of this potential problem and schools do not recognize the connection to the traumatic brain injury.

• Developmental milestones may not be reached as the student grows. Ability to reason abstractly, use deductive or inductive problem-solving skills, organize homework for multiple teachers or subjects can be affected several years after the injury. This change in learning potential is sometimes not related back to the traumatic brain injury when it occurs many years after the initial injury.

• The brain of a student is in a constantly developing and changing mode. Myelination of brain cells continues to impact learning potential for years after the injury. Thus, the student who begins to fail as pragmatic, social skills, and adult personality traits should be emerging is not often identified as continuing to have challenges as a result of a traumatic brain injury that occurred years earlier and teaching strategies that may help are not considered.

Remembering that a child/adolescent continues to grow and change, we find accom

modating to the developmental potential or lack of reaching a developmental milestone

of the student with traumatic brain injury is often a challenge. It is also a joy to work with

a student who has potential to grow and evolve into a functioning adult.

The Case of John John was injured in a car crash the summer between kindergarten and first grade. He was unconscious at the scene and was hospitalized for 2 days with a diagnosed traumatic brain injury and broken leg. His preschool and kindergarten academic records indicated that he was a normally-developing child with prereading and math skills intact. He was able to read introductory first grade materials and was communicating with ease in all academic and social situations. After the crash,

Executive

functioning Difficulty with many of the processes listed above, plus an inability to recognize strengths and weaknesses. Does not recognize when homework was completed correctly and may not do the same type of assignment well the next day; cannot outline what behaviors were successful in the classroom; does not describe what problems are experienced when trying to follow directions.

Source: From De Pompei, 2003.

Table 18.1 (Continued)

Cognitive Processes, Challenges to a Student with TBI, and Possible Classroom Behaviors

Underlying

Cognitive Process How Process Can Be Affected after TBI Possible Classroom Behaviors he entered first grade where he continued to demonstrate adequate learning skills in first and second grade. His grades were passing to outstanding in all academic areas. However, he began to stutter at the end of first grade and, by the end of

second grade, had been referred to the speech-language pathologist. He began

failing most academic requirements for reading and language arts in the third

grade, and by fourth grade was referred to special education for a complete

evaluation. School personnel considered him to be learning

disabled (LD) and no

reference to the traumatic brain injury was made in any evaluation. There were

no assessments of cognitive processing completed. John is an example of a youngster who performed well after his initial injury

on previously learned information, but failed to meet developmental milestones

as he grew. As there was no annual evaluation in place, his learning difficulties were not recognized until they became severe and interventions that may have facilitated learning were not instituted in a timely fashion. When the problems were recognized, the association with the traumatic brain injury was lost and he was diagnosed as LD rather than TBI.

The Effect of Cognitive-Communicative Challenges on Learning and

Behaving in the Classroom

The Interrelationship of Language, Executive Functioning, and Self-Regulation

Singer and Bashir 17 discussed the concept that language, executive functioning, and self

regulation (behavior) are interrelated and emphasized that employing metacognition for

academic success is critical. They stated that the role of language in both executive func

tioning and the self-regulatory process is not yet well acknowledged, but is essential to

both processes. Vygotsky 18 stated that speech plays a central role in the development of

self-control, self-direction, problem solving, and task performance. He argued that speech

is learned in the course of social interaction and is the medium for learning and knowing

how to regulate personal behavior. Wertsch 19 and Bashir, Conte, and Heerde 20 suggested

that children learn appropriate language and then use verbal scripts to regulate thinking

that guides participation in the learning and communication demands of school. Children

use these scripts to respond to the varied discourse styles and instructional demands of

teachers and other communication partners. Through the use of scripts, children acquire

appropriate behaviors for learning. 21 “In school, language becomes both the object of

knowledge and the means through which knowledge is acquired. Thus, within the early

school years, and beyond fourth grade in particular, the role of language becomes almost

inextricably intertwined with executive functioning and the self-regulatory process.” 17(p. 267)

In this conceptual framework, language skills form a base for development of executive

functioning and self-regulation and become an integral part of those functions.

Challenges to Language, Executive Functioning, and Self-Regulation for a Child with

Cognitive-Communicative Problems

When a student with traumatic brain injury is faced with learning and behaving chal

lenges, teachers and therapists should appreciate the part that language plays in the

development of executive functioning skills that can lead to increased self-monitoring.

The student with cognitive-communicative problems will be at risk in any learning situ

ation and will also have problems with the development of executive functioning and

self-regulation skills. Teachers and therapists will often try to modify behaviors in the

classroom without first assessing and intervening with language-based learning. Thinking

about development and treatment from Singer and Bashir's 17 framework may be beneficial

when developing plans for educational intervention.

Cognitive–communicative problems can be directly related to problems with curricular

based knowledge and skills areas. Each grade level has published curricula that guide

teachers in knowing what should be achieved during the academic year. The relationship

of language demands on the curriculum and the effect on a child with traumatic brain

injury is outlined in Figure 18.3. (The information in this figure is intended to provide an

idea of what the curriculum demands could be and is not intended to be all-inclusive.)

By obtaining the curriculum for a specific grade level and reading through the knowledge

and skills expected, a therapist or teacher should be able to anticipate the challenges to

the student with traumatic brain injury and propose teaching modifications that account

for the learning challenges of the student.

The Case of John (Continued) John was evaluated and found to have the following curricular-based learning challenges: Language Arts: Vocabulary development essentially stopped after first grade. He demonstrated word-finding problems and fluency difficulties were based in his lack of ability to express himself verbally. Language example of John's discussion about his need for a computer. Therapist: "Is there anything else that would help you?" John: "Yeah, to have my old own special thing (gestures typing) so I, I, I,

um, can work all, all of my, my, um, assignments on one thing because of what I'm to a sharing a bunch of things with a bunch of other students and I cannot do that." Therapist: "Books? Like your books in class? Is that what you are sharing?" John: "No, no! My, ah, own own, ah, laptop computer. See once first I use one thing, ev, ever, everybody else wan to use it." These same word-finding problems were also reflected in spelling and writing attempts. His reading and spelling were found to be at the second grade, third month level. Writing was at kindergarten, ninth month level. He used gestures well and was often assumed to be communicating better than his language capacity indicated he could. History: John was unable to understand concepts of time and place and could not deal with "when" questions. He could not sequence temporal events and experienced difficulty with most history-based concepts. Science: John had no concepts for sequencing beyond two steps. He was unable to use deductive reasoning and saw no cause-effect relationships. Math: John was able to complete most addition, subtraction, multiplication, and division problems. He could not apply the math skills to word problems.

The student will often face challenges with language skills within the curriculum. Following are examples

of the demands and possible interventions: ENGLISH AND LANGUAGE ARTS Language Demands on Curriculum Challenge to Student with TBI Possible Proactive Solutions

1. Interpret "wh" questions in spoken and written form 1. Lack of problem solving skills to sort out different meanings of key words to aid in answering "wh" questions 1. Teach main idea of "wh" questions (who means person, what means fact, etc.)

2. Process grammatical structures, sometimes rapidly 2. Slowed information processing – unable to sort rapidly; inability to learn new grammatical structures and use functionally 2. Give information at slower pace; review grammatical structures and help to use functionally in spoken and written output

3. Understand abstract word meanings (antonyms and synonyms) 3. Difficulty knowing similarities and differences 3. Teach similarities and differences and how to recognize in spoken and written materials

4. Employ accurate recall and use of retrieval for word meanings and facts 4. Short- and long-term memory problems

4. Encourage vocabulary development within specific curriculum areas by use of memory devices, such as notebooks, associations, and categorization

Add specific language demands

for your client List possible problem areas Suggest interventions for the therapist and teacher SOCIAL STUDIES (HISTORY AND GEOGRAPHY) Language Demands on Curriculum Challenge to Student with TBI Possible Proactive Solutions

1. Employ temporal terms, concepts, and relationships 1. Difficulty with episodic and temporal events 1. Use compensatory strategies for episodic memory

2. Knowledge of past, present, future 2. Unsure of relationships that include time plus space 2. Teach concepts of time and make relationships functional

3. Use of organizational and sequencing abilities 3. Poor development of executive functioning 3. Supply compensatory strategies for sequencing and organization

4. Ability to take notes from lecture, identify main ideas and supporting information 4. Inability to locate main ideas and lack of recognition of supporting data 4. Teach main idea vs. supporting data

5. Ability to recall and retrieve related information 5. Memory impairments for recall 5. Develop compensatory strategies for recall and retrieval

Add specific language demands

for your client List possible problem areas Suggest interventions for the therapist and teacher MATHEMATICS Language Demands on Curriculum Challenge to Student with TBI Possible Proactive Solutions

1. Ability to use syntactic and semantic components of language to solve verbal math problems 1. Difficulty with semantic aspects of word problems 1. Aid in finding the main idea of the verbal math problem — what information is needed to solve the problem

FIGURE 18.3

Language Demands on the Curriculum: Implications for the Student with Traumatic Brain Injury. (From

Blosser, J. and DePompei, R., Pediatric Traumatic Brain Injury: Proactive Interventions, 2nd ed., Delmar, New

York, 2002, pp. 298–301. With permission.)

Treatment of Cognitive-Communicative Strengths and Needs: An

Integrative Approach for School

Cognitive-communicate and behavioral deficits following traumatic brain injury will

require special interventions throughout the student's education. Although long-term

deficits following traumatic brain injury are well documented, empirical research on the

effectiveness of particular instructional practices for dealing with subsequent learning

problems in students with traumatic brain injury is lacking. Given this absence of research,

Ylvisaker and collegues 22 stated that teachers must examine effective teaching practices

and proven instructional interventions for students with other types of learning difficul

ties. They recommended identifying students by functional need and connecting identified

needs with research-based strategies.

2. Recall and use "math language" when needed — many complex concepts are carried in a few words: "divide," "multiply," "add" 2. Unable to recall the concept associated with a single word, misses the instruction to "add" 2. Teach the meaning of single words that carry considerable intent — aid in recall of the concepts and processes underlying the single word

3. Employ sequencing skills to complete a process 3. Sequencing skills are often impaired 3. Work on meaningful, functional sequencing skills

4. Use language to understand the word problem and then complete the math to solve the problem 4. Poor recall, inability to find relevance within the word problem

(Oftentimes, the child with TBI can do the math if he/she can understand the words that formulate the problem) 4. Develop ability to find the main question within the problem and associate the concepts necessary to solve it

Add specific language demands

for your client List possible problem areas Suggest interventions for the therapist and teacher SCIENCE Language Demands on Curriculum Challenge to Student with TBI Possible Proactive Solutions

1. Knowledge of concepts such as more than/less than, when/then, before/after 1. Inability to recognize relationships and concepts that are not concrete in nature 1. Teach relationships within the word pairs

2. Recognition of cause and effect 2. Inability to recognize relevance of cause and effect 2. Aid in recognizing the relevance of cause and effect

3. Recall of specific terms and processes 3. Vocabulary development may be sporadic and inability to recall newly learned words is problematic 3. Devise memory strategies and compensatory aides for new vocabulary

4. Demonstration of learned knowledge in projects that often require sequencing of events and steps 4. Problems sequencing 4. Employ memory aides for sequencing multiple steps (including written cues)

Add specific language demands

for your client List possible problem areas Suggest interventions for the therapist and teacher

FIGURE 18.3

Continued.

Identifying Student Needs

Determining the individual needs of a student will require careful evaluation of the

student’s functioning. To obtain a comprehensive picture of the student’s functioning,

assessment information from a variety of sources (e.g., neuropsychology, speech pathol

ogy, occupational therapy) should be combined with functional evaluation of the child's

skills. Pearson 23 recommended that, in addition to assessment of underlying cognitive

processes (how will deficits in short-term memory, long-term memory, sequencing, or

organization affect performance in the classroom), team members should be readily able

to answer questions such as the following:

• At what grade level does the student read? What is the average reading rate for the child's age and how does the child compare with peers?

• Can he do grade level math? Does he use his fingers to calculate?

• Can he follow classroom directions (single-step, multi-step)?

• Can he correctly sequence steps?

• Can he write? Is he able to keep up taking notes? Is the writing legible?

Evaluation of actual task performance in settings where the student's adaptive skills are

called into play is critical, because assessments given under ideal conditions do not reflect

the kind of difficulty a student may face in a busy classroom with less guidance and

structure. Ongoing functional assessment of the student in the school environment is

required to accurately determine the student's current functioning and needs in order to

develop interventions.

This segment discusses two methods for such interventions. First, suggestions for

addressing underlying cognitive processes in the classroom are presented. This is followed

by discussion of teaching techniques that may aid the acquisition of academic skills. It is

hoped that use of these strategies will establish outcomes for the student that develop

independence for learning and generalization of what was learned to new situations. The

overall outcome is to move the student away from special education services and into the

regular classroom whenever possible.

Strategies for Addressing Underlying Cognitive Processes

Results of the comprehensive evaluation may reveal that the student has a number of

specific deficits in underlying cognitive processes. To determine which teaching methods

may be most effective in meeting an individual student's particular needs, educators

need to examine instructional interventions and teaching practices that have been proven

effective for addressing similar deficits in students with other types of learning difficul

ties. For example, organizational impairments following traumatic brain injury will

necessitate proven instructional strategies for organization, such as task analysis (break

ing a given task into components or steps) and advanced organizational support (pro

viding an oral or written preview of information to be covered in a lesson). Lack of

strategic learning ability will require specific strategy instruction (see Deshler, Ellis, and

Lenz 24 for a comprehensive review of strategy research

and methods). Additionally, a

variety of effective teaching practices that have been found to be correlated positively

with student achievement (e.g., the provision of structured lessons, guided practice,

immediate feedback, clearly stated expectations, frequent review, and small-group

instruction) may be particularly beneficial for meeting the needs of students with trau

matic brain injury. 25

In conjunction with matching specific teaching methods to identified needs, a number

of teaching strategies and accommodations should also be considered to address problem

areas. These strategies can be successfully employed in general education settings or in

the context of special education environments. A sampling of common deficits following

traumatic brain injury are identified below, followed by examples from Tyler, Blosser, and

DePompei’s 26 and Tyler and Mira’s 27 comprehensive lists of teaching strategies for students

with brain injuries.

Attention/Concentration

To improve attention and concentration, educators should:

• Reduce distractions in the student’s work area (remove extra pencils, books, etc.).

• Provide preferential seating (an area that has the least amount of distraction and is closest to where instruction is taking place).

• Divide work into small sections. Have the student complete one section at a time.

• Establish nonverbal cueing system (e.g., eye contact, touch, etc.) to remind the student to pay attention.

Memory

To aid memory, educators should:

• Teach the student to use external aids such as notes, timers, calendars, and assignment books as self-reminders to compensate for memory problems.

• Frequently repeat and summarize key information.

• Use visual imagery, when possible, to supplement oral content.

• Teach the student to categorize or chunk information.

• Relate new information to the student's relevant prior knowledge.

• Demonstrate techniques such as mental rehearsal and use of special words or examples as reminders.

• Ask the student to verbally rehearse and summarize information.

Organization

To improve organization, educators should:

• Provide the student with written checklists of steps for complex tasks.

• Color-code the student's materials for each class (textbook, notebook, supplies).

• Provide an assigned person to review the schedule at start of school day and organize materials for each class.

• Supply outlines coordinated to class lectures (require the student to take notes within each section).

Decreased Speed of Processing

To help the student compensate for decreased speed of processing:

• Deliver instruction in small increments.

• Allow the student to have additional time to process information and complete tasks.

• Provide sufficient time for the student to respond to verbal questioning.

• Pair verbal instructions with written instructions.

• Allow the student to take exams in settings that do not have time restraints.

Problem Solving

To help the student to develop problem solving skills, the educator should:

• Have the student generate possible solutions to problems as they arise in an activity.

• Teach the student the steps involved in problem solving (e.g., identify problem, list relevant information, evaluate possible solutions, create an action plan).

Addressing Academics Deficits

Following a traumatic brain injury, a student may require specialized assistance or

accommodations to continue to participate in the regular curriculum. A number of

adaptations which will increase the success of student learning can be provided during

the teaching of academic subject matter. Tyler, Blosser, and DePompei 26 provided the

following examples of suggested techniques for addressing underlying deficits while

teaching subject matter.

Math

Educators should:

• Demonstrate mathematical concepts using concrete items. Allow the student to use manipulative times to solve math problems.

• Create functional activities for the student to practice mathematical concepts (e.g., planning a budget, purchasing small items from a school store).

• Practice word problems with pictures or stories that relate personally to the student.

• Allow the student to use a calculator to aid solving multiple-step problems.

Reading

Educators should:

• Review key vocabulary words prior to reading material.

• Highlight key words with colored marker.

• Provide the student with key questions to answer before reading.

• Ask the student to orally summarize content after reading small segments of a large passage.

Writing

Educators should:

• Provide for alternative response modes for work (e.g., let the student dictate responses, tape record answers).

• Allow the student to take exams orally.

• Provide specialized writing paper (e.g., raised lines).

In some cases following traumatic brain injury, even with accommodations, a student

may no longer be able to acquire information and skills using traditional methodologies

and curriculum provided in the general education settings. In such cases, specialized

intervention techniques are required. One such specialized approach is the use of the

Direct Instruction model. The Direct Instruction model provides a highly structured,

systematic instructional approach that incorporates several teaching practices that have

been consistently linked to pupil achievement outcomes (see Adams and Engleman 28 for

a comprehensive description of the model and summary of research).

Direct Instruction techniques have been shown to be effective in teaching both academic

and behavioral skills to children with brain injuries. 29 Glang, Singer, Cooley, and Tish 29

stated the Direct Instruction model is thought to be effective with children with brain

injury because it specifically addresses many of the common learning problems typical of

these students. For example, Direct Instruction provides rapid instructional pacing and

high levels of student engagement which address attention and concentration difficulties.

The model also provides sufficient practice of skills, teaches generalizable strategies, and

delivers corrective feedback to address difficulties students with brain injury face in

learning new concepts and information.

Assessing Teaching Strategies

Once instructional practices are employed, the effectiveness of these practices must be

continually evaluated. Also, because of the rapidly changing needs of the student follow

ing traumatic brain injury, ongoing functional assessment of the student in the school

environment is required to accurately determine the student’s current functioning.

The Case of John (Continued) Based on results of the

comprehensive evaluation and functional assessments, the Individualized Education Program (IEP) team developed an educational program to meet John's unique learning needs. John received specialized instruction in reading and language arts. John's special education teacher used commercially developed Direct Instruction reading and spelling materials, which provided the structure, practice, and immediate feedback John needed to succeed. The special education teacher provided support for John in his regular education history, science, and math classes. By assisting John with developing timelines and sequencing information, providing visual-spatial displays, and preteaching content vocabulary, John was able to participate in the general education curriculum. Special accommodations, such as reduced writing requirements, preferential seating, and peer assistance were provided throughout the day. John also received school-based speech–language services for 30 minutes, 3 times per week. During this time, John's word finding problems were addressed. The decision to stimulate

language and not work directly with the fluency problem was based on the thought that, with increased expressive competence, fluency patterns of repetition and word substitution would decrease. Shortly after the IEP was implemented, John began showing progress. John's family and teachers reported that, in addition to making academic gains, John's emotional well-being had also improved since he had begun receiving the help he needed.

Laws and Regulations that Affect Education, Provision of Services, and

Transition for Students with Traumatic Brain Injury

Because of long-term physical, cognitive, language, and psychosocial difficulties, students

with traumatic brain injury may require special education services, special assistance, or

accommodations. Students can access such services under the Individuals with Disabilities

Education Act (IDEA) or Section 504 of the Rehabilitation Act.

IDEA

The Individuals with Disabilities Education Act (IDEA), an outgrowth of the Education for

All Handicapped Children Act of 1975 (P.L. 94-142), guarantees a free appropriate public

education for children 3 to 21 years old. To receive services under IDEA, a multidisciplinary

team must evaluate and determine a student to have a qualifying condition that requires

special education services. Since 1990, IDEA has recognized traumatic brain injury as one

of the categories that qualify students for special education services. Once the team has

determined a student is eligible for special education, an individualized education program

(IEP) must be devised and carried out. The IEP is, essentially, a document that describes

the action plan for the student's educational program and serves as a contract between

parents and the school for the delivery of educational services to the student.

Through IDEA, a full continuum of special education placement options, ranging from

homebound services to placement in the general education classroom with special edu

cation support, is available. Regardless of setting, the term special education means spe

cially-designed instruction to meet the unique needs of the student and may include direct

skills instruction, the teaching of compensatory strategies, and vocational education, as

well as the provision of modifications and accommodations. Related services such as

speech-language therapy, occupational therapy, physical therapy, counseling, adaptive

physical education, and behavior management services are

also available through IDEA.

According to Tyler and Savage, 30 due to the underlying medical cause of the disability,

the resulting deficits, and the evolving needs of the child, IEPs written for students with

traumatic brain injury require procedures that vary from traditional IEP development. For

example, information from a variety of sources and disciplines outside the school system

needs to be translated to determine present levels of functioning. Goals need to address

cognitive processes rather than strictly academic impairments and IEP reviews need to

be conducted more frequently (e.g., every 2 to 3 months, initially) to address dramatically

changing needs. In addition, the student's initial IEP should be a joint venture among the

health care facility, the school, and the family.

Section 504

Not all students need, or are eligible for, special education even though a brain injury

may affect learning. With classroom adjustments and curriculum modifications, a student

may still be able to participate in the general education program by receiving services

under Section 504 of the Rehabilitation Act of 1973. Section 504 is a civil rights act that

protects the civil and constitutional rights of persons with disabilities. According to

Section 504, schools receiving federal financial assistance may not discriminate against

individuals with disabilities. Because some students with disabilities may need adjust

ments or modifications to benefit from their educational program, classroom teachers and

school staff are required to provide them. Unlike IDEA, Section 504 is a regular education

management responsibility.

To receive services under Section 504, a person must be considered disabled. According

to Section 504, a person may be considered disabled if the individual (1) has a mental or

physical impairment which substantially limits one or more major life activities (e.g.,

walking, breathing, learning, working), (2) has a record of such an impairment, or (3) is

regarded as having such an impairment. To determine eligibility for Section 504, a student

must be evaluated by a team of individuals who are familiar with the student. The evalu

ation typically consists only of gathering documented information from a variety of sources

and, since most students with traumatic brain injury have documentation from outside

sources, additional evaluation may not be required. The team then reviews the evaluation

data to determine the nature of the disability and how it affects the student’s education.

To document services, a Section 504 plan describing services or accommodations is

developed by the team. The plan lists specific adjustments to the learning environment

and modifications to the curriculum. The plan also indicates who is responsible for car

rying out and evaluating each adjustment or modification. Based on the student’s needs,

any number of accommodations can be provided with a 504 plan. They include environ

mental, curriculum, methodology, organizational, behavioral, and presentation strategies.

Tyler and Wilkerson 31 offer information about accommodations that may be provided

through a Section 504 plan. Table 18.2 provides a sampling of their suggestions for possible

accommodations to meet common concerns following brain injury.

Because Section 504 protections extend to a larger population of students than IDEA

does, Section 504 should be considered as a venue for receiving needed support for

students who do not qualify for services under IDEA. Additionally, since IDEA does not

apply to students who have graduated from high school or those who have reached age

22, Section 504 serves as the vehicle for obtaining services in postsecondary settings.

Transitioning Students with Traumatic Brain Injury

Following a traumatic brain injury, transitioning is often thought of as a one-step activity

of moving a child from the hospital to the school. While the importance of careful planning

for school reintegration has been well documented in the literature, 2,3 there are a number

of other important transitions that occur throughout a student’s education career. In reality,

transitioning occurs repeatedly over the lifetime of the student with traumatic brain injury.

Certainly, the student will transition from medical interventions to home, school, and

community. Once in school, the child will encounter transitions with the passage from

grade level to grade level, the change from elementary to middle school, and middle to

high school. Beyond that, the student will transition from high school to postsecondary

education, employment, and community living.

IDEA requires that, beginning at age 14, a transition plan for movement out of school

to postschool activities, employment, independent living, and community participation

specific outcomes must be identified and supported by transition services which may

include academic support, community-based education focused on employment, func

tional and independent living skills, personal and social content, and career awareness.

Because the same cognitive-communicative challenges exist for all transitions, planning

for any transition must be completed with as much proactive planning and anticipation

of challenges as the IEP process requires.

The following is a list of steps for planning transitions. It should be noted that the steps

are the same whether the transition is from hospital to school, within school, or from

school into community.

Step One: Plan in a Timely Manner

One of the keys to adequate planning is taking sufficient time to devise a well thought

out plan that accommodates individual strengths and needs. Transition planning should

occur well in advance of the time of the actual event. Therefore, hospitals should contact

schools well in advance of an anticipated return date (preferably, as soon as the child is

hospitalized). School staff should begin planning for in-school transitions months prior

to the child’s move to a different grade level or school. Transition plans focusing on TABLE 18.2 Section 504 Plan Accommodation Consider the following accommodations for students qualifying for 504 services: Memory Deficits Written, as well as verbal, direction for tasks Frequent review of information Monitored planner (check off system) Fatigue Reduced schedule Planned rest break Fine Motor Difficulties Note taker for lectures Oral examinations Scribe for essays Processing Delays Increased time to complete assignments/tests Extended time to provide verbal answers Complex directions broken into steps Attention Visual and/or verbal prompts Preferential seating Technology Computer/word processor for responding and homework Tape recorder for class work and class lectures Use of communication devices

vocational, postsecondary educational, and community living must be in place beginning

at age 14, or sooner, if necessary.

Step Two: Develop Transition Plans that Are Specific to the Strengths and Needs of

the Student

All members of the team should be prepared in advance of the meeting. Some questions

that the student and family should think about prior to the meeting include:

- What type of education is desired: regular education, special education services, trade school, two-year college, four-year college, none?

- What vocational tracks may be of interest?

- What type of independent living might be desired?

• What leisure activities are of interest?

• What are the student’s hopes and dreams for the future?

• What strengths does this student have to achieve any of the above desires?

• What challenges to achieving the above goals might exist?

• How can a specific plan be devised to address these challenges in the next few years?

• Who will need to participate in order to work toward these goals?

• What evaluation tools will be employed to determine if there is movement toward achieving these goals?

• Who will participate with the student to determine if the goals are being met or if they should be altered?

• How often will a reassessment of this plan be completed?

Step Three: Be Involved in the Meetings

Decisions and plans must be completed at the meeting. Lash 32 and Lash, Kahn, and

Wolcott 33 provide outlines for parents, students, teachers, and advocates that address skills

necessary for planning reintegration to school or preparing for work and adulthood. They

outline necessary skills of assessment, information gathering, referral, service coordina

tion, advocacy, and evaluation as essential to the planning and implementation process.

The reader is referred to these sources for an in-depth discussion of these areas.

The discussion should focus on the resources and teaching strategies necessary to aid

the student in the classroom and beyond. Some ideas may include:

Resources

• What community resources might be available? For example, Office of Students with Disabilities located on every state college or university campus; Bureau of Vocational Rehabilitation services, work-study programs at high schools, volunteer opportunities in the community.

• What other agencies might be able to help — Drug and Alcohol Boards, YMCA, Medicare, Departments of Mental Health or Mental Retardation/Developmental Delay, Family Services, Independent Living Centers?

• What opportunities for transportation, housing, and personal assistance might exist through agencies, churches, and social or private organizations?

Strategies

• What cognitive challenges may need to be accommodated and how will these behaviors appear in the classroom, workplace, or community?

• What accommodations might work (planners, coaches, reminders, adapted equipment, reduced schedules, technology applications for accommodation, note-takers, communication devices)?

• Who should be involved in assuring these accommodations are provided and are ongoing in support of the student?

Step Four: Maintain Contact with the Hospitals, Schools, and Community Resources

over the Entire Education of the Student

As the student transitions from setting to setting, do not assume the plan or information

is being transferred from teacher to teacher, supervisor to supervisor, or school to school.

Annual reviews of progress and modifications of plans are essential to continued success.

It is also crucial that the plan be shared with all individuals who work with the student

at work, school, or in the community whenever there is a change in personnel or location

throughout the year.

A checklist for transitioning is depicted in Figure 18.4.

The Case of John (Continued) When John was 14, the checklist was employed to establish a transition plan for him. The planning team consisted of John, his grandmother (legal guardian), the director of special education, two classroom teachers, the work-study coordinator, speech-language pathologist, representative of the Rehabilitation Services Commission, and a representative of a local rehabilitation center that held a grant to effect school-to-work transition for youth with disabilities. The original plan included assessing John for his vocational interests as well as discussion about his challenges in academic and social areas. His strengths included fine motor coordination, outgoing personality, math computation, use of gestures to augment communication attempts, and mechanical aptitude. John was placed in regular classes that emphasized managing skills for daily independent living, home economics, art, and math. He was placed in an LD classroom for assistance with language arts. He began in a vocational school where he learned auto mechanics. He had a job coach with him for all new classes. He attended the local rehabilitation facility 2 days a week where he was taught additional job skills which included socialization skills training, assistance with strategies for following directions, and self-advocacy training. He called periodic meetings of his IEP and transition teams to discuss progress and additional challenges. Accommodations were made, at his request, for training for job personnel about his poor organization and he provided an in-service regarding his communication challenges and how he adapted to them. Over the following 3 years, adaptations to his transition plan were completed six times. Training of personnel regarding John’s strengths and needs was completed four times as situations in teaching, coaching, and employment changed. Presently, John is employed half-days at a local car dealership where he is apprenticing as an auto mechanic. He continues his academic work the other halfday where he attends two regular classes and continues with the assistance of the LD teacher. He continues to be challenged academically in language arts. He

1. Identify key players at each agency

2. Determine what policies and procedures exist for all agencies involved

3. Provide all pertinent information about the student, including tests,

cognitive challenges, behaviors that can be anticipated

a. Obtain all written records

b. Generate a profile of student strengths and challenges

c. Identify the challenges that may interfere with the successful performance of the student

d. Provide samples of present work levels that represent capabilities and levels of performance

4. Relate the challenges and strengths to the new setting

a. Discuss accommodations needed

b. Offer choices based on the demands of the setting and the needs of the student

5. Determine the agency’s readiness to accommodate the student

a. Provide adequate staff training

b. Assess environment for necessary changes to accommodate physical, cognitive needs

6. Determine what assessments may be needed for placement in the agency

7. Outline strategies for supporting performance

8. Determine which placement, personnel can best meet student needs

9. Observe the environment to determine any supports not in place or

additional strategies that can help

10. Maintain ongoing communication of all involved parties after the plan is

begun

11. Modify the plan as often as indicated and prior to a serious problem

emerging

12. Outline a plan of action if problems emerge so staff can be proactive, rather

than reactive

13. Outline a functional evaluation plan to determine what is working and what

should be changed

14. Maintain contact among the key personnel identified in Step 1

15. Add any other steps pertinent to this student

FIGURE 18.4

Transition Planning Guide. should graduate this spring at age 19 and the car dealership anticipates hiring him into a full paying position.

Summary

This chapter has focused on the cognitive-communicative challenge that can emerge after

traumatic brain injury. These challenges often are overlooked in the struggle to provide

adequate educational programming. When strategies are employed consistently and per

sonnel collaborate to provide ongoing transition and intervention, students can modify

behaviors and become contributing adult members of society. These plans can be modified

for youth with many levels of severity. While all will not transition to gainful employment,

college, or independent living, it is our belief that all can be accommodated into society

for a better quality of life. Hippocrates suggested long ago that we use our skills for those

who are mildly injured and also for those who are severely injured — that they all deserve

our attention and efforts. We think he is right!

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19

The Contribution of the Neuropsychological Evaluation to Traumatic Brain Injury Rehabilitation

Jay M. Uomoto

CONTENTS

Introduction

One of the earliest accounts of the physical and cognitive consequences of acquired brain

injury was penned by the renowned neurologist, Kurt Goldstein 1 in his book published

in 1942, Aftereffects of Brain Injuries in War. In this comprehensive volume, Goldstein

described characteristic symptoms of the patient with brain injury based upon his clinical

experiences in treating and monitoring numerous patients, some over the course of 10

years. Of note were his precise insights as to the scope and genesis of disorders of motor

output, sensory input, visual-spatial, brain stem, and frontal lobe functions. Goldstein's

neurological insights converged with his methods of assessment of cognitive functions

and impairments, and described his approach to what would today be considered the

neuropsychological assessment.

These investigations are carried out for the following reasons:

- To evaluate some of the mental functions usually separated in psychology, such as memory and attention.

- To evaluate the patient's general level of performance. Some mental and physical performances are investigated over a period of time. The results obtained here are also useful for our judgment of the subject's capacity in general.

- To ascertain the circumscribed mental defects, in detail, as a basis for procedure in retraining.

- To study the subject's working capacity in special kinds of labor. (p. 92)

It is important to observe that much of what Goldstein wished to accomplish with

what he termed the psychologic laboratory examinations defines the essential goals of the

neuropsychological evaluation in the context of traumatic brain injury (TBI) rehabilita

tion. These goals are defined as (1) comprehensively delineating the cognitive impair

ments that have resulted from traumatic brain injury, (2) assaying cognitive assets to

thoroughly describe the patient's overall functional capacities, (3) utilizing neuropsycho

logical findings in the service of rehabilitative therapies, and (4) integrating neuropsy

chologic insights into the enterprise of improving quality of life, including return to work,

school, and community.

The use of the term neuropsychology is attributed to Sir William Osler 2 in an address to

the Phipps Psychiatric Clinic at Johns Hopkins Hospital in 1913. In this context, Osler

wished to draw attention to the interactions between brain function and psychiatric

disorder. In modern neuropsychology, this same interaction defines the field as the study

of brain-behavior relationships. 3 Although utilized for different purposes in a broad range

of neurological conditions, in traumatic brain injury rehabilitation, the neuropsychological

evaluation can be critical to defining effective rehabilitation therapy for the patient.

Neuropsychological testing procedures have been used in rehabilitation settings for at

least 30 years, primarily for the four purposes given above. The practice of neuropsychol

ogy in TBI rehabilitation has been enhanced by advances in neuroimaging techniques,

outcome research, advances in the neurobiology of cognition, and neuroplasticity. Thus,

neuropsychology has more to bring to the table in the process of improving the lives of

those who are survivors of TBI.

The Context of the Neuropsychology of Traumatic Brain Injury

Neuroimaging and the Neuropsychology of TBI

Over the past 10 years, there have been significant advances in neuroimaging techniques

that have had import to the role of the neuropsychological evaluation in health care service

delivery. Such techniques as positron emission tomography (PET), single photon emission

computed tomography (SPECT), functional magnetic resonance imaging (fMRI), and mag

netic resonance spectroscopy (MRS) have augmented our understanding of brain–behav

ior relationships and, at the same time, reduced the need to employ neuropsychological

testing as a first-line method for identifying the presence and location of brain lesions.

Technologies such as PET and SPECT examine regional blood flow, whereas fMRI mea

sures regional oxygen content; both image cortical and subcortical regions.

Much research has been conducted to understand the relationship between neuropsy

chological functioning and regional cerebral glucose metabolism in the brain. Kesler,

Adams, and Bigler 4 examined 52 patients with TBI, utilizing MRI, quantitative magnetic

resonance imaging (QMR), and SPECT, along with neuropsychological and psychological

testing procedures. Measures of recent memory and intellectual functioning correlated

with the number of brain abnormalities that were detected by all three of these imaging

techniques combined, and with QMR and MRI taken individually. SPECT abnormalities

did not correlate with memory and intelligence measures. Further, they found that the

MRI abnormalities in the frontal region correlated with measures of psychological distress.

Cerebral activation using fMRI found frontal, parietal, and temporal brain regions being

associated with working memory functions in both healthy individuals and patients with

TBI; the latter group showing greater diffusion of activation and an emphasis on right

hemispheric activation in the TBI group. 5 Changes in cerebral activation patterns have

been suggested by recent evidence using PET and fMRI. For example, Ricker, Hillary, and

DeLuca 6 studied the processes of reorganization of neuropsychological functions after TBI,

citing the frontal lobes as the leading brain region for learning and memory functions.

Cerebral blood flow (CBF) has been found to be associated with neuropsychological

outcomes 1 year after TBI. 7 Specifically, CBF values were associated with recent verbal

memory, adaptive reasoning, and processing speed in patients with severe TBI. The vul

nerability of prefrontal and cingulate gyrus regions in severe brain injury has been detected

using PET in patients with TBI, where it has been found that these patients also demon

strated executive functioning and behavioral disorders. 8 These frontal-subcortical path

ways are implicated in some of the typical neurobehavioral

symptoms after brain injury, 9

including poor problem-solving, disinhibition, poor working memory, and impaired com

plex attention processing. Abnormal findings are also detectable in mild brain injury

utilizing these newer imaging techniques, 10 and regional brain activation changes relative

to working memory capacity are detectable by fMRI. 11 Neuropsychological assessment

and regional brain activation do not necessarily overlap completely, however, as concluded

by Umile, Plotkin, and Sandel 12 who found that cognitive test performance statistically

predicted SPECT findings, but the reverse was not true in mild TBI. The reverse was found

to be true, however, in a more severely impaired subject population where Friedman et

al. 13 found that proton MRS (1H-MRS) predicted general neuropsychological functioning

at both acute and postacute phases of recovery.

The important finding here is that, at the present time, until functional neuroimaging

techniques become more refined and available for routine clinical use, neuropsychological

assessment will continue to provide the most comprehensive clinical picture of a patient’s

cognitive assets and deficits relative to the practical needs of the patient in the rehabilita

tion setting.

Pathophysiology and Neuropsychological Functioning in TBI

Traumatic brain injury is often the result of acceleration and deceleration forces that are

applied to the head and brain. When the skull remains intact, this is referred to as a closed

head injury (CHI). In an open head injury (OHI), skull integrity is breeched where a blunt

trauma to the head may result in a depressed skull fracture. Penetrating head wounds

resulting from a projectile (e.g., a bullet) entering through the skull would be considered

an open head injury. Lucas 14 delineates mechanisms of the primary injury and potential

secondary effects. In OHI, the primary effects include brain tissue damage along the missile

track, intracranial bleeding, and meningeal and cerebral lacerations. With CHI, brain

contusions and hemorrhages can occur, and the common phenomenum of diffuse axonal

injury (DAI) frequently occurs. Filley 15 states that varying degrees of DAI occur in TBI

where shearing forces act on the long fibers of the white matter of the cortex due to

acceleration (e.g., a stationary head struck by a moving object) and deceleration (e.g., a

moving head stopped by a stationary object) actions, common to what occurs in motor

vehicle accidents. The gray matter of the cortical mantle moves across the deeper white

matter structures of the cortex producing stretching and shearing forces along the axons,

producing the diffuse axonal injury. The extent and severity of DAI is thought to be

reflected in gross outcome measurements of the depth and length of coma. Three areas

of the brain most susceptible to DAI, according to Filley, are the brainstem, cerebral

hemispheres, and corpus callosum. Executive functioning, working and recent memory

deficits, and impairments in complex information processing are commonly found as

neuropsychological deficits in TBI. What Luria referred to as cortical tone 16 can also be seen

particularly early postinjury. Here, the patient demonstrates difficulty regulating and

maintaining alertness and focused attention to the task at hand. These common neurobe

havioral problems correlate with Filley's three common regions of DAI after TBI. Filley

also found that the superimposition of cortical lesions with DAI produced poorer neu

robehavioral outcomes in TBI than with DAI alone. 17 Thus, in TBI, the neuropsychological

outcomes can be widespread and pervasive, covering a number of neurobehavioral syn

dromes and an array of cognitive impairments.

Due to the inner skull structures upon which the brain rests, particularly vulnerable

are the orbitofrontal and anterior temporal convexity regions of the cortex. From a purely

localizationalist point of view, impairments in these regions explain typical neurobehav

ioral syndromes of disinhibition and decreased regulation of behavior seen in these

patients. However, Schnider and Gutbrod 18 note that "damage after CHI (closed head

injury) is never circumscribed" (p. 487) and "frontal dysfunction does not necessarily indicate

frontal damage." (p. 488) In traumatic brain injury — especially since DAI can be prevalent,

resulting in dysfunction across many areas of the cortex — there is no specific or common

neuropsychological profile, save generalities regarding memory, attention, and executive

functioning. Complicating the neuropsychological picture is the fact that there are numer

ous frontal to subcortical circuits where any lesion along these pathways, though not

necessarily localized to the frontal lobe, can result in the same neurobehavioral syndrome.

Likewise, due to the network of connections between frontal and subcortical structures,

the same lesion in two different individuals with TBI may have an entirely different

cognitive and neurobehavioral outcome. Luria 16 spoke of the integrated nature of higher

cortical functions nearly 30 years ago, even before the advent of functional neuroimaging

technology: That is why mental functions, as complex functional systems, cannot be localized in narrow zones of the cortex or in isolated cell groups, but must be organized in systems of concertedly working zones, each of which performs its role in complex functional system, and which may be located in completely different, and often far distant, areas of the brain. (p. 31)

Whereas dysfunction along the orbitofrontal-subcortical circuit can produce behavioral

disinhibition, impairments in the dorsolateral-subcortical circuit underlie executive cogni

tive processes. Chow and Cummings 19 describe this circuit as controlling processes such

as organizational strategies, memory retrieval, ability to shift set and concepts, and

response inhibition. These cognitive processes are commonly assessed by neuropsycho

logical testing procedures. Impairments in the anterior cingulate–subcortical circuit results

in apathy, initiation deficits, reduced responsivity to tactile-sensory input, and paucity of

verbal output.

Neuropsychological Recovery after Traumatic Brain Injury

Recovery of cognitive functions and reduction of neurobehavioral consequences has been

studied over the years. One of the earliest of these prospective studies was conducted by

Dikmen and her colleagues 20,21 who studied a cohort of adult TBI patients and a friend

control group at 1, 12, and 24 months postinjury. Neuropsychological impairments across

many domains of cognitive functions were found at each time interval, the extent of

cognitive impairment at each being related to the length of coma. Improvements occurred

in the first year, consistent with other studies 22 on cognitive recovery. Dikmen and her

colleagues also found further, but more specific, types of cognitive improvement occurring

in the second year postinjury; however, the extent of recovery was dependent on severity

of injury. More recent studies have also examined the rate of neuropsychological recovery

within the first year postinjury. Kersel et al. 23 found 31 to 63% of recovery in such functions

as simple and complex attention, verbal memory, executive functioning, and perceptual

abilities. Novack and his colleagues, 24 prospectively, found improvements in memory,

processing speed, language, and constructional abilities at 6 and 12 months postinjury.

Gains in community reintegration, but continued deficits in driving abilities, were also

found in that study, where severity of the TBI determined the amount of recovery.

Neuronal injury and glial cellular damage has been shown to account for some of these

neuropsychological impairments, both shortly after injury (2 weeks) and more distant to

the injury (6 months). 25 Diffuse axonal injury has also been related to the rate of recovery

of cognitive functions. 26 These studies led to the idea that the majority of neuropsycholog

ical recovery occurs within the first 2 years postinjury. That notion has been more recently

challenged by Sbordone et al. 27 who found cognitive, social, physical, and emotional

improvements beyond 2 years postinjury. These researchers suggest that recovery contin

ues for at least 10 years postinjury; a finding that is highly discrepant with the earlier

prospective studies. It is important to note, however, that the latter research was conducted

with a retrospective research design that relies upon judgment of recovery compared to

preinjury status up to 10 years in the past. A balance between the earlier prospective work

and the retrospective study by Sbordone et al. was struck in a recent longitudinal study

of neuropsychological recovery at 1 and 5 years postinjury by Millis et al. 28 Neuropsycho

logical data from the National Institute on Disability and Rehabilitation Research Traumatic

Brain Injury Model Systems of Care was analyzed where recovery of attention, recent

memory, oral word fluency, cognitive efficiency, visuoconstructive, sensory-motor, and

reasoning abilities was variable across the 5 years. Using a change index score, they found

that 22.2% of the sample demonstrated cognitive improvement, whereas 62.6% remained

unchanged, and 15.2% declined. Clear improvement was shown to occur most on measures

of information processing speed, visuoconstruction ability, and verbal recent memory.

These longitudinal studies implicate a somewhat sobering clinical picture of successful

reintegration into community, vocational, and school reentry activities for the patient who

has sustained a traumatic brain injury. It is often helpful to employ the findings of these

longitudinal studies in the clinical setting. For example, Boake et al. 29 studied the use of

neuropsychological testing data to predict long-term productivity after TBI. Testing com

pleted prior to discharge from the acute inpatient rehabilitation setting was predictive of

competitive employment or enrollment in full-time regular education. They found that

tests of memory had prognostic value (Wechsler Memory Scale-Revised; Rey Auditory

Verbal Learning Test). Further, the Trailmaking Test (particularly, Part B) had significant

prognostic value regarding long-term productivity. They note this may be the case with

Trailmaking due to its sensitivity to multiple cognitive

domains. Leahy and Lam 30 found

that the Stroop Color-Word Test discriminated individuals with TBI who were competi

tively employed or were enrolled in degree-oriented education. Again, this may be due

to the demands of this test for several cognitive abilities including complex attention,

executive functioning, response inhibition, and speed of processing. These kinds of infor

mation can be useful in sequencing rehabilitative therapies throughout the postacute phase

of the patient's care in order to better target realistic goals for the patient in the short and

long term. Testing during the inpatient rehabilitation setting may identify TBI patients at

high risk for poorer productive outcomes, and the process of planning for subsequent

rehabilitation can begin early.

Neuropsychological Assessment vs. Neuropsychological Testing

Before discussing the variety of neuropsychological evaluation approaches and test pro

cedures, it is important to differentiate the process of assessment as opposed to the

technical aspects of testing. Assessment, in the context of the neuropsychological examina

tion, refers to the comprehensive process of evaluating the patient, whereas testing refers

to only one aspect of the examination. Assessment begins at the very first contact with a

referral source or with the patient, and is concluded when feedback is provided to all

interested parties. Table 19.1 describes the various components involved in the neuropsy

chological assessment process. Not all components are included in every neuropsycho

logical examination. The neuropsychologist may employ various components depending

upon the referral question.

These components comprise an in-depth examination of the patient that covers a broad

range of brain–behavior relationships. In the context of brain injury rehabilitation, the

neuropsychological assessment provides an active ingredient to planning interventions

and defining cognitive rehabilitation strategies that may be executed by the interdiscipli

nary rehabilitation team. The neuropsychological assessment is an active ingredient due

to the fact that information regarding deficits often defines the obstacles that will poten

tially interfere with the patient's benefit from a rehabilitation therapy. For example, if a

patient evidences marked recent memory impairment, verbal instruction alone to complete

TABLE 19.1

Components of the Neuropsychological Evaluation

Component of the Evaluation Comment

1. First Contact with Referral

Source Ascertain questions to be answered by the assessment; begin determination of assessment approach; define other data that may be of assistance for completing the evaluation.

2. First Contact with Patient/

Family Understand the patient and family's conceptualization of traumatic brain injury relative to

the need for the assessment; examine discrepancies between patient's insights regarding the TBI vs. family/friend's view; determine alignment of expectations of what will be accomplished by the examination.

3. Medical Record

Review-Post-TBI Examination of early records, including field observations of the patient [e.g., Glasgow Coma Scale scores]; emergency room observations of retrograde amnesia, loss of consciousness, posttraumatic amnesia to assist with grading severity of TBI; evidence for early behavioral agitation; track the chronology of events postinjury including medications, treatments, neurosurgical interventions, medical complications, progression of the symptom complex, rehabilitation therapy, patient and family response to the rehabilitation process.

4. Other Record Review Examination of educational records to assist with determination of premorbid cognitive functioning level, history of psychiatric impairment and substance abuse, determination of premorbid neuropsychological risks or conditions, medical history that may be contributory to the current evaluation.

5. Preinterview Questionnaires Background information may be ascertained on demographics, logistics, medical history, psychological history, notation and rating scales of past and current symptoms, educational attainment and performance; provides information to structure the clinical interview.

6. Clinical Interview-Patient Review medical and psychosocial history, ascertain current symptom complex from the patient's point of view; assist in determining congruency with early head injury severity indices; determine awareness of neuropsychological and neurobehavioral deficits; assist with ascertaining the patient's experience of quality of life post-TBI; obtain observational mental status functioning; determine contributory conditions to cognitive dysfunction, including depression, anxiety, anger, fatigue and sleep disturbance, pain symptoms, and substance use.

7. Clinical Interview-Collateral Review variable mentioned above for the clinical interview with the patient to examine for congruency of that information and obtaining further details; obtain information to judge premorbid compared to post-TBI functioning; assist with determining

change in cognitive and neurobehavioral functioning; assist with the alignment of expectations for treatment and recovery of function in the patient.

8. Neuropsychological Testing Administration of neuropsychological tests by the neuropsychologist or psychometrist (a person trained in the standardized administration of neuropsychological and psychological tests). The length of the examination varies depending upon the referral question; can extend from a brief mental status examination to a full day of testing. Testing may involve administration by both the psychometrist and computer-assisted administration of tests. Administration of psychological tests of mood, personality, and coping.

9. Test Scoring and

Interpretation The neuropsychologist and/or psychometrist scores test protocols; computer scoring programs may be employed; generation of test score summary sheets; behavioral observations of test administration is recorded to assist in determining validity of obtained test scores.

10. Report Generation A comprehensive report is generated that incorporates the above information; referral questions are answered within the body of the report.

a set of exercises prescribed by the physical therapist or to properly sequence the steps

for completing an activity of daily living, knowledge of the type and extent of that memory

problem will be useful to the therapist involved. The therapist may, in turn, decide to pair

verbal instruction with visual demonstration of the exercise set, and provide the patient

with pictures of the steps of an exercise routine. Breaking a complex set of steps down

into component parts, and training by mastery and repetition of the ADL sequence may

be necessary, based on the neuropsychological information about memory impairment.

To fully understand a patient’s memory capacity, both in terms of assets and deficits, many

of the components above are necessary for the accurate determination of that patient's

memory abilities. It is in the application of the neuropsychological test findings to the care

of the TBI patient that the assessment becomes a powerful instrument to improve the

functional status of the patient. 31

Neuropsychological Assessment Orientations

A number of training programs and subsequent models of neuropsychological assessment

has emerged since the beginning of clinical neuropsychology. Often related to a particular

researcher or research program, an array of orientations or approaches to neuropsychology

has emerged. 32 All have been applied in brain injury rehabilitation, and have provided an

active ingredient to the process of recovery of function in TBI. The major approaches are

Fixed Battery Approach

The fixed battery approach refers to the administration of a uniform set of neuropsycho

logical tests across all patients evaluated. This provides for a systematic comparison of

patients across the same sets of tests. The fixed battery approach usually incorporates tests

that cover a full range of brain-behavior functions, including sensory-motor, language,

attention and concentration, memory, visuoconstructive, visuospatial, information pro

cessing speed, and executive functioning domains.

Among the most commonly utilized fixed battery approaches is the Halstead-Reitan

Neuropsychological Test Battery (HRNB). 33–36 First developed by Ward Halstead in 1947 and

later modified by Ralph Reitan in 1955, the HRNB consists of eight core tests: Category

Test, Tactual Performance Test, Speech Sounds Perception, Seashore Rhythm, Finger

Oscillation, Trailmaking Test, Aphasia Screening Examination, and the Reitan-Klove

Sensory Perceptual Examination. It generates the Halstead Impairment Index that pro

vides a gross indication of impairment severity. A General Neuropsychological Deficit

Scale can be generated, also, from the HRNB that provides indications of level of perfor

mance, pathognomonic signs, pattern analysis, and lateralization indicators. Other tests

11. Feedback Session Feedback regarding the results of the examination are explained to the patient and family; modification of the report may occur depending upon new questions that may arise; recommendations are made to the patient and family; other providers may be invited to the feedback session, depending upon clinical need; feedback may be provided to case managers, vocational counselors, educational specialists, or other health care providers.

TABLE 19.1 (Continued)

Components of the Neuropsychological Evaluation

Component of the Evaluation Comment

are often used in conjunction with the HRNB, including the Wechsler Adult Intelligence

Scale-Revised and 3rd Edition versions, measures of recent memory, further measures

of sensory-motor integrity, and personality functioning (e.g., Minnesota Multiphasic

Personality Inventory-2).

Another widely used fixed battery approach is the Luria-Nebraska Neuropsychological

Battery (LNNB) developed by Charles Golden and his colleagues. 37-40 Utilizing testing

procedures of A. R. Luria 41 and systematized by Anne-Lise Christiansen, 42 the LNNB was

developed to capture some of Luria's original bedside examination methodology, orga

nized into a psychometric format. While having been highly criticized in the past on basis

of reliability and validity, these criticisms have given way to the cumulative empirical

research as to its enduring psychometric soundness and clinical utility. There are two

published versions of the LNNB, Form I and Form II, the latter of which has been thought

to be particularly useful with older adults. 43 The LNNB allows for both actuarial interpre

tations, based upon the empirical research on the instrument in different populations, as

well as allowing for qualitative analysis, particularly on the item analysis level of inter

pretation. It is a rich clinical instrument that can be useful in the rehabilitation setting as

it allows the clinician to apply LNNB findings to an analysis of intact vs. impaired

functional cognitive systems. The LNNB consists of 11 clinical scales (motor functions,

rhythm, tactile functions, visual functions, receptive speech, expressive speech, writing,

reading, arithmetic, memory, intellectual processes), 5 summary scales (pathognomonic,

left hemisphere, right hemisphere, profile elevation,

impairment), 8 localization scales (left

frontal, left sensorimotor, left parietal-occipital, left temporal, right frontal, right sensori

motor, right parietal-occipital, right temporal), and 28 factor scales that assist the clinician

in illuminating elevations on the clinical scales.

Flexible Battery Approach

In flexible battery approaches, the neuropsychologist may employ a different set of tests,

depending upon the referral question and the type of neurological problem being ana

lyzed. The hypothesis-testing approach that has been championed by Muriel Lezak 44 is based

on the idea that the presentation of the patient and the referral question generate initial

hypotheses regarding the neurocognitive condition of the patient. Tests are selected to test

out these clinical hypotheses. Confirmation and rejection of specific hypotheses can then

lead to further neuropsychological testing to follow-up clinical observation of test perfor

mance by the patient. Tests such as the Wechsler Adult Intelligence Scale, Rey-Osterrieth

Complex Figure Test, Rey Auditory Verbal Learning Test, and the Wisconsin Card Sorting

Test are employed particularly in TBI due to the nature of commonly found impairments

in this population.

Process Orientation Approach

Original Lurian methodology called for the qualitative analysis of the patient’s perfor

mance on tasks that the clinician employs. Anne-Lise

Christensen organized a set of Luria's

behavioral neurology oriented procedures into a systematic set of tasks called Luria's

Neuropsychological Investigation (LNI). 42 The approach calls for a set of procedures, includ

ing the preliminary conversation (stage one) which is the clinical interview. The next step

involves the examination of motor, auditory, kinesthetic, and visual analyzers (stage two),

followed by examination of specific cognitive functions (stage three) based upon perfor

mance of earlier stages of the examination. In the fourth stage of the examination, syn

drome analysis, the clinician identifies the neuropsychological syndrome according to

Luria's localization of functional systems in the brain. The LNI has been used for the

purposes of brain injury rehabilitation and has been used specifically to evaluate those

with TBI. 45

Another popular approach to the neuropsychological examination of patients has been

led by Edith Kaplan, called the Boston Process Approach. It often combines the use of fixed

neuropsychological tests, but within a framework of examining not only the score out

come, but the types and processes of the errors involved. 46 Kaplan and her colleagues

utilize standardized tests, such as the Wechsler Memory Scale or the WAIS-R, and modify

the administration procedures to introduce methods of scoring the protocol to analyze

errors and to test the limits of the patient's cognitive

capacity. Additional items and

multiple-choice formats are added to the instrument to better analyze the performance of

the patient. The WAIS-R-NI is a good example of this approach 47 where the patient's

constructions of the Block Design test are tracked where certain kinds of errors (e.g.,

constructing the block patterns outside of the gestalt of the square) may be more indicative

of right hemispheric impairment.

Content of Neuropsychological Assessment

In reviewing several neuropsychological testing procedures, it is important to not only

describe the instrument and cognitive domain that it represents, but in the context of

traumatic brain injury rehabilitation, the ecological validity implications are paramount.

Ecological validity refers to a test's ability to predict everyday functioning. Sbordone 48

describes this concept as follows: Ecological validity can be defined as the functional and predictive relationship between the patient's performance on a set of neuropsychological tests and the patient's behavior in a variety of real-world settings (e.g., at home, work, school, community). This definition also assumes that demand characteristics within these various settings are idiosyncratic and fluctuate as a result of their specific nature, purpose, and goals. (p. 16)

The neuropsychological examination done in the context of TBI rehabilitation is not

often used to identify lesions but rather for the purposes of ecological validity. They are

useful when attempting to predict the patient's functioning in the environment, and to

assist with predicting the patient's behavior in

“idiosyncratic” settings that do not remain

static. One of the problems with neuropsychological testing, according to Sbordone, 49 is

that neuropsychological tests, by themselves, do not well predict everyday behaviors or

vocational functioning. It is, therefore, incumbent upon the neuropsychologist to translate

assessment findings into meaningful statements about a particular patient, with specific

deficits, under specific environmental conditions (e.g., inpatient rehabilitation unit setting,

safety issues in being home alone without supervision, a job setting with noise distractions,

college chemistry classroom setting). Therefore, ecological implications of particular test

ing procedures are stated for the following testing procedures.

Cognitive Screening and Mental Status Examinations

Instruments that provide global information about general cognitive functioning can be

useful in the assessment of patients with traumatic brain injury to provide a brief look at

level of ability. This tends to occur in the early phases of recovery where the patient may

not be capable of engaging in a more complex or comprehensive examination. Table 19.2

provides a listing of common cognitive screening measures and their characteristics. These

measures provide some coverage of important cognitive domains such as recent memory,

attention, visuoconstructive and abstracting skill (e.g., Dementia Rating Scale, Cognistat,

RBANS). Others provide a global index of cognitive

functioning (Mini-Mental State Exam

ination, Clock Drawing Test).

Ecological Implications

These measures can help the rehabilitation team answer such questions as:

• Does the patient have the mental capacity to understand his/her own cognitive condition?

• To what extent is the patient oriented and in need of supervision?

• Can the patient be expected to follow a schedule or keep up with simple instructions?

• What is the gross capacity of the patient to learn routines and carry over instruction from one time or setting to another?

• What is the gross attention ability of the patient?

• Is there any relative preservation of cognitive ability that can be capitalized upon for simple tasks.

If the patient fails aspects of these cognitive screening measures, the rehabilitation team

may need to provide interventions such as the posting of a calendar in the patient’s room

for orientation purposes, cue the patient to the tasks at hand and encourage learning by

repetition, determine the length of a session based on level of sustained attention, and

train the patient to the setting and not assume transfer of learning to a new setting. Some

measures, such as the RBANS, allow for repeat administration where tracking cognitive

TABLE 19.2

Tests of Cognitive Screening and Mental Status Examinations
Test Comment

Cognistat

(Neurobehavioral Cognitive Status Examination) Assesses five major areas: language, constructional ability, memory, calculation skills, and reasoning/judgment

Dementia Rating Scale-2 Provides subscales scores for Attention, Initiation/ Perseveration, Construction, Conceptualization, and Memory; yields a total score

Mini-Mental State Examination (Folstein) Standard measure of mental state based on the 30-point scale; widely used for gross dementia detection; runs the risk of a high false negative rate

Repeatable Battery for the Assessment of

Neuropsychological Status Brief measure of immediate memory, language, visuospatial/constructional, attention, and delayed memory; an alternate form is available for repeat testing

Screening Test for the Luria-Nebraska

Neuropsychological Battery Very brief measure that determines whether or not a full LNNB may be helpful; screener includes stimulus materials for adults and children

Severe Impairment Battery Assesses the lower range of cognitive impairment; suited for severely impaired patients

Kaufman Short Neuropsychological Assessment

Procedure (K-SNAP) Measures attention-orientation, memory and perceptual skills, intelligence, and planning

Shipley Institute of Living Scale Produces Vocabulary, Abstraction, and Total Scores; Conceptual Quotient can be used as an index of impairment; estimates WAIS or WAIS-R Full Scale IQ

improvements can occur. This may be particularly important when making discharge

plans and organizing postacute services.

Cognitive screening measures may also be helpful in tracking the TBI patient’s cognition

in determining transfers to and from subacute and acute rehabilitation settings. The

patient’s ability to engage in 3 hours per day of rehabilitative therapy may depend upon

the cortical arousal level and integrity of sufficient sustained attention and orientation to

benefit from this intensive level of therapy. In special situations, such as the patient with

combined spinal cord injury and traumatic brain injury, making initial judgments about

cognition may determine length of stay in that the dually diagnosed patient, due to

decreased learning capacity and memory, may require more supervision, reminders, and

repetitive learning of such activities as executing proper transfers, self-catheterization, and

repositioning to avoid decubitus ulcers.

General Level of Performance Perhaps someone with expert knowledge of the human brain will understand my illness, discover what a brain injury does to a man’s mind, memory, and body, appreciate my effort, and help me avoid some of the problems I have in life. 50(p. xxi) — From L. Zasetsky in A. R. Luria’s The Man With a Shattered World

A. R. Luria’s method of behavioral neurology often involved the detailed examination of

the patient 50 as documented in the above work. His observations of the patient laid the

foundation to understand brain-behavior relationships and are used as examples of what

occurs after TBI. His patient, L. Zasetsky, suffered a penetrating head injury from a bullet

wound during World War II.

Based upon a larger set of neuropsychological test findings, indices of general neurop

sychological performance and impairment serve similar functions as cognitive screening

measures. They tend to have greater reliability since they are based upon scale scores rather

than item-level scores. As mentioned above, the Halstead Impairment Index is one of the

more commonly cited general performance indices that have been used in outcome research

in patients with TBI. The General Neuropsychological Deficit Scale, as noted above, is a

score that is derived from a wider set of HRNB tests. The LNNB can generate its own

Impairment Index, utilizing elevations on specific Clinical Scales and the Pathognomonic

Scale. Table 19.3 presents measures of general neuropsychological level of performance.

Ecological Implications

An index of general performance is an indication of overall neuropsychological integrity

and can be used to judge and predict a patient's ability to function independently in global

life functions. A Halstead Impairment Index of 0.9 (i.e., 90% of the indexed tests on the

HRNB fell in the brain-impaired range) would alert the rehabilitation team that the

patient's cognitive reserve is limited to independently compensate for cognitive deficits

in real-world settings. That patient's capacity to independently generalize learned skills

to new settings may be limited. This is due to the fact that an HRNB II of 0.9 indicates a

broad range of impaired higher level cognitive functions — cognitive skills that are needed

to bear upon complex tasks and behaviors. Likewise, a LNNB Impairment Index that falls

in the mild range may be associated with a greater potential for independent living where

compensatory strategy training, modifications to the home environment, and training the

patient with organizational aids may be feasible and effective. Mild level of general

impairment does not necessarily connote mild impairments across all tests in a battery,

and could mean normal functioning on some tests combined with severe problems on

specific tests. Compensating for the cognitive problem that falls in the severely impaired

range (e.g., utilizing a memory aid for scheduling appointments and organizing informa

tion that impacts everyday functioning) may require the assistance of a rehabilitation

therapist or family member to implement in everyday tasks or contexts.

Sensory-Motor Integrity When the doctor learned what my first name was, he’d always address me that way and try to shake hands when he came over. But I couldn’t manage to clasp his hand … Suddenly, I’d remember and try to shake hands again but would only manage to touch his fingers. 50(p. 46) — L. Zasetsky

Output of motor movement for everyday routine actions (e.g., picking up a jar, using the

steering wheel while driving, folding the laundry) may, on the surface, appear to be a

reflexive action without involving higher level cognitive actions. Luria posited that verbal

mediation is a significant driver of human actions, what he described as the regulatory

function of speech. Thus, the integration of higher cortical functions with motor move

ments and the ability to interpret tactile inputs is intricate. The interplay of motor functions

and higher order processes occur and are relevant for consideration in brain injury reha

bilitation. Table 19.4 describes commonly used tests of motor functions.

Ecological Implications

Whether motor input impairment occurs in the peripheral nervous system (e.g., peripheral

neuropathy), in the spinal cord (e.g., nerve impingement), at the subcortical level (e.g.,

TABLE 19.3

Measures of General Levels of Performance Measure Comment

Halstead Impairment Index Calculation of the 7 indexed tests of the HRNB; ranges from 0.0 to 1.0, with latter meaning 7 out of 7 of the tests fall in the impaired range

General Neuropsychological Deficit Scale Calculated off of 42 variables from the adult HRNB and allied procedures; higher scores indicate more impairment

Luria–Nebraska Neuropsychological

Battery–Impairment Index Calculated by examining the difference between the obtained T-score and the Critical Level; similar in conception as the NDS above

Wechsler Adult Intelligence Scale–III(WAIS-III)

Full Scale IQ FSIQ not generally considered a neuropsychological measure; helpful in estimating long-term cognitive abilities

Kaplan Baycrest Neurocognitive Assessment Evaluates a broad range of functioning including attention/concentration, immediate memory, delayed memory, verbal fluency, spatial processing, and reasoning/conceptual shifting

MicroCog: Assessment of Cognitive Functioning Evaluates

attention/mental control, memory, reasoning/ calculation, spatial processing, reaction time, information processing accuracy, information processing speed, cognitive functioning and cognitive proficiency; this is a computer-assisted administration system

cerebellar contusion), or at the cortical level (e.g., subdural hematoma along the motor

cortex), impairment in higher level abilities can be affected. Reduced motor input due to

tactile sensory discrimination problems interferes with judgment of distance in low light

settings, for example. Centrally mediated problems, such as dysmetria, may be com

pounded by impairments in sensory motor inputs. Training patients to scan and sweep

their tactile environment may be less successful when sensory motor input of the fingers

or hands is impaired. Reduced tactile discrimination and motor dexterity may prove

disruptive to those patients that may work in assembly line work, electrician work,

musicians that utilize fine motor movement (e.g., violinists), and other professions that

require fine motor dexterity. Organization of the motor act is measured by Item 21 of the

LNNB that requires the patient to clench-extend the fingers alternatively between both

hands. Cognitive functions that are brought to bear on this item include fine motor speed,

alteration and switching of motor acts, thus requiring organization and rapid sequencing,

and the ability to translate visual representation and verbally mediated instructions into

accurate motor actions. Impairment on this item has implications for learning by visual

demonstration, difficulty keeping and maintaining a sequence, and difficulty in maintain

ing motor coordination. All of these may be required to keep up with the instructions of

the physical therapist to learn the proper way to range the arm, or may implicate problems

in coordinating syncopated movements in gait training (i.e., proper equal weight bearing

on both feet, swinging the arms alternatively to maintain balance during gait). Changes

in tactile-spatial discrimination (Items 70 and 71 of the LNNB measure two-point discrim

ination distance; aspects of the Reitan-Klove Sensory Perceptual Examination, such as

Finger-Tip Number Writing) can impair the patient's ability to employ fine motor dexterity

for such tasks as accurately executing keyboarding on the computer, or for a person with

low vision, the ability to discriminate Braille symbols, or the mechanic who needs tactile

senses to reach and manipulate parts on an engine carburetor that is not visible. Deficits

of motor integrity can affect writing output ability, the ability to manipulate and utilize

TABLE 19.4

Tests of Sensory-Motor Functioning Test Comment

Motor Scale-LNNB Multifactorial scale that examines simple motor output abilities to motor programs that require tertiary zone abilities; used clinically and in research contexts as a stand-along measure

Tactile Functions Scale-LNNB Assesses a wide range of tactile input abilities, including tactile-spatial analysis, two-point discrimination

Reitan-Klove Sensory Perceptual Examination Given as a part of the HRNB to assess sensory-motor integrity; includes tests of tactile, auditory, and visual modalities

Finger Oscillation Test Part of the HRNB; motor speed and lateralization hypotheses can be assessed

Hand Dynamometer-Grip Strength Motor output strength and lateralization of deficits can be assessed

Grooved Pegboard, Purdue Pegboard Test Motor dexterity and speed is assessed; lateralization can be assessed

Benton Finger Localization Localization of fingers — conditions include hands visible and hands hidden from view

Benton Motor Impersistence Maintenance of movement and posture is assessed

Benton Tactile Form Perception Assesses spatial analysis and tactile recognition; assesses stereognosis

Tactual Performance Test Part of the HRNB; though multifaceted in nature, the TPT requires significant tactile-spatial analysis

tools, and could affect a person’s ability for recreational and leisure pursuits, such as doing

needlepoint or playing golf, as well.

One patient with TBI that this author evaluated was a liver transplant physician who

evidenced problems on the Tactile Functions scale of the LNNB, with emphasis upon

problems in his left (nondominant) hand. The patient described the need to use his left

hand to reach underneath the liver while using his right hand to manipulate surgical

instruments. The tactile senses of the left hand were required to identify structures of the

liver and provide kinesthetic input regarding the position of the liver during transplan

tation procedures, and thus required judgments that had to be made on a moment-to

moment basis during surgery. With impairments of these functions, the patient could no

longer take the lead in doing transplant surgery. This illustrates one example of the critical

nature of sensory-motor integrity to higher order abilities in a functional task.

Language Functioning and Pragmatics of Communication By this time, I could remember a great many letters by associating them with different words, but when I tried to visualize a particular letter — “k,” for example — or hunt up a word for it, I needed quite a bit of time in order to recognize it and point it out to my teacher. 50(p. 68) — L. Zasetsky

The intricate relationship between higher mental processes and spoken language, accord

ing to Vocate, 51 was central to Luria’s view of cognition: He [Luria] argues that “mind” is impossible without its synergetic relationship with spoken language and that both arise from the physical reality of the human brain and human society. 51(p. 129)

She goes on to summarize Luria’s thought by stating that “spoken language is the means

by which the individual becomes capable of conscious and voluntary processes” (p. 143) and

that language “is a component in the complex functional systems of other higher mental

processes.” (p. 146) Indeed, language acquisition is a lynchpin to the acquisition of knowledge

and engagement in the sociocultural environment. When there is dysfunction of language

ability after TBI, there usually exists significant disruption in the patient’s ability to interact

with the social environment (e.g., family members, coworkers, friends). Table 19.5

describes common neuropsychological tests that evaluate language functioning in the

patient with TBI. It should be noted that speech therapists are expert in language assess

ment. There is considerable overlap between measures used by speech therapists and by

neuropsychologists.

Ecological Implications

Language impairment after TBI can come in many forms, including different forms of

aphasia, impairments of oral word fluency, and disorders of pragmatic communication

skills. Expressive language disturbances influence everyday activities such as use of the

telephone. If a patient cannot properly communicate safety conditions over the telephone,

that patient’s safety at home, without continuous supervision, is threatened. Paraphasias

can disrupt interpersonal communications and can be experienced as markedly frustrating

to the patient. Global aphasics experience marked limitations in independent living ability

due to the limits imposed by both receptive and expressive language abilities. Those with

receptive language impairments experience problems with following instructions pre

sented by the therapist. They may require alternate modalities (visual presentation) or

multiple modality (presenting information by use of both visual and procedural-kines

thetic input) instruction to accomplish a task. For example, a patient with both expressive

and receptive language dysfunction may need to have the

therapist demonstrate how to

put on an ankle-foot orthosis, but may also need the therapist to physically direct his/

her hands and legs to learn the procedure, and minimize the sole use of verbal instruction.

Working Memory and Complex Attention Processing I try a little harder to remember and make sense of the person's remarks. And when I talk to my mother or sisters, I have to strain my nerves and memory even more to understand what they're saying to me so that I know what I'm to do or say. 50(p. 93) — L. Zasetsky

Working memory refers to that ability to register and manipulate information. Baddeley

referred to this concept as the central executive system. 52 It requires the patient to hold

initially encoded information while being able to manipulate that information and store

the newly manipulated information for immediate future use. Working memory is invoked

when executing mentally, for example, a four-digit subtraction task. Often, visual repre

sentation, auditory attention, retrieval of long-term information, and executive abilities

can be employed in working memory tasks. Once information has been initially processed,

information can then be encoded into recent memory storage. Thus, there is a direct

relationship between working memory and recent memory. Individuals with TBI have

difficulty in working memory that some believe is a result of dysfunction of the central

executive system, and related to higher order executive functioning deficits. 53 Some argue

that patients with TBI do not, primarily, exhibit problems in working memory but in recent

TABLE 19.5

Tests of Language Ability and Dysfunction Test Comment

Woodcock Johnson Psycho-Educational

Battery–Revised A battery of tests of academic achievement that contains subtests that examine written and oral language usage and reading comprehension abilities

Multilingual Aphasia Examination Focuses on oral expression, spelling, oral verbal comprehension, reading and the assessment of articulation

Boston Diagnostic Aphasia Examination Comprehensive set of measures that correspond to a full range of aphasia types

Token Test Commonly used to evaluate the ability to follow commands of increasing complexity

Boston Naming Test Confrontation naming task that allows for semantic and phonemic cueing

Controlled Oral Word Association Test Measures word fluency; executive processing may influence performance on this test

Receptive and Expressive Scales of the LNNB Contains items that measure a range of aphasic disturbances

Reitan–Indiana Aphasia Screening Examination Part of the HRNB; tasks are easily passed by normal adults; identifies pathognomonic signs of aphasia

Western Aphasia Battery Evaluates reading, writing, calculation ability, and nonverbal skills; yields an Aphasia Quotient and a full battery Cortical Quotient

memory processes of encoding, consolidation, retention, and retrieval. 54 Complex attention

processing includes the ability to sustain and focus attention on a task. Alternating and

divided attention also come under this category of cognition. The research literature clearly

shows that attention deficits are common among those with TBI (e.g., Van Zomeren,

Brouwer, and Deelman). 55 Impairments in attention appear to occur across the spectrum

of TBI, including mild TBI, the latter showing impairments on tests of attention that

requires information processing speed. 56 Table 19.6 presents some common measures of

working memory and complex attention.

Ecological Implications

Working memory impairments can be significantly disabling due to the need for this

aspect of cognition in most human activities. While those without brain injury may

function at a preconscious level, for those with brain injury, working memory can be

experienced as confusion, derailment, and poor task maintenance. Working memory

impairments are evidenced early after traumatic brain injury, and may significantly

TABLE 19.6

Working Memory and Complex Attention Processing Measures
Test Comment

Working Memory Index–WAIS-III Comprised of the Arithmetic, Digit Span, and Letter–Number Sequencing subtests

Processing Speed Index–WAIS-III Comprised of the Digit Symbol-Coding and Symbol Search subtests; requires motor writing output

Speech–Sounds Perception From the HRNB; measures sustained auditory attention; ability to accurately perceive verbal information; is sensitive to the presence of brain damage

Seashore Rhythm Test From the HRNB; measures focused auditory attention and presence of brain damage

Rhythm Scale From the LNNB; assesses sustained and focused attention; examines pitch perception

Paced Auditory Serial Addition Test Sustained attention test; significant demands on working memory; information processing speed is also assessed without the need for motor writing output; used frequently in TBI

Ruff 2 & 7 Selective Attention Test Measures both accuracy and speed of selective attention; normative sample includes those with TBI

d2 Test of Attention Speed and accuracy of selective attention is measured; can be used with children and adults

Brief Test of Attention Assessment of auditory divided attention; broad normative base

Visual Search and Attention Test Visual letter and symbol cancellation task; examines ability to sustain visual attention

Continuous Performance Test Examines lapses in attention, vigilance, and impulsive responses

Auditory Consonant Trigrams Test Evaluate alternating and divided attention in the auditory modality; executive functioning also influences performance

Digit Vigilance Test Produced for visual tracking and target selection of visual stimuli

Stroop Color-Word Test Attention, cognitive flexibility, and response inhibition are assessed; commonly used are the Golden and Trenerry versions

Test of Everyday Attention Evaluates divided, alternating, selective and sustained attention; approach uses everyday materials that may better approximate realworld situations

Symbol Digit Modalities Test Visual tracking, motor speed; comparisons between written and oral performances can be provided

Trailmaking Tests, Parts A and B Part of the HRNB; cognitive flexibility and speed of information processing are assessed

Color Trails Test Similar concepts as Trailmaking Test but uses colors instead of letters; can be given without verbal instruction; alternative forms are available

contribute to posttraumatic amnesia. In the acute rehabilitation, clinicians may be required

to cue the patient to the task at hand, and may need to direct the patient through the

component steps of a task. In the severe TBI, an occupational therapist may need to break

down the morning ritual of brushing teeth and washing the face into much smaller parts.

This type of incapacity can be puzzling to family members who may assume that the

patient may have forgotten how to brush the teeth (i.e., long-term memory loss) when, in

fact, that patient has difficulty registering information related to the context of teeth

brushing, and may have difficulty not only with simultaneously processing positioning

the tooth brush appropriately while alternating the brushing motion but in making the

decision as to when to discontinue the task. Difficulties with alternating and divided

attention can result in the patient being easily distracted from the task at hand. In an office

environment, a secretary with divided attention problems may not be able to focus atten

tion on the telephone while, in the background, coworkers are moving about the room.

This is akin to the cocktail party phenomena where most without brain injury may be

able to focus on one conversation while ignoring others, then turn the attention to another

speaker, again without being distracted by extraneous conversations. The patient with TBI

may have difficulties shifting the focus of attention

efficiently and will encode incomplete

information and may incorporate information from extraneous conversations due to dif

ficulties sifting out appropriate auditory stimuli. Often, patients will describe being easily

overstimulated and overwhelmed when there are too many noise or visual distractions

in the immediate environment. Reading tasks can be affected by impairments in visual

sustained attention. Tracking words across the page with the aid of a ruler or use of a

finger to cue eye movement can help compensate for a patient’s difficulties with sustaining

attention on the written text. Having the patient articulate the words aloud while they

read may also assist with self-cueing and focusing attention on a reading task.

Speed of Information Processing

Several neuropsychological tests judge the accuracy and speed of information processing.

Individuals without brain injury are usually capable of completing tasks both accurately

and within a reasonable period of time. After TBI, one or both aspects of information

processing may be impaired. With the publication of the Wechsler Adult Intelligence

Scale-III comes four indices that are factor analytically derived from the subtests of the

test. The Verbal Comprehension, Perceptual Organization, and Working Memory Indexes

require accurate responses and the patient is penalized less for time of completion. An

exception to this is the Block Design test where the

correct response is recorded but more

points are awarded with a more rapid correct response. The Processing Speed Index

provides a measure of information processing efficiency. Speed of information processing

for response inhibition, as measured by the Stroop Color-Word Test, and motor output

speed on the Purdue Pegboard has been shown to be associated with general functional

outcomes (operationalized by the Glasgow Outcome Scale) in patients with moderate to

severe TBI. 57 The analysis of speed vs. accuracy is also obtainable on tests such as the Ruff

2 and 7 Selective Attention test where selective attention accuracy (errors of omission and

commission) and amount of information processed (accurate target detection speed) are

measured. The relative mix of accuracy and speed can be calculated from a subset of items

from Form I of the LNNB termed the Power and Speed Indexes. As with most neuropsy

chological tests, there are few that purely measure a particular construct. For example,

the Stroop Color-Word Test measures information processing speed and response inhibi

tion, as well as shift set maintenance. There is considerable overlap between attention

abilities and information processing speed. Table 19.6 includes measures of information

processing speed.

Ecological Implications

During the acute inpatient stay, the patient is often engaged in many rehabilitative ther

apies, each with different tasks and learning goals. The rate of learning these routines and

benefitting from treatment may depend on the patient's capacity for information process

ing speed. It may be important, therefore, to pace the patient through a mobility or

ambulation exercise in a way that does not exceed the patient's ability to keep up with

instructions. Repetition of instruction and slowing down the rate of verbal output on the

therapist's part can improve the patient's understanding of the task. In the postacute

phase, therapists may elect to improve either accuracy or speed, depending upon the task

to be mastered. Those patients where behavioral impulsivity and disinhibition may be

problematic may benefit from an approach that focuses on pacing the speed of response

and inserting verbal self-cueing methods between the instruction and execution of the

task. In making job modifications, the patient with brain injury may require that tasks be

done on a project-driven basis rather than a time-to-work product basis. It may not be

possible for the patient to work full-time and produce the amount of work prior to TBI,

but working part-time, on a limited set of projects, may better accommodate speed of

information processing deficits.

Recent Memory Functioning I used to spend all my time lying on my right side or sitting up for a little while trying to recall some of my past. I couldn't remember anything at will, whereas, when I wasn't thinking about anything in particular, some words would occur to me along with the

tunes of different songs. I’d hum to myself. 50(p. 89) — L. Zasetsky

Recent memory is a multifaceted concept covering verbal, visual, and tactile-spatial

domains, as well as episodic (event-related memory) and procedural (recall and repro

duction of actions) aspects. While the scope of this chapter does not allow for a thorough

review of memory functioning in TBI, some highlights are in order to better describe

ecological implications. For a comprehensive discussion of the neuropsychology of mem

ory, see Squire and Schacter. 58

A number of studies have examined memory dysfunction in TBI. A common measure

of recent memory is the California Verbal Learning Test where Wiegner and Donders 59

found attention span, learning efficiency, delayed recall, and inaccurate recall being com

ponents of memory disorder among patients with TBI. Patients with TBI have been found

to have a rapid rate of forgetting new information and difficulties with the consolidation

of new material. 60 Material-specific memory, or that ability to recall information based on

the properties of the stimulus material (verbal, visual-spatial), has been found to underlie

episodic memory in TBI. 61 Capitalizing upon enhancing stimulus materials may, therefore,

assist the learning process in this population.

In clinical practice, recent memory tests assess immediate recall of information for which

efficient encoding of information is required. Immediate

recall paradigms include both

verbal (e.g., Logical Memory I of the Wechsler Memory Scale–III) and visual (e.g., Imme

diate Recall of the Rey Complex Figure Test) components. Delayed recall of initially

presented material across 20- to 30-minute time intervals are common among memory

tests. Recognition trials in which the patient must choose among several verbal or visual

stimuli to identify what was initially presented assess recall accuracy, false positive, and

false negative rates. Recall trials often require rote retrieval of information and are generally

more difficult for the patient. Recognition trials allow for an assessment of storage capacity

(i.e., if the patient accurately recognizes information, it is assumed to be stored). Verbal

and visual stimuli may be placed within a context such as a paragraph story that has a

beginning, middle, and ending; visual stimuli may be recognizable objects or pictures.

Other recent memory tests may require the patient to impose an organizing principle (e.g.,

word-list learning tests such as the Bushcke Selective Reminding Test or the Rey Auditory

Verbal Learning Test) in order to recall stimuli. Still others may cue the patient to categorize

earlier presented information (e.g., on the California Verbal Learning Test, the examiner

asks the patient for all of the tools and vegetables that are on the list). Table 19.7 presents

some common memory tests that are utilized in the context of brain injury rehabilitation.

Ecological Implications

Among the various types of cognitive problems presented by the patient with TBI, memory

disorders may be more easily compensated for with the use of compensatory strategies

(cf., executive functioning problems). Upon identifying the type of memory problem the

patient presents, other functional systems may be employed to compensate. A traditional

example is the patient with recent verbal memory deficits in delayed recall where a

memory book and training on the routine use of the memory book can capture information

that may be lost due to recall deficits. Employing an organization strategy, assuming

relatively intact new learning and executive ability, allows for the patient to successfully

utilize the memory aid. A patient with the same verbal memory deficit may be aided by

TABLE 19.7

Recent Memory Functioning Tests Test Comment

Wechsler Memory Scale–III Battery of subtests that measures verbal and visual memory; working memory also included; normed with WAIS-III

California Verbal Learning Test Word-list learning test of verbal memory; many indices can be calculated including the effect of interference, category cues, and recognition on memory performance; norming includes TBI

Rey Auditory Verbal Learning Test Word-list learning test; several different norm tables are available

Buschke Selective Reminding Test Word-list learning test; widely used in research with TBI; executive functioning ability influences test performance

Memory Assessment Scales Measures recent verbal and visual

memory across 12 subtests

Tactual Performance Test Part of the HRNB; measures incidental tactual memory; requires problem-solving, tactile-spatial analysis, and speed of information processing

Hopkins Verbal Learning Test-Revised Measures verbal recent memory

Rivermead Behavioral Memory Test Evaluates everyday memory ability; extended version allows for assessment of subtle memory deficits

Rey Complex Figure and Recognition Trial Measures visuospatial memory; provides a recognition trial; can measure visuoconstruction ability and planning ability; qualitative scoring systems are available for other versions of this test

Benton Visual Retention Test Visual recent memory is assessed; can be used in children and adults; measures visuoconstruction ability

Brief Visuospatial Memory Test Visuospatial memory is assessed; six alternate forms are available

Recognition Memory Test Allows for a distinction between left and right hemispheric dysfunction by examining recognition of words and faces respectively

Memory Scale-LNNB Brief scale containing an array of items for immediate visual and verbal recall; word-list learning includes predictive judgments made by the patient in calculating the error score

training to visualize information to be recalled, and to learn new information in multiple

modalities including visual, tactile, and by verbal repetition. Rehearsal of important infor

mation, paired with cueing techniques (e.g., a watch alarm, using visual reminders such

as a green dot placed in strategic places in the house or work setting), may also aid recall

accuracy. Consistency of recall of information may require compensatory or environmental

manipulations that assist with complex attention problems that may play into recall

deficits. Reducing extraneous noise in the environment may allow the patient to better

encode and store needed information. Improving lighting conditions while reading may

also improve encoding of written material, thus improving storage efficiency. One of the

difficulties in training the patient in compensatory memory techniques is the problem of

“remembering to remember” otherwise known as metacognition. Supervisory attention and

executive abilities must be intact, to a certain degree, in order for the patient with TBI to

successfully utilize memory aides. With the proliferation of personal computers and per

sonal digital assistants (PDAs), assistive technology may show promise in developing

compensatory aides for this population. Unfortunately, those with TBI will often have

executive functioning problems. This poses an additional challenge in the brain injury

rehabilitation setting where multiple and integrated compensatory techniques may need

to be trained and integrated into the patient’s daily routine.

Visuospatial Analysis and Visuoconstruction Ability Ever since I was wounded, I’ve had trouble sometimes sitting down in a chair or on a couch. I first look to see where the chair is, but when I try to sit down, I suddenly make a grab for the chair since I’m afraid I’ll land on the floor. Sometimes that happens because the chair turns out to be further to one side than I thought. 50(p. 47) — L. Zasetsky Not only would he “lose” the right side of his body (an injury to the parietal area of the left hemisphere inevitably produces this symptom), sometimes he thought

parts of his body had changed — that his head had become inordinately large, his torso extremely small, and his legs displaced. It seemed to him that, in addition to the disintegration of objects he perceived, parts of his body had undergone some form of fragmentation. 50(p. 42) — A. R. Luria

Impairments of visuospatial and visuoconstructive abilities can occur after TBI and may

take on many different forms. The patient may evidence problems with visual-spatial

analysis of graphical percepts. On Block Design of the WAIS-III, for example, the patient

may not be able to construct visual designs using different patterned and colored blocks,

and may lose the whole or gestalt of the design. More esoteric problems in TBI may

present as something like Gerstmann's Syndrome 62 in which the combination of agraphia

(difficulties in motor writing with spelling and word order altered), acalculia (deficits

in execution of arithmetic calculations), finger agnosia (inability to name or move a

designated finger after it has been labeled), and right-left confusion (discrimination of

instructions that require orientation of the right vs. left side of the body) occurs. Any

or all of these components can be evidenced in TBI, likely due to the cortical proximity

of brain regions that mediate these activities (emphasis on the left parietal region).

Impairments of perceptual-motor integration refer to the general inability of the patient

to properly visualize information, translate the visual percept into an accurate cognitive

representation, and then execute an accurate motor

response, such as copying a design

that corresponds to the original percept. In constructional dyspraxia, the patient’s writ

ten reproductions of designs may be distorted, rotated, and with evidence of loss of the

spatial configuration of the original visual stimuli. Assembly of materials may be

impaired due to visuoconstructive impairments. Table 19.8 shows some common tests

of visuoconstructive skills.

Ecological Implications

Mechanical abilities rely heavily on intact visuoconstructive skills. In the early phases of

rehabilitation, activities of daily functioning can be affected by impairments of these skills.

Dressing activities that require sequencing of steps and accurate right-left orientation

skills may be impaired. Therapists will often face the patient when demonstrating a

technique or skill, and this requires the patient to translate what is seen to actions, requiring

accurate right-left orientation. Rather than facing the patient, it may be beneficial to work

side-by-side to reduce the need for the patient to translate the visual orientation of the

task. Later, in the postacute phase, community mobility, driving ability, and detailed

activities, such as filling out a job application or organizing the kitchen, may be affected

by visuoconstructive impairments. Pathfinding skills may need to be aided by verbal

instruction, enhanced visual cues, and rehearsal of the task to encourage procedural

learning. Reading ability may also be affected where dyslexia (impairments in reading)

may have a component of dysgraphia; in combination, they reduce reading efficiency.

Large print materials and cueing techniques may be helpful in these situations. Alternate

learning systems such as books on tape may be needed as well.

Executive Functioning Capacity I can’t understand how wood is manufactured, what it is made of. Everything — no matter what I touch — has become mysterious and unknown. I can’t put anything

TABLE 19.8

Visuospatial Analysis and Visuoconstruction Ability Tests
Test Comment

Perceptual Organization Index–WAIS-III Composed of the Picture Completion, Block Design, and Matrix Reasoning subtests

Rey–Osterrieth Complex Figure Test Design reproductions can indicate impairments of perceptual–motor integration

Benton Judgment of Line Orientation Measures visuospatial judgment

Benton Visual Form Discrimination Measures visual accuracy and discrimination ability

Benton Facial Recognition Ability to match unfamiliar faces is tested; can assess prosopognosia

Benton Right–Left Orientation Measures the ability of the patient to accurately identify body parts on the appropriate side of the body

Hooper Visual Organization Allows for the measurement of visuospatial integration without a motor response

Line Bisection Test Measures problems with visual neglect

Visual Object and Space Perception Battery Eight subtests measure spatial perception, spatial estimation, spatial

localization

Visual Functions Scale-LNNB Items measure visuospatial, visuoconstruction, and visual judgment abilities; executive functioning abilities are required for some of these items together myself, figure anything out, or make anything new. I've become a completely different person, precisely the reverse of what I was before this terrible injury. 50(pp. 98-99) — L. Zasetsky

The term executive in executive functioning ability is a term apropos to the construct being

measured. It refers to the capacity to encode and utilize information from a variety of

sources, process that information quickly and efficiently, and then engage in decision

making based on those inputs — much like what a business executive engages in on a

daily basis. Executive processes are most often associated with frontal lobe functioning

and a plethora of research has been conducted to examine the executive abilities associated

with this brain region (see Miller and Cummings 63 for a comprehensive examination of

the human frontal lobes). Luria 16 described executive abilities as residing within the

tertiary zone of the brain, and is the unit responsible for the "programming, regulating,

and verifying mental activity." (p. 43) What Luria 64 also understood was the interconnections

of the tertiary zones with other zones in the brain, and delineates a neuropsychology of

problem-solving not only involving the frontal lobes, but also implicating parietal-occip

ital and basal-frontal functional systems. A significant amount of research has been

devoted to understanding the nature of executive

functioning impairments in TBI and the

extent to which such deficits are remediable. Executive functioning deficits, measured by

the Wisconsin Card Sorting Test and the Tower of Hanoi test, are related to acute neuro

physical damage in TBI survivors. 65 A study by Greve et al. 66 demonstrated that patients

with TBI can be clustered into four different executive functioning groups: (1) intact

performance, (2) impaired response maintenance, (3) problem-solving impairment, and

(4) impairments in ability to shift cognitive set. Executive functioning ability may also

overlap with neurobehavioral impairments such as emotional dyscontrol and reduced

motivation. 67 Changes in executive functioning can be related to recovery in TBI. 68

According to a well-known model of frontal systems by Stuss and Benson, 69,70 self

awareness is the highest human cognitive capacity which is served by a number of other

executive abilities. Figure 19.1 depicts the Stuss-Benson model.

The model is consistent with Lurian theory with the tertiary zone comprising the first

three tiers of the model, and the fourth tier related to Luria’s secondary zone. These aspects

FIGURE 19.1

The Stuss-Benson model of frontal system functioning.

Anticipation Self-Awareness Alertness Attention Memory Visual-Spatial Language Autonomic Emotional Motor Sensory-Perceptual Goal Selection Pre-Planning Drive Sequencing SelfMonitoring

of executive functioning are well represented in many of the tests employed by neurop

sychologists (see Table 19.9).

Ecological Implications

A problem noted by Cripe 71 in connection with testing for executive abilities is the ability

to generalize test findings to real-world settings. In the clinical setting, testing occurs in

a controlled environment with a minimization of distractions, usually administered by an

examiner who can cue and encourage the patient’s behavior. This is in contrast to real

world settings that are less structured and require the patient to impose structure and

organization to function, require planning and self-initiation on the part of the patient,

and where the environment may be competitive in nature in the absence of a test examiner

who can encourage and redirect the behavior of the patient. Laboratory tests may not best

represent what the patient can and cannot do in the real-world environment.

Nevertheless, tests of executive functioning can be predictive of outcome. For example,

in a recent study, Sherer et al. 72 found that the Trailmaking Test (Part B) is particularly

effective in predicting productive outcomes in patients with TBI. This is thought to be

true due to this test requiring dual-task performance (simultaneous processing) and speed

of information processing. While not specifically cited as a test of executive functioning,

tests like the Trailmaking Test or Color Trails Test

require cognitive flexibility, working

memory, and speed of processing, all in concert. This harkens back to what Luria described

as the regulation and verification of higher mental processes. Remediation of executive

abilities may be difficult since high level processes are required to benefit from interven

tions. Providing compensatory strategies for cognitive abilities that serve executive skills,

such as assistance for complex attention, recent memory, and visuoconstructive deficits,

TABLE 19.9

Tests of Executive Functioning Test Comment

Wisconsin Card Sorting Test Used widely in clinical and research contexts; shorter 64 trial version available; examines problems with perseveration and ability for novel problem-solving

Category Test From the HRNB; short version available; booklet version available but not recommended for use with the standard HRNB battery

Trailmaking Test/Color Trails Test Attention, speed of information processing and cognitive flexibility are measured

Stroop Color-Word Test Response inhibition aspect relates to executive functioning ability

Cognitive Estimation Test Examines the ability to make estimated judgments on everyday types of activities and items

Ruff Figural Fluency Test Design fluency is assessed; nonverbal equivalent to word fluency test

Executive Control Battery Executive dyscontrol; qualitative analysis of performance is assessed

Intellectual Processes-LNNB Evaluates higher-order cognitive skills, many that require executive abilities

Frontal Lobe Score–LNNB Comprised of specific items throughout the LNNB that have been found to be impaired in patients with frontal lobe damage

Tower of Hanoi Reasoning and planning skills are required

Delis–Kaplan Executive Function System Battery of subtests, each measure an aspect of executive abilities; similar types of tests to some of the tests seen in this table

Behavioral Assessment of the

Dysexecutive Syndrome (BADS) A multiple subtest measure geared toward obtaining ecologically valid data of executive functioning; includes a questionnaire of behavioral symptoms of executive functioning problems that can be filled out by the patient and by a collateral informant

will likely have an impact on the patient's net executive functioning capacity. Specific

strategies for directly managing executive functioning ability often relies upon approach

ing the patient on many fronts. This includes providing consistent and continuous feed

back (e.g., video and audio taped feedback, immediate feedback on tasks), structuring the

patient's problem-solving approaches, and assisting the patient in organizing and simpli

fying the home or work environment. Component analyses of the task at hand (e.g.,

studying for a college examination) can reveal steps in which executive dysfunction can

impair (e.g., trouble with organization of study notes). These types of analyses may be

used to identify strategies for remediation or compensation, rather than attempting to find

a treatment approach for executive abilities in general. Further strategies can be found in

Eslinger, 73 Sohlberg and Mateer, 74 and Wilson. 75,76

Mood Functioning It’s depressing, having to start all over and make sense out of the world you’ve lost because of injury and illness, to get these bits and pieces to add up to a coherent whole. 50(p. xxi) — L. Zasetsky

Mood impairments and personality functioning are important aspects of functioning in

the patient with TBI. Although the assessment of mood states and interpersonal propen

sities are not considered neuropsychological variables in and of themselves, it is an essen

tial element of the evaluation to understand the whole person. Clearly, mood disorders

are common in TBI 77 and may be a function of the neurobiology of neuropsychological

disorder. 78 Premorbid cognitive ability appears to be related to experienced distress in

individuals after TBI. 79 One of the difficulties faced by clinicians in assessing mood after

TBI is the fact that many measures rely on self-report (e.g., MMPI-2, Beck Depression

Inventory) and some, like the Symptom Checklist-90-Revised, may not have been normed

on TBI populations 80 leading to distortion on the profiles produced by these types of

measures. 81 Some commonly utilized measures are listed in Table 19.10.

Ecological Implications

Mood dysfunction, including depression, anxiety, and anger, can result in excess disability

in psychosocial functioning and in cognitive functioning. 82 Treatment of depression can

result in improved cognitive functioning, as found by Fann et al. 83 The criteria for major

depressive disorder includes concentration deficits and its alleviation may, in turn, result

in some cognitive improvement. In the patient with TBI, other neurobehavioral conditions,

such as apathy and reduced affect regulation, may mimic depression, and such symptoms

may overlap with depression. In either case, depression can be appropriately assessed

when utilizing multiple sources of data including self-report (e.g., Beck Depression Inven

tory, Geriatric Depression Scale), structured interview formats (e.g., Hamilton Depression

Rating Scale), and collateral observations by family, rehabilitation staff, and friends. Cop

ing skills of the patient can moderate some of the effects of mood disorder in patients

with TBI; however, the patient's capacity to employ psychological coping strategies may

be dependent upon the intactness of executive abilities. Reduced self-awareness can act

to reduce the frequency with which a patient may deem it necessary to change their own

behavior and invoke coping strategies (e.g., use of positive self-statements in response to

stressful situations). A combination of pharmacotherapy and psychotherapy may,

therefore, prove beneficial to the patient who presents with mood disorder following TBI.

Many patients with mood disorder find general mood benefits from physical reactivation

through physical therapy and home exercise programs. Reengagement in pleasant

activities 84 may also have mood elevating benefit. After TBI, the patient's ability to inde

pendently engage in community recreation and leisure pursuits may be limited. Postacute

rehabilitation strategies that target recreation and leisure skill improvement will also have

the added benefit of improving or maintaining euthymic mood. Other moderating vari

ables that play a role in mood stabilization and cognition include chronic pain, sleep

disturbance and fatigue, current medication regimen, and substance use — all of which

should be assessed at the time of defining rehabilitation goals.

Directions for the Future

One of the most frequently cited case studies of traumatic brain injury is the tragic case

of Phineas Gage, the railroad foreman who sustained a devastating penetrating head injury

in 1848 when a tamping iron was driven through his left frontal lobe, secondary to a blast.

Macmillan 85 documents some of the changes that Gage's physician, John Harlow, observed

in his patient shortly after the accident:

TABLE 19.10

Tests of Mood Test Comment

Beck Depression Inventory/Beck Anxiety Inventory Self-report measures of depression and anxiety (respectively); can sometimes be difficult in a severely cognitively impaired patient to complete

Geriatric Depression Scale Self-report measure of depression, normed for older adults; yes–no format

Center for Epidemiological Studies Depression Scale

(CES-D) Commonly used in research; self-report represents a

balance between mood, somatic, and cognitive aspects of depression

Hamilton Depression Rating Scale Used frequently in psychiatric research; structured interview results in clinician rating; a self-report version is available

State–Trait Anxiety Inventory Self-report measure that examines state anxiety and trait anxiety

State–Trait Anger Expression Inventory–2 Measures various aspects of anger expression, including state anger and trait anger; an Anger Expression Index is provided as well

Minnesota Multiphasic Personality Inventory–2

(MMPI-2) Standard personality inventory that has been used extensively in TBI; measures mood states, coping, and interpersonal propensities

Personality Assessment Inventory (PAI) Comprehensive measure of mood, coping, interpersonal propensities, and treatment response indicators

Millon Behavioral Medicine Diagnostic Measures interpersonal coping methods in response to medical illness; assesses mood states and treatment responsivity indicators

Neuropsychology Behavior and Affect Profile Evaluates changes in personality and emotion after brain injury

Neurobehavioral Rating Scale Measures aspects of mood and behavior that represent consequences of brain injury Remembers passing and past events correctly, as well before as since the injury. Intellectual manifestations feeble, being exceedingly capricious and childish, but with a will as indomitable as ever; is particularly obstinate; will not yield to restraint when it conflicts with his desires. 85(p. 91)

Gage experienced a dramatic change in his life of being a successful railroad worker to

working as a side show for the Barnum and Bailey Circus, displaying the tamping iron

and touted as “the only living man with a hole in the top of his head.” 85(p. 98) Stuss, Gow,

and Hetherington 86 comment on Gage: Although he miraculously survived and demonstrated good physical recovery and many preserved cognitive abilities, his emotional behavior and personality were so significantly changed that his friends stated that he was a different person: “No longer Gage.” 86(p. 349)

This story has been repeated numerous times when examining the neuropsychological

consequences of TBI. Little has changed regarding common neuropsychological and neu

robehavioral outcomes in TBI. Yet, we clearly know more about the specific neurobiological

mechanisms of dysfunction and regional brain metabolism that is altered in TBI; refine

ments in assessment technology have allowed for more precise tracking of effective reha

bilitation strategies. From Phineas Gage, we have a clear delineation of the task in front

of rehabilitation professionals: to push not only for care, but to begin working on cure.

The future holds promise for survivors of TBI, especially with regard to research into

neuroplasticity. Basic research approaches will likely lead to more transitional research

involving the enhancement of recovery 87 and the implementation of neuroprotective mea

sures early post-TBI. Clinical protocols that call for the regular use of neuropharmacolog

ical agents of cognitive enhancers are likely to enhance functional improvement. Further

research into the synergistic effect of combined evidence-based cognitive rehabilitation

procedures with cognitive enhancers is likely to illumine a biopsychosocial approach to

treating TBI. This will certainly expand the role of

setting with the neuropsychologist filling roles as an assessor and interventionist.

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20

Evaluation of Traumatic Brain Injury Following Acute Rehabilitation

Mark J. Ashley

CONTENTS

Introduction

The field of traumatic brain injury (TBI) rehabilitation has changed considerably over the

last 25 years. The field was born in the late 1970s of a need realized largely by the private

insurance community in the U.S. People with TBI were living far longer than ever before

and rehabilitation efforts for these individuals were not well developed.

In the early 1980s, a number of hospital and nonhospital based rehabilitation programs

developed utilizing a variety of program models and concepts. The number of facilities

available to people with TBI increased dramatically in the mid-1980s, only to contract

again in the early 1990s with the advent of managed care. Early rehabilitation efforts were

largely developed using treatment techniques developed for other populations and

applied to the TBI population. The last 25 years have seen a great deal of refinement of

interventions and improved predictably of outcome.

The impact of managed care on TBI rehabilitation has been considerable, 1,2 as it has been

in many areas of medicine. Perhaps the largest single impact, however, can be seen in the

amount of treatment provided to people with TBI. The 1980s saw a broadening of insur

ance coverage for rehabilitation for people with TBI, but as managed care took hold,

significant decreases in length of stay (LOS) were noted. The average LOS for acute

hospitalization decreased from 29 days in 1990 to 19 days in 1999. LOS for acute rehabil

itation hospitalization decreased from 48 days to 28 days from 1990 to 1999. It is clear that

severity of injury did not change during this time. 3 Kreutzer et al. 2 reported decreases in

lengths of stay averaging 3.65 days or 8% annually for acute and inpatient rehabilitation

treatment of traumatic brain injury between 1990 and 1996.

It can be argued that alternative treatment settings allowed LOS to be decreased as noted

above for these periods, and it is likely that such availability did, in fact, contribute to

shorter LOS. The point, however, is that these individuals were discharged from acute

care settings far earlier than had ever been accomplished before. Consequently, alternative

care settings were increasingly faced with individuals who were admitted with ongoing

medical needs or with, perhaps, as yet unrecognized problems. The trend toward shorter

LOS continues today and provides a substantial challenge to the families and professionals

involved with this population. The evaluation of a person with TBI becomes far more

complicated than ever before as a result.

TBI, unlike any other diagnosis, can impact an exceptionally broad spectrum of systems.

Additionally, recovery from TBI can occur over a protracted course of time 4–11 with residual

deficits observable for many individuals on a lifetime basis. TBI will impact the injured

person and his/her immediate family for life for persons who sustain moderate to severe

injury. 12–18 Data suggest that even a small percentage of people who sustain MTBI will

experience symptoms that persist for months or years postinjury. 19,20

Evaluation of a person with TBI, then, truly requires a

great deal of investigation, time,

and thoroughness. Unfortunately, many forces conspire to thwart the completion of such

evaluative efforts. Discharge planners have relatively little notice of impending discharge

requirements. They are plagued with lack of financial coverage for ongoing rehabilitation

or placement in supervised settings for many individuals. Discharge planners understand

that families are ill-equipped to provide all the necessary care for an injured family member,

but often have no choice in such placements. The discharge planner may be unaware of

resource availability due to the busy nature of his/her caseload and a resultant inability

to carefully research discharge options which may exist locally, regionally, or nationally.

The evaluation of a person with TBI is frequently required on short notice and must be

conducted in a busy, if not harried, environment where insufficient time has not allowed

for complete collection and collation of necessary information for the evaluator. The

evaluation today must be conducted far more quickly, without sacrificing thoroughness

or accuracy. More than ever, discharge planners and others need to know the results of

the evaluation, whether an individual is acceptable for admission to the next level of

rehabilitation and whether the individual can be admitted to that next level. The evalua

tion, then, must be conducted quickly and thoroughly, a report of the findings generated,

and all parties informed of the findings and available ongoing treatment options, often in

the span of 24 to 48 hours. The evaluator must be supported by a team of professionals

who can rapidly react to the demands of today's rehabilitation and funding milieu. Of

course, some evaluations may be conducted in a home, skilled nursing facility (SNF), jail,

or psychiatric hospital. In many of these situations, there is far less time pressure to

complete the evaluation.

This chapter will outline the comprehensive nature of information which should be

collected during an evaluation. It should be recognized that complete collection of the

information to follow is unlikely in today's rehabilitation and funding environment;

however, information which is not collected should be earmarked for later collection,

should the evaluation recommend progression to a next level of rehabilitative intervention

or admission to another care setting. It should also be understood that the intention of

this chapter is provide information to the facility-based evaluator who must conduct

evaluations at the bedside, in the home, or in another institution. Thus, the evaluation

outlined is not designed to be exhaustive, but rather to identify the major issues at hand.

Some of these issues may require much more extensive work-up than is intended to be

represented here.

Preparation So much of our time is preparation, so much is

routine, and so much retrospect, that the pith of each man’s genius contracts itself to a very few hours. — Ralph Waldo Emerson

Evaluations proceed best when the evaluator has the opportunity to prepare in advance

of the evaluation. Demographic information such as name, age, date of birth, date of injury,

social security number, home address, telephone numbers, insurance carrier information,

and so on, should be recorded for easy reference during the evaluation. Precious time will

not be taken up by these activities in this manner. The evaluator should be very familiar

with the complexity of TBI and with the scope of service availability on a local, regional,

and national level. All too often, evaluations are conducted to determine whether an

individual is appropriate for admission to a specific rehabilitation or assisted living setting.

This does not pose a significant problem when the individual is appropriate for admission;

however, the evaluator has an ethical responsibility to recognize when an individual may

be better served in an alternate environment. In order to accomplish this, the evaluator

should be aware of services offered at a variety of settings other than that in which he/

she is employed. Careful consideration must be given to advice offered for the types of

treatments or care that should be delivered next for an individual as well as to where

those services might be available. Occasionally, evaluations are conducted for the sole

purpose of securing an admission to a facility, in which

case, the evaluator has breeched

ethical principles. 21

The evaluator is best served by review of medical records prior to seeing the individual.

Collection of medical records can be quite challenging. Medical records are available from

treatment centers; however, access to the records can be quite difficult. Medical records

departments are charged with maintenance of confidentiality and are frequently over

whelmed in their workload. Although some states have requirements for timed compli

ance with requests for medical records, obtaining records via mailed or even hand

delivered requests can be exceptionally arduous. Thus, discharge planners or referring

physicians or other professionals can facilitate access to records for an evaluator.

Medical records are often more readily available in the files of workers' compensation

carriers and, sometimes, accident and health carriers since these companies strive to pay

only those bills which are accompanied by medical records. The availability of such records

can be useful in cases where the individual being evaluated was injured not recently, but

some time in the past. It will not always be possible to review the entire medical record

prior to completion of the evaluation. The evaluator's role, then, is to note which records

have and have not been reviewed and to begin the process of obtaining the balance of the

records for immediate review and consideration upon

receipt. Incomplete record avail

ability should be noted in the evaluation report and the report should be amended should

newly received information materially change any information in the report.

Review of the medical record should begin with records created at the time of injury. The

accident scene detail should be reviewed to attempt to determine the nature of the injury,

likely levels of force encountered by the body, details pertaining to level of observed con

sciousness, length of elapsed time to emergency medical treatment, and Glasgow Coma

Scale (GCS) score observed at the scene. 22 The GCS is used to both assess the severity of

injury and track the course of recovery. Mild brain injury is defined by a GCS score of 13

to 15. A rating of 9 to 12 is classified as a moderate injury and a rating of 3 to 8 as a severe

injury. In instances where the GCS is used to document the course of recovery, notation of

medications being administered over the interval should be made as medications can mate

rially impact ratings of depth of coma. 23 Emergency room records may reveal information

as indicated above and will begin documentation of the observed injuries upon presentation

to the emergency department. Increasingly, details such as level of consciousness and trauma

scores are being placed and monitored in the charts as emergency departments become

more sophisticated in their approach to TBI intervention. These data points are important

to collect at they bear upon most outcome predictions available in the literature.

As the medical record progresses, it is tempting to confine one’s review to the more

easily read typewritten reports. Clearly, these records provide a fairly comprehensive

review of a case; however, important details may be found in the handwritten nursing,

therapy, and physician notes. As the evaluator reviews the case, questions will arise as to

how and when developments occurred or conflicting information may be found in dif

ferent portions of the medical record. The answers to such questions can often be found

in such handwritten notes. The record is best understood when reviewed and presented

in the evaluation report in chronological order.

Care should be given to noting admission and discharge dates, especially in the case of

multiple facility involvement. All conditions diagnosed must be included in the report

together with a detailed review of medications, their effects, and reasons for discontinu

ation. The evaluator is well advised to structure the collection of information so as to

increase the likelihood that the most thorough evaluation will be completed. To that end,

Appendix 20A provides such an evaluative format that is useful in structuring the eval

uation process and in report preparation. Information which is not collected is obvious

by its absence and, as the evaluator considers finishing the evaluation and whether enough

information has been gathered, the form provides a means for such assessment.

The evaluator should approach each evaluation in as uniform a manner as possible.

Certain of the sections to be reviewed in this chapter require use of some minimal equip

ment and familiarity with certain procedures. Standardized reporting of level of disability

is strongly suggested by accreditation agencies 24 and should begin at the time of the

evaluation. The evaluator will need rating scale forms available with the heading infor

mation already completed. This will speed completion of the rating scales, increasing the

likelihood that they are completed. Scales most often used are the Glasgow Coma Scale,

Rancho Los Amigos Scale, 25 the Disability Rating Scale, 26 and the Functional Independence

Measurement Scale. 27

The evaluation is conducted for the purpose of determining the history and current

status of the individual with an eye toward determination of the need or propriety of

additional treatment or placement. The evaluator should have a thorough working knowl

edge of various treatment approaches and techniques available so as to be in the best

position to make recommendation about ongoing treatment delivery. While the focus is

largely upon the injured individual, the evaluator has a role to play in education of both

the individual’s family and friends as well as the professionals currently involved with

the person. As such, evaluations will require an investment of energy and time unlike that

seen in many other diagnostic groups. Evaluations of people with TBI can require well

over 2 to 4 hours, and remain incomplete. There is a huge amount of information necessary

to collect that will shape the rehabilitative effort and the current and future discharge

planning. Information collected during the evaluation will set the stage for the more in

depth clinical assessments to be conducted once an individual is admitted to the next level

of care being considered. While it may be tempting to put off collection of some informa

tion until after the next admission, the propriety of that very admission may be impacted

by advanced knowledge of key variables. Prognostication of outcome is often requested

at the time of evaluation and the accuracy of such prognostication can only be detrimen

tally affected by a lack of comprehensive information.

The evaluation should begin with answers to the questions below:

- What is the purpose of the evaluation?
- Who requested the evaluation to be completed?
- What is expected following the evaluation and by whom?
- Who are the various people who are to be involved in the evaluation?
- What specific questions have been posed to be answered by the evaluation?

The evaluation’s purpose may be to determine whether an individual is ready for the

admission to a next level of care or treatment. It may be conducted for medical-legal

purposes. Insight into the purpose of the evaluation is often, though not always, provided

by the person who requests the evaluation. The purpose may or may not be well articu

lated. The evaluation may be conducted at the request of a person behind the scenes, with

or without the encouragement of the people currently involved in the individual's care.

Some diplomacy may be in order. It is quite important to understand what is expected as

an outcome of the evaluation. Because there is so much information that can be collected

in an evaluation, the amount of time to complete the evaluation will be dependent upon

what those expectations are. The evaluator should be very clear as to what information

he/she may be expected to provide, what opinions he/she may be asked to provide, and

the information he/she will have to obtain in order to adequately answer these questions.

The people involved can be quite variable from case to case.

Likewise, roles played by these parties may not be obvious. It should not be assumed

that a person's spouse is the primary decision maker, for example. Some spouses defer to

parents, siblings, friends, or others. Thus, the evaluator must determine who the key

players are and their roles to ensure that communication flows smoothly both before,

during, and after the evaluation. It is usually advisable to have the major players present

and/or available during the evaluation. The evaluator can use their presence as an oppor

tunity to educate regarding the findings of the evaluation either as the evaluation unfolds

or in summary at the end of the evaluation. Caregivers, understandably, have information

as their most intense need and desire. 28,29

The evaluation can be conducted using a variety of formats in combination with one

another. Direct interview and assessment of the injured person may or may not be possible

as a means of information collection. It may be necessary to glean information from

observation of the injured person as he/she interacts with other allied health professionals

or with family and friends. It will be important to be able to interview these parties as

well to obtain information that is unlikely to be well represented in the existing medical

record. This includes information concerning preinjury matters such as educational

achievement, vocational history, social and family history, and sometimes, medical history.

In the event that information is relied upon from medical records to substantiate a par

ticular matter, care should be taken to note the currency of the report since recovery in

TBI sometimes occurs at unpredictable rates.

Evaluation

Current Medical Status

The person’s current medical status is a primary focus of the evaluation, especially in

these days of shortened LOS. Current medical status cannot be truly understood, though,

without reference to medical history, both prior to and since injury. Every effort should

be made to thoroughly review medical history information. Laboratory studies should be

reviewed for reported abnormalities, with particular attention paid to neuroendocrine

function, 30,31 blood dyscrasia, serum anticonvulsant levels, prothrombin times, infectious

disease reports, and alkaline phosphatase levels. Current medical status reporting should

include a detailed review of bowel and bladder status and continence. This should include

catheter requirements, stool softeners, levels of independence and awareness, and any

medical issues noted. Dietary status should review nutritional intake, swallowing status,

and level of independence. A good depiction of the history of swallowing evaluations is

in order in the event that the person suffers from dysphagia.

A full description of medications, dosages, and indications should be provided. Seizure

history or its absence should be noted. Medication history since injury should be reviewed

and reported chronologically, together with indications, effects, and reasons for discon

tinuance. All allergies must be clearly documented. The individual’s most current height

and weight statistics, together with behavioral health concerns such as alcohol or substance

abuse, must be reported.

Dental status should be reviewed either via the records or via examination. 32 Broken or

missing teeth will need to be addressed. The reliance upon dentures, orthotics, or dental

appliances should be noted. The oral cavity should be examined for description of the

dentition and gums. Some anticonvulsants and other medications can cause gum hyper

plasia. 33 Oral hygiene and level of independence and efficiency should be reported. Oral

tactile defensiveness may be a clue to painful teeth or gum.

It is important to review the person’s sleep as sleep disorders following TBI appear to

occur related to the TBI. 34,35 Check for sleep routine, including bedtime, arise time, night

time awakening, reasons for awakening, and how the person feels upon awaking in the

morning. Note caffeine or other stimulant intake, as well as medications used to induce

or maintain sleep. Discussions of sleep can be found in Chapter 9 and Chapter 24.

The person’s preinjury medical status should be documented. This should include the

person’s personal history as well as family history that might become contributory to

developing health concerns in the future. This should include both physical and emo

tional health issues. Careful investigation should be conducted into the history of pre

vious trauma to the head or whiplash, as this information may be instrumental in

understanding the postinjury course of recovery, particularly in case of mild traumatic

brain injury. 36

Lastly, medical interventions which may be necessary in the future should be recorded

such as revisions of orthopedic appliances, gastrostomy, or tracheostomy sites, cranio

plasty, and so on. Such procedures may be best undertaken either prior to or during

additional rehabilitation depending upon the nature of the case. Additionally, knowledge

that more than one surgical procedure will be necessary in the future may allow for

scheduling of both procedures under a single anesthesia.

Audiometry

Audiometric evaluation is not generally performed in the early phases of rehabilitation

for traumatic brain injury (TBI). Where formal audiometry has been undertaken, the dates

of testing and detailed findings should be reported. In instances where formal testing has

not been undertaken, observation of the individual’s functioning within the environment

can provide valuable insight into audiometric function. Historical information is of great

importance to be gathered during this process. It is important to know whether there was

a blow to the head, the integrity of the tympanic membranes, and whether otorrhea was

reported. 37,38 Each of these is important for the possible identification of disarticulation of

the ossicular chain within the middle ear. 37,38 Temporal bone fractures may result in

cochlear or vestibular damage. 37,38 A blow to the head in the temporal region may impair

Cranial Nerve VII function by damaging the nerve as it exits the skull, possibly impacting

either lacrimation alone or lacrimation and salivation.[39,40] Additionally, historical informa

tion, such as exposure to noise of a chronic nature in the pursuit of recreational or

vocational interests, might portend the development of sensory neural hearing loss. Of

course, sensory neural hearing loss of this type does not arise from the traumatic brain

injury but may complicate communicative and other restorative efforts. Likewise, an

individual's chronic exposure to ototoxic medications, such as certain antibiotics and

aspirin, might lead to loss of hearing. Reports of tinnitus are common and may be

described in varying terms. Terms used by the person to describe tinnitus can be important

in understanding its underlying cause. A high pitched whistling or buzzing sound is most

often experienced. The tone is most noticeable in quiet areas and is masked by normal

environmental noise levels. Some tinnitus, though, is reported as a roaring and may

suggest significant otological pathology. The evaluator must note these issues as well as

whether the tinnitus is constant or variable.

Behavioral observation and interview may assist in identification of hearing loss. The

evaluator should note whether the individual attempts to read lips or localize environ

mental sounds, exhibits an auditory startle reaction, or turns the head to one side during

conversation. The individual may report the presence of ringing in the ears, whistling,

buzzing, or, in some instances, a roaring sensation in the ear. The latter is often accompa

nied by a sense of oral fullness and fluctuating hearing loss. Further discussion of audi

ological and vestibular issues can be found in Chapter 5 and Chapter 6 .

Cognition

Evaluation of cognition begins with assessment of orientation to person, place, time, and

date. These questions are simply asked; however, the evaluator’s name should not be used

as a reference point. Rather, the name of an individual more familiar to the injured person

should be selected.

The presence of attentional deficits can be determined either by observation or by

interview with other professionals involved with the individual. An attempt should be

made to determine if the individual’s ability to persist with a task (persistence) is better

or worse than the individual’s ability to persist with mental activities (concentration). It

is important to discern a difference, if any, between these two types of attentional tasks. 41

Further investigation into attentional skills can be conducted by evaluation of whether

an individual is able to change between activities efficiently and without a loss of infor

mation. Some individuals will be unable to change from one activity to another and exhibit

perseverative tendencies. Others may be able to change between activities but do so slowly

and lose information in the process. Finally, the evaluator should attempt to determine

whether the individual is able to demonstrate vigilance by screening large amounts of

information for a target stimulus.

Evaluation of very brief attentional store mechanisms such as iconic (visual) and echoic

(auditory) can be easily undertaken in the scope of a field evaluation. The examiner can

prepare cards, as demonstrated in Appendix 20B, for presentation of iconic store stimuli.

The presentation of several 3 × 5 cards with three rows of three letters each 42 can be utilized,

presenting each card briefly. Examiners should note that the card is presented anywhere

from 2 to 5 seconds and, following presentation and removal of the card from sight,

examiners indicate which row they would like the person to recall. As the examiner goes

through various cards, the row requested should be chosen randomly and the accuracy

of response noted. Line recall should be somewhere in the neighborhood of 75% and card

recall in the neighborhood of 90%, with a small amount of rehearsal. Echoic store can be

evaluated by the presentation of randomly presented numbers, zero to nine. Normal

performance is in the neighborhood of six to seven numbers forward recall and four to

five numbers backward recall. 43 The task can be further complicated by asking the person

to order presented numbers from largest to smallest, thereby assessing both immediate

recall and working memory.

Central to the processes of cognition is an individual's ability to identify perceptual

attributes of objects and events in their environment. 41 The evaluator should attempt to

discern the individual's fluency with this task by presenting up to three objects and asking

the individual to provide a description. The examiner can model the description or can

enumerate the variables desired, such as color, size, weight, shape, function, detail, texture,

and construction. The total time required and the spontaneity of response, once the task

is demonstrated, should be noted. The degree to which the evaluator needs to assist the

individual in coming up with features should be noted. In order, then, to undertake this

evaluation, the examiner might describe an object to the patient using the eight previously

detailed features. A pencil could be 5 inches long, 3 / 8 of an inch in diameter, hexagonal

in shape, yellow, pointed, or cylindrical, weigh approximately 1 / 2 ounce, be constructed

of wood, have a lead point or rubber eraser, and be used for writing. The individual is

asked to carry out a similar description with up to three objects. This task should be able

to be completed in less than 30 seconds per object and notation of any perseverative

response should be made. Of particular interest is whether an individual focuses on the

object's function vs. description of how the object is constructed.

Next, the evaluator should determine the degree to which the individual is able to

use perceptual features to categorize. This can be done with objects that are common

and within the environment. It may be necessary to model the task for the individual.

The evaluator should observe if the individual is able to categorize and determine which

methods and techniques are used for categorization (see Chapter 13). As part of the

evaluation of categorization, the examiner should attempt to determine if the individual

can decide which items do not belong in an examiner-defined category. Use of real

objects allows the examiner to create a group of objects that share a perceptual feature

and to determine if the individual can decide what attribute is shared by all of the

objects. For example, grouping of four or five metal objects should elicit a response that

all the objects are made of the same material or of metals. Next, the evaluator should

determine if the individual can decide which objects do not belong in a particular

category. The evaluator can determine if the person can extend categorical boundaries

by asking questions such as "Can a chair be used as a ladder?," followed up by a request

for a description of how this could be undertaken. Individuals who are very concrete

and unable to extend categorical boundaries will answer the question in the negative.

If an individual answers the question in the affirmative, the evaluator should determine

whether the response is a randomly selected one or, in fact, is based upon sound

reasoning. The intention is to identify the ability to alter the function of an object to an

acharacteristic function based upon a particular feature. In the pencil example, the pencil

could be used as a lever or as a weapon. The examiner can show the person an object

and ask them to name three other objects not currently in the room that share a named

feature with the one being shown.

Proverb interpretation can be undertaken to determine the degree to which an individual

is functioning at an abstract reasoning level. Additionally, drawing a floor plan of the

room in which the individual is sitting, including windows, walls, doors, and placement

of furniture, as well as a floor plan of the place where the individual lives, can provide

additional insight into visual perceptual skills, as well as abstraction capabilities. In the

instance where the proverb is literally interpreted, it becomes apparent that the individual

is functioning at a fairly concrete level. Floor plan execution and proverb interpretation

can yield information about the individual’s ability for planning, sequencing, cognitive

distance, 44 visual imagery, and visual praxis. 45

The ability to sequence can be evaluated by asking the individual to go through a

detailed description of how to change a tire, or bake a cake, or some other gender and

experience appropriate example. In a somewhat similar vein, problem solving can be

evaluated by asking the individual what they would do in the event of a given scenario.

One such example might be, “What would you do if you came home and found a family

member lying on the floor, unconscious, and bleeding heavily from a deep cut on the

arm?” Acceptable responses should be noted, as well as the time required to provide those

responses. Once an acceptable response is obtained, the examiner adds a complication,

such as being unable to awaken the person. A logical response might be that they would

then call for help. The next complication added would be that the telephone does not

work. A logical response to this complication might be to leave the individual and go to

a neighbor’s for help. Finally, the complication that the neighbors are not home can be

provided. Some individuals will become quite frustrated with these task complications,

others will provide unique and unrealistic responses to the complications, and still others

will be able to provide a reasonable response to the complications. The response pattern

should be noted, as well as the time to respond.

Next, it is important to evaluate whether learning is rule governed or nonrule gov

erned. 46 A deck of cards can be utilized to evaluate an individual’s abilities in this regard.

First, the cards are slowly dealt, face-up, into two piles, which are separated on the basis

of whether they are black or red. The individual is asked to tell the examiner the rule the

examiner is using to place a card in either pile. The individual should be able to identify

a rule within five to ten cards per pile. If the individual is able to identify the rule properly,

the examiner should continue by simply changing the pile into which the red cards and

black cards are delivered (to the converse pile). Again, the individual should be able to

tell the examiner that the rule has changed and what the new rule is. This is an evaluation

of a “reversal shift” capability. The testing progresses with the examiner changing the rule

entirely, placing face cards in one pile and nonface cards in the other. Again, determination

of the change in rule and the nature of the rule is the target for this “nonreversal shift”

activity. Care should be taken to evaluate the level of capability and/or frustration present

during this task and the task is discontinued should the individual be unable to complete

the task or become frustrated with it. Previous administration of the Wisconsin Card Sort

may provide the information that can be obtained from this procedure. Whether the

individual is a reflective thinker or has an impulsive thought style should be evaluated

and noted as cognitive tempo. 41 Speed of processing should likewise be evaluated.

Through much of the evaluation of cognition, the examiner can rely both on formalized

evaluative procedures that might have been undertaken by professionals involved in the

case and by observation of the individual's behavioral interaction with the environment

and individuals in it. In this method, behavior is used as a representation of cognition. 47

Education

The educational history of the individual should be obtained by interview with family, as

well as a review of academic records. Those individuals who are in the process of com

pleting or have completed high school may have academic records available to them

personally. In any event, academic records can be requested of grade school and high

school institutions and should be reviewed to gain insight into both academic performance

and the possibility of previous observations or notations regarding injuries, attentional

deficits, learning disabilities, or behavior problems.

All too often, a formal or informal academic skills evaluation is absent from a rehabil

itative evaluation. In many instances, these areas are relegated to the speech pathologist

or occupational therapist. In some specialized facilities, however, educational specialists

are utilized to evaluate and remediate these skill sets.

In a field evaluation, a cursory look at mathematics, reading, writing, money manage

ment, and telephone skills is in order. For mathematics, the individual's ability should be

evaluated to count with a random number of objects, add and

subtract with either objects

or without, identify sizes, write number symbols up to 100, count by 2s, 5s, and 10s up

to 50, add and subtract without renaming up to 3 columns, add and subtract with renaming

up to 3 columns, multiply 1 digit by 1 digit, multiply 2 digits by 1 digit, distinguish the

value of a decimal fraction compared to a whole number, and find a percentage of a whole

number. Reading skills, such as the ability to recognize random letters in the alphabet,

read simple sight words, read functional sources (e.g., labels, newspapers, signs), and

answer three comprehension questions about material read from a functional source,

should be evaluated. Spelling and writing skills can be evaluated by asking individuals

to write any given letter of the alphabet, copy a sentence, write two or three sentences

about themselves, and spell two of four words at a sixth-grade reading level (i.e., direction,

activity, vegetable, gentle).

A history should be taken pertaining to money management skills. It should be deter

mined who managed money in the family and the extent to which the injured individual

participated in those activities. It should include experience with the management of real

money, such as coin identification and making change, as well as whether the individual

utilized a checkbook and how he/she managed the checking account. Finally, telephone

skills can be evaluated by asking the individual to dial a

number, determining whether

the appropriate communicative techniques are utilized for the telephone, whether the

individual is aware of emergency phone skills, and whether the individual is able to use

a telephone directory. Discussion regarding money management skills with the family

will allow determination of whether responsibilities have been given over to a family

member or caregiver since injury.

The evaluator may wish to bring along grade-level, standardized math and reading

exercises and problems to be used in the evaluation. Care should be taken not to assume

capabilities not demonstrated. It is often tempting, based upon an individual's educational

or vocational experience or, sometimes, based upon their linguistic skills, to forgo this

portion of the evaluation.

Family

It should go without saying that collection of information pertaining to the family will be

of great help in determining key players and their roles. It may be that the evaluation

setting will not lend itself to a casual collection of this information or complete access to

this information in that family members may or may not be present in all settings. In any

event, the information should be collected, either by direct interview or telephone inter

view. The individual's marital status and prior experience with marriage/divorce should

be discerned. Previous spouse names should be collected. All children from current and/

or former marriages should be identified by name and age. Siblings, also, should be

identified by name, age, and location. It is often helpful to attempt to discern siblings'

occupational endeavors. These individuals may be quite insightful during treatment, may

have worked in similar or identical fields and be helpful in identification of vocational

aptitudes and skills, and may represent potential vocational placement options following

completion of the medical rehabilitation. The parents' names, ages, locations, occupations,

and marital status should be obtained as well.

Of greatest interest is the family's education and awareness of the diagnosis, individual

deficit areas, and knowledge of the short- and long-term outlook for their family member.

Often, families, though they may have been given access to some information, report that

they feel quite at a loss to predict a longer-term outcome for the injured individual or

themselves. 29 Reviewing the evaluation findings with the family, in detail, will both serve

as an educational opportunity and an opportunity to determine gaps in their knowledge

and provide education. Many families report a frustration with the lack of information

and a coincidental relief when their questions can be answered by an evaluator, either

about past, current, or future events. The evaluator will be interested to know whether

the family has had counseling or is currently involved in counseling. Additionally, dis

charge options should be discussed with the family, determining their wish to be involved,

their ability to be involved, and the degree of involvement they wish to have.

Conservatorship or guardianship issues can be quite varied from state to state and

circumstance to circumstance. That is to say, some individuals may have no guardianship

or conservatorship proceedings involved in their case. Others, however, may have a

conservatorship over finance, a conservatorship over person, a conservatorship over both,

a power of attorney arrangement, or some other arrangement. Likewise, some individuals

may not have any of these in place and the evaluator may be in a position to advise that

these matters be considered with the family's legal counsel. Family members are often

poorly informed regarding the role of guardianship or conservatorship proceedings that

may have been undertaken or may have been recommended. Consequently, it is always

a good policy to obtain copies of any conservatorship or guardianship proceedings so

that the evaluator and/or treating facility can be aware of the nature of the proceedings

and the impact upon the individual's rights and liberties those proceedings may or may

not have.

Occupational/Physical Therapy

Investigation of occupational and physical therapy status

should begin with a review of

the patient’s treatment history and discussion with any currently involved professionals

in these disciplines. Active and passive range of motion is of interest in the upper and

lower extremities, head and neck, and trunk. These can be directly assessed or observed

as the individual moves in the environment. Likewise, strength in the upper and lower

extremities, as well as head, neck, and trunk, should be determined. The evaluator can

note functional capabilities or can proceed through formal strength grading by physical

examination. Sensation and proprioception should be evaluated. Comments regarding

overall muscle endurance, as well as cardiopulmonary endurance, should be provided.

Of interest in sensation testing is appreciation to light touch, to touch discrimination, and

temperature differentiation in all four extremities. Facial sensation will be discussed under

the Speech Pathology section of this chapter. Likewise, proprioceptive awareness of the

upper and lower extremities should be evaluated. When evaluating stereognosis, the

evaluator should be careful that the individual does not see the object being placed in

either hand. As the individual names the object, care should again be taken to note whether

naming difficulties are present in both hands or only the left hand. A deficit in stereognostic

naming in the left hand may point to a callosal lesion. 48 If language impairment is present,

the evaluator may ask the individual to identify the object he/she was holding from a

group of objects.

The presence or absence of clonus in the upper and lower extremities should be noted.

The evaluator is interested in fine motor coordination and dexterity. This can be observed

through direct assessment, object manipulation, or finger-to-thumb opposition, progress

ing through each of the four fingers. Gross motor skills, such as the ability to roll from a

supine to prone position and back, assume a quadruped position, assume tall kneeling,

assume half kneeling, and stand from a half-kneeling position, will be important to the

physical therapist. The individual’s ability for transfers should be assessed as indicated

from floor to chair or wheelchair, from wheelchair to chair, wheelchair to bed, bed to

wheelchair, wheelchair to car, and wheelchair to toilet.

Balance should be evaluated for both sitting and standing, if possible. The evaluator

can assess an individual’s abilities for challenged and unchallenged sitting and standing

balance, one-foot balance, and heel-toe walking. Weight shift during ambulation should

be noted, as well as posture, both sitting and standing. Gait should be evaluated for pace,

required devices (such as orthotics, canes, walkers, etc.), trunk rotation, and reciprocal

arm swing, and should include smooth and uneven surfaces. If the individual requires a

wheelchair, the type of wheelchair should be noted.

Evaluation of vestibular sensitivity should include review of complaints of headaches,

nausea, vomiting, dizziness, lightheadedness, or a feeling of imbalance. Historical infor

mation may point to vestibular dysfunction such as falls which occurred in low light

conditions, loss of balance in the shower, while dressing or playing with the children,

reliance upon night-lights, a feeling of imbalance, fear of heights or stairs, or discomfort

or motion sickness following car rides or activities which require plane changes. The

evaluator may wish to conduct a marching-in-place exercise, with and without vision, or

other vestibular tests the evaluator may be comfortable with (see Chapter 5). Walking in

a straight line, forward and backward, with eyes open and eyes closed can help to identify

vestibular involvement. Deviation will be toward the side of involvement. 49 Of course,

care must be taken to provide for proper safety precautions in guarding the person from

falls with any balance or coordination testing. These activities should not be undertaken

without proper training. Cerebellar testing can be done by heel-to-shin maneuver, finger

to-nose maneuver, and reciprocal alternating movements of the upper extremities.

The ability to complete activities of daily living (ADL) is of great interest. This should

include hygiene, toileting, dressing, grooming, feeding, meal planning, shopping, meal

preparation, laundry, and household cleaning. The degree to

which the individual partic

ipates in these activities, the level of independence exercised, and the degree to which the

individual participated in these activities prior to injury will all be important. Part and

parcel to the evaluation of ADL skills is a review of the individual's typical daily routine.

This should simply include a description of the individual's time to arise and all activities

generally engaged in throughout the day until bedtime. Careful evaluation of the person's

ability to initiate tasks as either part of routine or apart from routine should be conducted. 50

Essentially, the evaluator needs to construct a conception of the individual's daily and/

or weekly schedule of activities. This should be contrasted to the daily or weekly schedule

of activities the individual engaged in prior to injury. Driving habits prior to injury can

be discussed as a part of this undertaking and the individual's ability to drive following

the injury should be documented. Different states have different requirements regarding

reporting to their motor vehicle departments and the evaluator should be aware of those

reporting requirements and/or whether the individual's injury or seizure condition, if

present, has been reported.

Evaluation of gustation and olfaction is not often done. The evaluator may wish to carry

a standard set of scratch and sniff patches to test olfaction. The presence of deficits in

olfaction is fairly common following traumatic brain injury

51 and should be suspected

when the individual suffers weight loss, loss of appetite, or diminished meal volume

consumption. Likewise, these same behaviors may point to difficulties with dentition and/

or swallowing.

Psychosocial

Among the many areas traumatic brain injury impacts in a person’s life, perhaps none

can be more profound than the changes in personality that are attributed to TBI by injured

individuals, their families, and their friends. 29 A reasonable goal for rehabilitation is to

attempt to return the individual to his/her preinjury lifestyle as much as possible. To

that end, it becomes quite important to understand the individual’s personal history.

Information such as where the individual was born and raised, how frequently he/she

moved, a military service history, and religious affiliation will provide great insight into

preinjury personality.

An evaluation of the individual’s ability to describe his/her deficits and limitations

should be conducted. The evaluator should attempt to discern how comprehensibly the

individual can describe his/her deficits and the degree of assistance needed to do so.

Difficulties in acknowledgment or acceptance of disability should be identified, docu

mented, and described. The individual may have difficulty due to cognitive processing

problems, denial, rationalization, projection, repression, suppression, displacement, subli

mation, or regression. The evaluator should obtain an idea of the individual's self-concept.

How does the individual see himself? Does the individual demonstrate a consistency of

self from preinjury to current status? Does the individual see himself as others do? Finally,

the evaluator should attempt to determine the impact of the injury on self-esteem.

It is important to attempt to determine the degree to which the family is supportive

of the individual, is understanding of the individual's deficits and limitations, and is able

to participate in a rehabilitative milieu. Problem areas in the family should be identified,

in particular as they may impact the rehabilitative undertaking. A similar approach

should be taken with friends, attempting to determine the quality and quantity of visi

tations or interactions.

The preinjury personality may have been more formally assessed somewhere in the

individual's treatment. Formalized testing and dates, as well as report summarization,

should be included in the evaluation. Additionally, the family's characterization of the

preinjury personality and the individual's characterization should be reported. Informa

tion about membership in organizations, hobbies, recreational interests, preinjury goals,

and current goals should be collected. The evaluator will need to request information

regarding social and legal history. Results of formal neuropsychological and/or psycho

logical testing should be reported, with the dates of testing, the tests administered, and

the findings.

Discussion of sexuality may be conducted either in the Psychosocial portion of the

evaluation or in the Medical portion. The evaluator should attempt to discern the indi

vidual’s ability to engage in various levels of social interaction and maintenance of social

boundaries. Family may be best able to provide an historical reference to the person’s

expression of sexuality prior to injury. This should be compared to behavior following

injury. It is important to attempt to determine whether emotional and sexual intimacy

have been altered or impaired since injury.

TBI often impacts an individual’s ability to handle frustration or to engage in socially

appropriate behaviors. These deficits may manifest in impulsive anger, verbal aggression,

physical aggression, or in behavioral manifestations that are outside of societal norms.

The evaluator must note episodes of impulsive anger, frustration, verbal aggression,

physical aggression, and any behaviors which have been noted to be problematic. The

individual or family should be able to provide insight into coping mechanisms prior to

injury and may be able to provide insight into current strategies. It is important to evaluate

how the individual shows frustration, whether he/she

engages in withdrawal or aggres

sion, and whether there is anxiety, nervousness, psychosomatic complaint, lability, or

depression. Information may be available regarding previous psychological or psychiatric

treatment. The evaluator should discern whether paranoia, hallucinations, delusions,

addictions, depression, regression, or psychosomatic complaints have been noted or

observed. The individual's motivational capabilities should be identified, both for those

areas in which the individual seems highly motivated or, perhaps, "overly motivated," as

well as a lack of motivation or initiation.

Speech/Language Pathology

Deficits of interest in speech/language pathology following traumatic brain injury are

typically in the areas of cognition, motor speech disorders, dysphagia, language disorders,

fluency, and voice. As part of the evaluation of motor speech disorders and dysphagia, an

oral peripheral examination is undertaken. Observation of the facial symmetry, at rest and

in movement, is undertaken to determine whether any asymmetries are present. Facial

sensation should be evaluated at all three branches of Cranial Nerve V 39,40 as this nerve is

particularly vulnerable to injury in the temporal region where it exits the skull. The

mandibular rest position is noted, as well as the ability to extend and lateralize the

mandible. Position of the tongue, at rest and in various maneuvers, is noted, again, with

an expectation for no tremor, no fasciculations, and symmetry of movement. An oral

peripheral examination form is attached in Appendix 20C of this chapter. It is not likely

that the evaluator will conduct an otoscopic examination; however, otoscopic examination

has probably been performed and the results should be noted. Likewise, swallowing is

most generally evaluated at the acute level and the most recent swallowing evaluation, as

well as the history of evaluation of dysphagia, should be noted. The evaluator should look

for consistency in the management of foods, liquids, secretions, and radiographic evalua

tion of swallowing. The examiner can undertake a quick apraxia assessment by asking the

individual to undertake several activities without demonstrating those activities. These

include (1) stick out your tongue, (2) blow, (3) show me your teeth, (4) pucker your lips,

(5) bite your lower lip, (6) whistle, (7) lick your lips, (8) clear your throat, (9) cough, (10)

smile, and (11) puff your cheeks. Articulatory agility, or the ability to make various speech

sounds clearly and quickly, should be noted. Throughout the evaluation, the individual’s

ability to maintain topic can be determined. 52,53 Any difficulties with fluency (stuttering)

should also be noted. Should a fluency disorder be present, the evaluator should determine

if this preexisted the injury. Voice can be characterized as breathy, nasal, hoarse, soft, or

loud. Evaluation of intonational changes in conversation

should be included as their

absence can materially impact communicative intent and success. 54 History of endotracheal

intubation should be noted and an attempt should be made to determine pulmonary

capacity. A nasal quality in voice may suggest a velopharyngeal paresis. 55

Traumatic brain injury does not generally result in pure receptive or expressive aphasias

as are often demonstrated in cerebral vascular accidents (CVA). However, evaluation of

expressive and receptive language skills should be undertaken and/or test results

reported. Most frequently observed are difficulties with anomia, paraphasias, and neolo

gisms. A paraphasia is a whole-word substitution, such as “tar” for “car.” Neologisms are

nonsense words or syllables. 56,57 Finally, the ability to communicate intent should be

assessed with a description of the means utilized to communicate.

Vision

A visual evaluation early after TBI is difficult to undertake and is, therefore, often post

poned. Clearly, cranial nerve involvement (see Chapter 6) is often included in a neurolog

ical evaluation and some work-up of visual perceptual skills may be available in the

Occupational Therapy history. The evaluator should note whether the individual had

prescriptive lenses prior to injury and for what purpose, as well as whether those lenses

are currently available and in use. Documentation of

complaints of visual acuity should

be included and any formal ophthalmologic examination which has been undertaken

should be reported, with dates and results. Individuals may report difficulty seeing,

blurred vision, double vision, changes in vision with fatigue, difficulty reading, and in

some instances, may report image persistence (being able to see an object after looking

away from it) or lack of recognition of familiar objects, places, or persons. 58,59 Some of

these reports may not be spontaneous and may require the evaluator’s active investigation.

The evaluator can test visual fields to confrontation and can evaluate ocular motility

and gaze convergence. Evaluation of visual fields is conducted by covering one eye and

moving an object from the ear forward into the lateral field of the uncovered eye. The

person is asked to maintain a straight ahead focus and indicate the earliest point at which

the object comes into the peripheral field of vision. The maneuver is repeated from over

the head to check superior quadrants, under the chin to evaluate inferior quadrants and

the opposite side of the head to the covered eye to evaluate nasal fields. The entire process

is repeated for the other eye. Evaluation of ocular motility is performed by asking the

person to track, with eyes only, the movement of an object which is moved in front of the

person from left to right to left, up and down, and in a circle. The evaluator is looking for

smooth and convergent movements of the eyes, without overshooting or jerky movement,

which could imply brainstem involvement of Cranial Nerves III, IV, VI, or VIII. 60,61 Finally,

behavioral observation may help to discern the presence of visual field cuts or neglect as

when an individual bumps into objects or appears to miss information in the environment

predominantly in a particular visual field or quadrant.

Information about visual perceptual skills may be available from the occupational ther

apy department or from ophthalmologic or optometric evaluation. Of interest are depth

perception, binocular or stereo vision, visual figure-ground, visual praxis, and visual

organization skills. The examiner may wish to carry subtests of standardized visual per

ceptual tests in order to investigate visual perceptual skills.

Vocation

The individual’s preinjury vocational endeavors should be chronicled in the evaluation.

This should consist of a chronological review of at least the last 10 to 15 years of employ

ment, complete with job position, companies, locations, and salaries. A complete voca

tional history provides a great deal of information about an individual’s work ethic,

intellectual capability, social experience, and vocational experience. If large gaps in

employment history are noted, reasons for unemployment should be determined. Like

wise, if an individual has a history of frequent job

changes and positions of short duration,

reasons for those job changes should be listed. An individual who frequently changes jobs

may have a history of inappropriate social skills as they pertain to job settings or difficulties

with maintaining employment. By the same token, some professions, by their very nature,

subject an individual to frequent changes in employer. Consequently, any conclusions

drawn regarding an individual’s work ethic, personality, or vocational history should be

drawn from a comprehensive review of these factors. This section should culminate with

the job held at the time of injury or the most recent position and salary. Families or injured

individuals, themselves, may be able to provide insight into positions the individual

disliked and liked, as well as goals the individual had and/or has. The individual’s goals

for vocational involvement should be determined, together with the family’s goals and

expectations. Finally, any vocational evaluation or testing that has been completed should

be reported, with dates and results.

Report Preparation

Appendix 20A to this chapter and, indeed, the very format of this chapter, can be used

in report preparation. Findings under each heading can be listed within their own sub

section in a report; however, the most important section of the report is likely to be the

Impressions and Recommendations section. This section of the report must be clear,

concise, and able to answer most questions of most readers. Unfortunately, reports are

read by many varied professionals and it is not possible to anticipate all of those questions,

nor is it advisable. Thus, when the report is prepared, it should be prepared with the

referral questions in mind, very clearly stated, and answered as clearly as possible in the

Impressions and Recommendations section.

A good practice is to utilize a standardized scale reporting in an effort to quantify the

individual's functioning status in a means that may be immediately understandable across

treatment settings. Scales which allow this are the Disability Rating Scale, the Rancho Los

Amigos Scale, the Glasgow Coma Scale, and the Functional Independence Measure. The

level of disability should be characterized in terms of the scale or scales utilized. The

referral question should be posed and answered, with a listing of factors which will

positively influence attainment of any identified goals, and factors which will impede

attainment of those same goals. It is often best to enumerate recommendations in a

numbered fashion, and it may be helpful to both the preparer of the report and its reader

if these recommendations follow the general outline of the report in order. Consequently,

following the outline of this chapter, recommendations of a medical nature would be

provided first, followed by Audiometry, Cognition, Education, Family, Occupational and

Physical Therapy, Psychosocial, Speech/Language Pathology, Vision, Vocation, and

Impressions/Recommendations.

The report should include whether the individual is an appropriate candidate for admis

sion to a specific care setting or treatment setting, if this question has been raised. The

report should answer whether ongoing rehabilitative services are in order and the expected

outcome of those services, if rendered, together with time and cost expectations. Again,

this information should be provided only if requested as the primary purpose of the

evaluation. Should the individual not be an appropriate candidate for a particular pro

gram, it is felt that the evaluator should attempt to provide alternate suggestions for the

referral source, injured individual, and/or family. The report should conclude with infor

mation about how to contact the evaluator with questions or comments.

Summary

The evaluation of a person with traumatic brain injury poses considerable challenge to

the professional. The evaluation is rarely complete enough and time allotted for evaluation

is all too often insufficient. In any evaluation, there will almost universally be more

information needed than provided and the art form to be realized is the successful col

lection of a maximal amount of information in the time allotted. The evaluator should

develop a sense for which information is most important and germane, and a routine

within the treatment setting for a collection of information that may not have been avail

able at the time the evaluation was conducted. The evaluation should be viewed as a

preliminary venture which sets the stage for a team of professionals to become involved

in more in-depth diagnostics and evaluations. Treatment plans which will subsequently

be established will be preferentially or detrimentally impacted by the quality of this initial

evaluation. It is this author's contention that allied health professionals in the field of

traumatic brain injury have an ethical responsibility to put forth the effort necessary to

conduct a thorough, comprehensive, and accurate evaluation.

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Appendix 20A: Patient Examination Report

An onsite patient examination was conducted of Mr. Xxxxxx Xxxxxxxxx on August 18,

1995. The examination was conducted at the request and authorization of Mr. Xxxxxx

Xxxxxxx, Assistant Vice President, Xxxxxxx Xxxxxxxxxxx Corporation. Present and/or

interviewed during the examination were Mr. xxxxxx

xxxxxxxxx, Ms. xxxx xxxx, Mr.

Xxxxxx Xxxxxxx, and Mrs. Xxxxx Xxxxxxxxx. The examination was conducted by Xxxx

X. Xxxxxx, XX, XXX-XXX, XXX, Xxxxxxxxx Xxxxxxxx of Xxxxxx xxx Xxxxx Xxxxxx in

Xxxxxxxx, California. The examination was conducted in Dr. Xxxxx Xxxx'x office.

MEDICAL HISTORY:

AUDIOMETRY:

COGNITION:

EDUCATION:

FAMILY:

OCCUPATIONAL/PHYSICAL THERAPY:

PSYCHO-SOCIAL:

SPEECH/LANGUAGE PATHOLOGY:

VISION:

VOCATION:

VOCATIONAL REHABILITATION:

IMPRESSIONS/RECOMMENDATIONS: Sincerely, NAME OF ORGANIZATION Name and Credentials of Examiner Title of Examiner

XXX/xxx

CLIENT: XXXXXXXXXX

AGE: XX

DATE OF BIRTH: XXXXXXXXXX

SOCIAL SECURITY NUMBER: 000-00-0000

DATE OF INJURY: XXXXXXXXXX

CARRIER CASE MANAGER: XXXXXXXXXX

CLAIM NO. XXXXXXXXXX

REINSURANCE: XXXXXXXXXX XXXXXXXXXX XXXXXXXXXX XXXXXXXXXX

CONTACT: XXXXXXXXXX XXXXXXXXXX (000) 000-0000

DATE OF EVALUATION: August 18, 1995

DATE OF REPORT: August 24, 1995

Appendix 20B: Iconic Store Cards N D Q H K X T Z P M J D A F R T M E A Y O W F L E R B A C M D T K Z O V S J P W O G B X H B T F O M S L E N X T F L A H U V N P F H T R M O Y L L Z G U C B N W P D S W L Q B U G J T Q M C Z R K G J

Appendix 20C: Oral Peripheral Evaluation

Apraxia Battery

1. Stick out your tongue

2. Blow

3. Show me your teeth

4. Pucker your lips

Client Name Date

Facial Symmetry Rest: Smile: Labial Strength: Pucker: Facial Sensation: Normal Normal Normal Normal V 1 Right Droop Right Weak Weak Weak V 2 Left Droop Left Weak V 3

Mandible Rest Position: Jaw Extension: Jaw Lateralization: Resistive Closure: Normal Normal Normal Normal Low Right Right Absent Weak Right Left Left Absent Weak Left

Tongue Rest: Tremor: Protrusions: Fasiculations: Protrusion Strength: Elevation: Lateralization (in cheek): Diadochokinetics: Oral Mucosa: Normal Absent Normal Absent Normal Normal Normal Normal Normal Right Atrophy Present Right Deviation Present Weak Weak Right Weak Depressed Lesion(s): Describe Mass: Describe Left Atrophy Left Deviation Left Weak _____ _____ _____

Velopharyngeal Mechanism Rest: Clefts: Ah: Hyper nasality: Gag: Normal Absent Normal Yes Absent Right Droop Present Right Droop No Present Left Droop Left Droop

Hearing:

Swallowing: Liquids

Vital capacity: (3 trials)

Sustained phonation: ah _____ s
_____ z _____

5. Bite your lower lip

6. Whistle

7. Lick your lips

8. Clear your throat

9. Cough

10. Smile

11. Puff your cheeks

Dentition: Good Repair Poor Repair

Dentures: Maxillary Mandibular

Occlusion: Normal I II III Describe

Corrective Lenses: Yes No

Hearing Aids: Yes No 1 or 2 Type:

Dysarthria: Yes No Severity: Mild Moderate Severe

Apraxia: Yes No Severity: Mild Moderate Severe

Other:

_____

_____

Smoking: Yes No How much _____

Recommendations:

_____

Speech/Language Pathologist

Case Management Themes

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Appendix 21A Facility Experience Yes No Comments

1. Has the facility been open longer than 2 years?

2. Does the program specialize in brain injury?

3. Does the program handle behavioral clients?

4. Does the program specialize in community reentry?

5. Does the program specialize in cognitive retraining?

6. Does the program specialize in vocational rehabilitation?

7. Does the program specialize in return to work? Personnel Qualifications Yes No Comments

1. Does the program employ all professional staff?

2. Does the program employ or contract with: — a physical therapy staff? — an occupational therapy staff? — a

speech-language pathology staff? — an educational staff? — a neuropsychology staff? — a clinical psychology staff? — a nursing staff? — a recreational therapy staff? — a social services staff? — a community staff?

3. Does the above-mentioned staff have professional licenses?

4. Are these licenses available for review?

5. Is each professional assigned to one facility 100% of the time?

6. Does the licensed professional provide more than half the treatment for his/her discipline?

7. Are assistants used to provide treatment?

8. Does the assistant provide more than half the treatment?

9. Is the assistant certified?

10. Does the program have a medical director?

11. Does the program regularly obtain medical consultations for patient health issues?

12. Does the program regularly obtain medical consultation for patient program issues?

13. Does the program have a core of senior staff with more than 2 years of experience?

14. Has the core of senior staff been employed by this program longer than 2 years? Peer Review Yes No Comments

1. Is the opinion of the professional community outside the program favorable?

2. Does the program seek input for programming purposes from the case manager?

3. Does the program consider the case manager part of the treatment team?

4. Is the staff able to answer questions concisely, in lay person terms?

5. Do the answers make sense?

6. Is senior and treating staff available for consultations or to answer questions?

7. After discharge, does the program continue to follow the client? Services Provided Yes No Comments

1. Is the program residential?

2. Is therapy performed in the residential setting?

3. Is therapy performed in a separate setting from the living environment?

4. Is therapy conducted in a community setting?

5. Is more than half of therapy conducted on a one-onone, therapist-to-client basis?

6. Are the programs custom-tailored to meet the individual needs?

7. Is the program able to prepare the client for the intended discharge setting? Patient Evaluation Criteria Yes No Comments

1. Was the preadmission evaluation performed by other than marketing staff?

2. Did the evaluation include a thorough review of medical records?

3. Were goals stated in the evaluation?

4. Did the evaluation include an estimate of discharge living status?

5. Did the evaluation provide a length of time the program will take to accomplish the goals stated in the evaluation?

6. Did the evaluation include a detailed projection of treatment costs?

7. Did the evaluation provide you with more information than you had before the evaluation? Communication and Documentation Yes No Comments

1. Does the program provide detailed weekly reports?

2. Are the reports clear, concise, and easy to read?

3. Are goals reevaluated on a monthly basis?

4. Are goals set appropriately?

5. Do treaters educate the injured individual?

6. Do treaters educate the family? Price Structure Yes No
Comments

1. Is fee-for-service billing available?

2. Is the program billing easily audited?

3. Are complete reports provided in the billing?

4. Does the program participate in discounting practices?

5. Does the program charge for evaluation services?

6. If the program charges a per diem rate, is the number of
hours of therapy and treatment defined? 661

0-8493-1362-7/04/$0.00+$1.50

22

Litigation and Settlement Options for the

Brain-Injured Survivor

William L. E. Dussault

CONTENTS

Appendix

Introduction

Individuals who have experienced traumatic brain injuries are often involved in litigation

to obtain financial recoveries for the injuries they have experienced. Personal injury attor

neys who work in this area typically do a wonderful job in the traditional aspects of

litigation and settlement of the legal case, but are just as often completely unfamiliar with

the long-term consequences of obtaining funds on behalf of the disabled client without

proper planning for the long-term use and management of the funds. The same lack of

awareness of the impact that resources held by a disabled person will have on that

individual's public benefit eligibility can make a well-intended gift or contribution from

a third party have disastrous consequences for the disabled individual.

In the U.S., a social service delivery system has been created over the last 35 years to

assist individuals who experience disabilities. The system elements include, but are not

limited to, publicly-funded case management, housing of many different varieties and

levels of supervision, monthly income, medical and therapy support, special education,

vocational services, and social services. These services have many things in common —

they are hard to obtain, require diligent advocacy, and are often inadequate in scope and

nature. But they also share the feature of providing a basic level of support for the disabled

individual which, if properly coordinated and managed with the individual's private

resources, can significantly extend the availability of the private resources and improve

the quality of life for the injured survivor.

The purpose of this chapter is to provide a basic overview of these benefit programs

(Collateral Source benefits) and to advise how private resources from litigation or other

sources may be managed in such a way as to maintain public benefit eligibility while still

using private resources as a supplement.

Public Collateral Source Benefit Analysis

There are a number of federally-funded public programs available for persons who have

experienced catastrophic injuries and consequent disabilities which can enhance their

lives, and, in many instances, increase their independence. The plaintiff's personal injury

attorney needs to be aware of the various benefit programs for several reasons. First, there

is an argument that, as the client's "attorney of record," the attorney has an obligation

under the Rules of Professional Conduct to assist the client with all of the client's legal

needs. This certainly includes the right to various benefits that arise due to the client's

disability.* Second, the attorney acts in the capacity of a fiduciary, especially for a client

that the attorney knows, or in the exercise of reasonable professional judgment, ought to

know, is unable to act on his/her own behalf. The standard of care owed to the disabled

client from the attorney as a fiduciary is, arguably, much higher and should include the

* See RPC 1.2(c) re. Scope of Representation, ABA Model Rules of Professional Conduct, Third Edition, Center

for Professional Responsibility, American Bar Association (1996).

duty to advise of programs that are, or should be, available to the client. Third, through

accessing various public benefit services on behalf of the client, the attorney can assist the

client to obtain financial, medical, rehabilitative, and supportive services during the pen

dency and subsequent to the completion of the litigation process. This will assist both the

client and the attorney in managing the stresses of an otherwise very difficult time. Finally,

by gaining access to, and working with, public benefit programs, the attorney can create

valuable allies in developing evidence of the client's long-term injuries and damages. As

tort reform proposals continue to mutate, new rules on the admissibility of evidence on

collateral source benefits are being generated and implemented on a state-by-state basis

around the country. For example, in the State of Florida, it is now possible for defendants

in a medical malpractice action to present testimony of collateral source benefits that may

be used to offset the plaintiff's life-care plan.*

Individuals with disabilities have a constellation of benefit programs available to them,

if they meet various eligibility criteria. An extensive social service delivery system has

been created in a rather haphazard fashion at the local, state, and federal levels. Programs

for those with disabilities can be extraordinarily expensive. The majority of funding

available for publicly supported benefit programs is generated through, or in conjunction

with, funding available under the Social Security Act, Chapter 42 of the U.S. Code. Most

people are not aware of the number of different programs established by Congress under

the aegis of this Act. All planning for individuals with disabilities must first consider the

need for continued eligibility for local, state, and federal benefit programs funded under

the Social Security Act.

Knowledge of the four basic disability-related benefit programs is critical.

Programs that Provide Income

Social Security Benefits (SSA) — Title II, 42 U.S.C. §402 to 431

This is the principal disability and retirement income program for American workers,

funded by FICA tax contributions. Disabled workers or individuals of retirement age will

receive benefits. To be eligible for disability benefits under Title II (known as Social Security

Disability Insurance or SSDI), a worker must meet two tests. First, the worker must have

worked and contributed sufficient funds into the Social Security system, and second, the

worker must meet a disability standard.

An individual may become eligible for these benefits if they have worked a sufficient

number of qualifying quarters of employment. For the typical worker, this will require

that the individual has worked in 20 of the most recent 40 calendar quarters prior to an

injury. A minimum amount of FICA payments will have to have been made for the worker

in those 20 calendar quarters of employment. Unmarried, dependent children and grand

children of a deceased or post-age 65-year-old worker who are under age 18, or over age

18 and disabled prior to age 22, qualify for benefits on their deceased/retired parent’s or

grandparent’s account.

The disability definition requires that the individual be medically disabled with suffi

cient severity that the individual is precluded from performing “substantial, gainful activ

ity” (competitive employment with earnings of $770 per month or more, indexed

annually). Title II benefits are not “means-tested;” that is, the disabled individual’s assets

and unearned income are irrelevant. Payment of the monthly benefit is typically made by

direct deposit to the disabled person’s bank account or to a “representative payee”

appointed to receive and manage the payment for the disabled person by the Social

* See Florida Statute, Section 768.76, 1993.

Security Administration. A worker will become eligible for Title II benefits 5 months after

the date the disability occurs.

Supplemental Security Income (SSI) — Title XVI

This program provides a guaranteed minimum income to the aged, blind, and disabled

who have not made adequate contributions to their personal Social Security accounts and

who do not qualify for payments under another's Social Security account sufficient to

qualify for a specific minimum amount of Social Security Disability Income. At the present

time, SSI provides a federal cash supplement of approximately $550 per month, indexed

annually. Some states also provide supplemental payments which increase the total

monthly amount received.

Eligibility for SSI is based on the same disability requirements as in SSA above and upon

financial need. There is no requirement for past employment or payment of FICA taxes

by benefit applicants. SSI payments are not available to "inmates of a public institution"

such as jails or prisons, and residents of Medicaid (known as "Medi-Cal" in California)

funded state residential or nursing care facilities. Eligibility is "means-tested;" that is, the

applicant must have assets "available" to him or her of less than $2,000, exclusive of certain

"exempt" resources such as the ownership of a home, a vehicle valued at less than $5,000

(or of unlimited value if the vehicle is specially equipped or used for special disability

related purposes), a funeral plan and/or burial plot worth

not more than $1,500, personal

furnishings, tools of a trade, and a “plan of self-support.” A “plan of self-support” is a

written plan outlining how a disabled person intends to become self-supporting. The plan

must be approved by the local Social Security office and, with that approval, can generally

be funded with up to $6,000 per year. Income tests are also applied.

Programs that Provide Medical Assistance

Medicare – Title XVIII

This program provides hospital (Part A) and supplemental medical insurance benefits

(Part B) for eligible participants. Congress is currently exploring possible expansions to

these coverages. In order to receive Medicare, an applicant must be eligible for Social

Security Title II benefits (SSA). If the applicant is filing against his own account, but is

still below retirement age, as would be the case with an injured worker, or if the applicant

is someone other than the individual against whose Social Security account the benefits

are based (i.e., disabled dependent children or adults receiving benefits on a deceased

parent’s account), a 2-year waiting period is required from the applicant’s date of eligibility

for SSA benefits before Medicare coverage is effective. For individuals who have sustained

a catastrophic injury, the typical waiting period is 29 months, comprised of the 5-month

waiting period for SSDI and the 24-month waiting period from that initial eligibility date

for Medicare. For an injured worker who receives medical insurance through work,

COBRA (Consolidated Omnibus Budget Reconciliation Act) health care continuation cov

erage is available for the full 29 months, but only if an election to continue coverage is

made at the date of termination of employment.

The Medicare program provides only listed hospital and doctor’s services. Payment is

made through a local contracting agency acting on behalf of SSA. Payment is not means

tested, but coverage is limited. Pharmaceuticals, custodial, and residential care are not

covered and there are significant co-payments and deductibles for covered services.

Figure 22.1 provides a convenient summarization of the Income and Medical coverage

entitlement programs available to persons with traumatic brain injury.

Medicaid — Title XIX

General

Medicaid is a federally-funded, state-administered program with individual states being

given a great deal of flexibility in use of funds. This program generally provides a wider

variety of services than the Medicare program. Eligibility for this program is based on SSI

(Title XVI) criteria for both disability and need. If an applicant meets eligibility require

ments, there is no waiting period for benefit eligibility.

The Medicaid program currently provides a significant portion of state-sponsored med

ical care: acute care, immediate postacute care, long-term residential care, and some in

home support programs for individuals with disabilities that arise due to catastrophic

injuries. Congress is currently considering revisions of the Medicaid Title of the Social

Security Act to significantly expand usage of Medicaid dollars for community programs

to encourage independence for individuals with disabilities. Medicaid is generally consid

ered to be the most important of the federal benefit sources for individuals with disability.

For that reason, more detailed information concerning Medicaid is set forth below.

Details

Because of the interplay between federal funding and state administration, there are

multiple levels of statutory, regulatory, and guideline authority for implementing the INCOME Title II - Social Security Act 42 U. S. C. § 402 Disability, Retirement, and Survivor’s Benefits (SSDI) Title XVI - Social Security Act 42 U. S. C. § 1380 Supplemental Security Income (SSI)

1. Direct monthly cash benefit paid to eligible person

or representative

2. Eligibility is dependent upon:

a. Disability; and

b. Contributions to Social Security system

3. Not means-tested

Establishes eligibility for: 1. Direct monthly cash benefit paid to eligible person or representative 2. Eligibility is dependent upon: a. Disability, and b. Means-tested — i. Assets and resources ii. Income test 3. Contribution to Social Security system is not required for eligibility

Establishes eligibility for: ⇓ MEDICAL AND CARE COVERAGE ⇓
Title XVIII — Social Security Act 42 U.S.C. § 1395 —
Medicare Title IXX — Social Security Act 42 U.S.C. § 1396 —
Medicaid

1. Managed through local private contractors

2. Medical insurance program, eligibility for which is

dependent upon eligibility under Title II — not

means-tested

3. Two types of benefits:

a. Part A — Hospital Benefits

b. Part B — Physician and out-patient services benefits

4. Program requires payment of deductibles,

copayments, premiums, and many goods and

services not covered 1. Managed through state agency under state and federal rules — complex 2. Is means-tested — generally related to SSI eligibility, but may be extended above SSI means-tested clients for certain benefit categories 3. Numerous services and items covered, including: a. Physicians, hospital, many therapies, prescription medications, and some medical devices; b. In-home care; c. Long-term care (institutional care); d. May even pay Medicare premiums

FIGURE 22.1

Summarization of the Income and Medical coverage entitlement programs.

Medicaid program. Medicaid is codified at Title XIX of the Social Security Act, 42 U.S.C.

§1392 et seq.

State Medicaid programs are governed by two general sets of requirements:

• Those states which follow the Supplemental Security Income (SSI) statute and regulations found at Title XVI of the Social Security Act, 42 U.S.C. §1382.

• Those states which follow the more restrictive requirements that were in place at the time the Medicaid statute was established. The more restrictive states that are not limited to the SSI rules are known as the Section 209 (b) states. There are fourteen 209(b) states. These are Connecticut, Hawaii, Illinois, Indiana, Minnesota, Missouri, Nebraska, New Hampshire, North Carolina, North Dakota, Ohio, Oklahoma, Utah, and Virginia. (See 42 U.S.C. §1396a(f).)

The primary means of determining eligibility for Medicaid are categorical. Specific groups

or categories of people are eligible if they fall within the group criteria. The major eligible

categories include those persons who meet the Temporary Assistance to Needy Families

(TANF) requirements and those needy individuals who meet the eligibility requirements

for Supplemental Security Income for the aged, blind, and disabled (the medically indigent).

States have the option of qualifying individuals for Medicaid long-term care support as

“medically needy” at income levels that are above the SSI eligibility criteria.

Funding for Medicaid programs is provided jointly by federal and state resources.

Federal statutes, regulations, and policies provide general guidelines for the program,

while states are authorized, within certain limits of flexibility, to establish requirements

on eligibility for state-operated, but partially federally-funded, programs. The federal

regulations are at 42 CFR 430 et seq.* The Center for Medicare and Medicaid Services

(CMS), formerly the Health Care Financing Administration (HCFA), promulgates program

instructions and guidelines to the states in a transmittal

collectively entitled the “State

Medicaid Manual”** which can also be found in the Commerce Clearing House Service

Medicaid and Medicare Guide.

For institutionalized persons, states are generally prohibited from using eligibility cri

teria more restrictive than those used by the Supplemental Security Income Program (42

U.S.C. §1396 A(a)(10)(C)).*** Guidance on various Medicaid issues can be found in the

federal SSI statute at 42 U.S.C. §1381–1383, the federal SSI Regulations 20 CFR 416 et seq.,

and in the federal SSI Policy Manual titled Programs Operations Manual System (POMS).

As the Medicaid statute has been amended over the past 7 years, resource and income

limitations for single individuals applying for benefits have significantly diverged from

the resource and eligibility limits applicable to married couples. In addition, the resource

and income limitations vary depending on whether or not a state is an SSI/categorical

state or a 209(b) state. It is not within the scope allotted to this chapter to attempt to

present the income and resource limitations on a state-specific basis. Each attorney or

family will have to take the responsibility to review the state income and resource limi

tations for single and married persons who may be in need of Medicaid eligibility within

the particular state of residence.

Prior to October, 1989, each state was given broad latitude in establishing the resource

eligibility requirements for Medicaid-funded long-term care. The result was very substan

tial intrastate variability in eligibility for Medicaid-funded benefits.

* For the Code of Federal Regulations, see http://www.access.gpo.gov/nara/cfr/cfr-table-search.html.

** For the State Medicaid Manual, see http://cms.hhs.gov/manuals/45_smm/pub45toc.asp.

*** For the U.S. Code, see http://www.access.gpo.gov/congress/cong013.html.

Effective in October, 1989, the Medicare Catastrophic Coverage Act of 1988 at Title III,

Section 3, made important changes in the Medicaid program for long-term care residential

options (acute care hospitals and nursing homes). The relevant provisions of the Act and

the technical amendments made to it by the Family Support Act of 1988 are codified at

42 U.S.C. §1396p(c) (Transfers of Assets) and 42 U.S.C. §1396r-5 (Other Provisions). More

changes were made in the Revenue Reconciliation Act of 1989. That 1989 federal amend

ment set forth minimum federal eligibility standard parameters that were required to be

met by each state.

The eligibility criteria for single (unmarried) individuals for Medicaid assistance

remained pursuant to the SSI/209(b) categorical models that were then being used by

each state. The SSI eligibility criterion required that, in order to be eligible on a means

tested basis, the individual had to have total resources actually available to the individual

of less than $2000.

For SSI purposes, a resource is cash or other liquid assets and any other real or personal

property that an individual (or spouse, if any) owns and could convert to cash to obtain

food, clothing, and shelter. If the individual has the right, authority, or power to liquidate

the property, it is considered a resource.

In determining resources that count against the applicant’s eligibility, certain exclusions

are established which include the following:

• An individual’s home, regardless of value, so long as the home is the principal place of residence of the applicant. The home exclusion also applies to any contiguous land and related buildings.

• Household goods and personal effects of reasonable value (generally considered up to $2000). Most states do not do an exhaustive review of personal property in determining eligibility.

• An automobile of value up to $5000 unless used for medically necessary or employment-related transportation, in which case no value limit applies (i.e., liftequipped van).

• Burial plots or funeral plans of value up to $1500 each.

• Life insurance with face value of up to $1500. If face value exceeds $1500, cash surrender value counts against the $2000 resource limitation. Term-life insurance will not count as a resource.

• Certain federal reparations and settlement funds.

Eligibility standards for married couples were significantly modified by the Medicare

Catastrophic Coverage Act of 1989. States were allowed to elect an exempt resource

allocation to be set aside for the nondisabled spouse who

would continue to live in the

community when the disabled spouse went to a hospital or facility for long-term care.

States could choose from a low of $12,000 to a high of $60,000 as the exempt resource

amount. The exempt resource amount was indexed and increased on an annual basis since

1989. The maximum exemption, as of the year 2003, is approximately $91,000 for the

nondisabled spouse.

The couple's home, regardless of value, was determined to be exempt, provided that

the home was transferred in ownership interest from the disabled and institutionalized

spouse to the community spouse within 1 year of the institutionalized spouse's date of

entry into a care placement under the Medicaid Financing Program. Both spouses were

allowed to have all of the remaining exempt resources as indicated in the items listed

above.

The Medicare Catastrophic Coverage Act provisions established time penalties if

resources were transferred to anyone other than an applicant's spouse without full value

being received in return (an uncompensated transfer). Those penalties were found at 42

U.S.C. §1396 p(c). The amendments established a 30-month "look-back" period. If uncom

pensated transfers were made within the 30-month period, a penalty disqualification time

was established in which an applicant could not receive Medicaid. The maximum length

of the penalty period was 30 months. This penalty period has since been amended.

The Medicaid Catastrophic Coverage Act also established provisions regarding the

treatment of grantor trusts created for the purpose of qualifying disabled individuals for

Medicaid benefits. Those restrictions were found at 42 U.S.C. §1396 a(k). Trusts established

for the purpose of qualifying individuals for Medicaid were termed “Medicaid Qualifying

Trusts” (MQTs). An MQT was defined as a trust or similar legal device established, other

than by will, by an individual or an individual’s spouse under which the individual may

be the beneficiary of all or part of the payments from the trust and the distribution of

such payments is determined by one or more trustees who are permitted to exercise any

discretion with respect to distributions to the applicant. If discretion was available, the

Social Security Administration was entitled to presume that payments would be made

under the discretionary provisions, whether the trustee agreed to make the payments or

not. The anomaly here is that an MQT, in fact, disqualifies the beneficiary for Medicaid.

Both the provisions concerning transfer of assets and the provisions regarding the

treatment of trusts were significantly amended by the 1993 Omnibus Budget Reconciliation

Act (OBRA) amendments to the Medicaid statute. The 1993 OBRA provisions are codified

in pertinent part at 42 U.S.C. §1396 p(a) through (e).

Estate recovery requirements, transfer

of asset rules, treatment of trusts, and definitions for transfer and trust provisions were

all impacted by the amendments.

Particular attention should be paid to subparagraph (c) of the 1993 amendments regard

ing the transfer of asset rules. There are no penalties for the transfer of ownership of assets

between spouses. For example, assume that one spouse became seriously injured and

expensive acute and postacute long-term care had to be provided. The couple had modest

means such as a house, car, and several thousand dollars in the bank. Perhaps the couple

also had a modest retirement or Individual Retirement Account (IRA) of less than a total

of $85,000. The disabled spouse (or an appropriately authorized legal representative) could

transfer ownership of all the assets owned by the disabled party or the couple to the

nondisabled spouse. The disabled spouse would then qualify for Medicaid funding to pay

for the needed extended care.

For transfers of assets to individuals other than a spouse, a transfer penalty period or

look-back period is imposed. The look-back period is computed under a complicated

formula that results in disqualification for benefits for a period of up to 36 months for

transfers of assets to a third party when the asset transfer is made without the donor

receiving full value compensation in return. The 36-month period is not capped. If an

application for benefit eligibility is made within a 36-month look-back period, it is possible

that a penalty period of longer than 36 months can be imposed. Assume an injured client

had bank accounts and stocks worth $40,000. The client's family approaches the attorney

to determine if the funds can be preserved during the pendency of the development of

the personal injury claim for which counsel has been employed. There are a series of

strategies that are available to allow preservation of some or even all of the funds they

include. Rather simple transfers to third parties can be made in a manner that would

preserve at least 50% of the funds. More complex transactions may be structured to

preserve all of the funds and pay them out for the client's use over an extended period

of time.

A penalty period of up to 60 months is called for when a transfer of assets belonging

to the disabled grantor or his/her spouse is made to a trust for the benefit of the disabled

grantor or spouse.

The trust provisions contain significant limitations on the use of trusts in Medicaid

planning. Planning with trust options will be discussed later.

As indicated above, SSI and SSDI benefits provide income via monthly payments of

cash to the individual. Medicare and Medicaid provide health care coverage. Through

state administration of Medicaid programs, housing and attendant care are also often

covered. Medicaid provides monies to the states which the states use to implement many

of the programs. Some of the programs function exclusively with federal money and

others with the matching of federal funds with state or local dollars. Because of the large

amount of funding available to state and local government service delivery agencies

through the Medicaid budget, states tend to adopt the Medicaid financial eligibility criteria

for entrance into many of their purely state-funded programs. Group-living arrangements,

including independent assisted-living, foster care, adult family homes, group homes,

institutional placements, and intermediate and skilled nursing placements, are often

funded, in whole or in part, through this system. Day activity programs, ranging from

adult day care, work training, sheltered workshop, and competitive vocational placement

programs, may also depend on Medicaid or SSI eligibility. Case management services

and social and recreational programs are also tied to this broad-based, disability-related,

social service delivery system.

The loss of SSI and Medicaid eligibility will often preclude the ability of an individual

with disability to access most, if not all, of the other programs available in the system.

Unfortunately, the availability of private funding, such as through a personal injury

settlement or judgment, will not guarantee that the individual can buy access to the same

system that is available if the individual meets the SSI and Medicaid eligibility criteria.

The government has a limited number of placements available within the publicly sup

ported system. Government contracts routinely restrict access to those placements by

significantly reducing public payments available to service delivery providers who accept

private payment for services. The disabled individual is caught in a “Catch 22.” Even if

they have funds available, the use of the available funds is foreclosed by the government

agencies’ insistence that the private service providers reserve their service slots to agency

clients. The privately-funded disabled individual is often restricted to a very few, very

expensive service providers who accept only private paying clients.

In order to gain the benefit offered by these various programs, one must obviously meet

the eligibility criteria. However, it must be acknowledged that the standard of living

available to an individual who has nothing but the services provided under the numerous

benefit programs will not be acceptable to most of the clients who will have access to our

services. Coordination of the two sources of funding, public and private, is absolutely

necessary to provide a reasonably comfortable lifestyle for the disabled person, regardless

of age.

In addition to the programs enunciated under the Social Security Act, there are a wide

variety of other programs that are established at the federal level that provide services to

individuals who experience disabilities as a result of catastrophic accidents. Included

among the more common programs are the Individuals with Disabilities Education Act

(IDEA), 20 U.S.C. §1400 et. seq, the Developmental Disabilities Act, The Rehabilitation

Act, HUD Section 8 rent subsidy provisions, food stamps, loan programs, and so forth.*

* See http://www.ed.gov/offices/OSERS/Policy/IDEA/.

Beyond federal, means-tested programs, each state offers an assortment of programs

and assistance to persons with disabilities which vary significantly from state to state,

but which are usually means-tested. Virtually all programs are funded, at least in part,

with federal funds. For all state programs which are funded with federal dollars, the

states must agree to apply eligibility criteria which is no more restrictive than federal

eligibility criteria. States are permitted to enact legislation and pass regulations regard

ing these programs so long as they do not contradict federal rules, statutes, and regu

lations on eligibility. Some common state programs include in-home aide or attendant

services, vocational training and placement programs, advocacy programs, and

“waiver” programs.

Waiver programs are Medicaid-funded programs in which

income, assets, and

resources are disregarded in determining eligibility for specific collateral source benefits.

These are known as “waiver” programs. Waiver programs are those for which a state

designs and submits a program for federal approval and funding for which the state

requests authority to disregard financial eligibility criteria for a specific type of disabled

clientele for a specific purpose. The following is an example of a waiver program that is

available in many states: In-home medical assistance for severely disabled children with substantial medical needs, often including aides/attendants, with the waiver applying to the home-care costs, so that those children will not have to be institutionalized at greater cost.

The type of program described above is intended to help families to keep their severely

disabled children at home and out of institutions. A family with a middle-class income

generally cannot afford the noninsured costs to do this without some form of assistance.

It is important to recognize that waiver programs vary from state to state, and reliance

upon a waiver program could eliminate interstate residence changes as a financial

impossibility.

When a settlement or judgment is achieved for a disabled individual, it may be easy to

assume that the individual’s need will be met with the proceeds. However, settlements

and judgments are seldom adequate to meet lifelong needs for these individuals after

deduction for attorneys’ fees and costs and outstanding

expenses of the individual that

often have accumulated to significant amounts. Federal statute requires that any assistance

the individual has received through the Medicaid program be reimbursed. These factors,

together with the exponential increases in medical costs seen in recent years, make it

unlikely that the individual will net enough money to provide for a lifetime of care. The

ideal is to coordinate use of the settlement or judgment proceeds with benefits under

collateral source benefit programs.

If the disabled individual receives title to the settlement or judgment proceeds, the result

will certainly be ineligibility for Medicaid, SSI, and other “needs” based programs. In

order to maximize the possibility that the disabled person will receive lifelong benefit

from the settlement or judgment proceeds, it is vital to retain or establish eligibility for

those programs.

In the 1993 Omnibus Budget Reconciliation Act, Congress enacted the first legislation

which specifically authorized the use of court-ordered trusts for receipt of assets of dis

abled persons in conjunction with eligibility for Medicaid assistance. The relevant portion

of the Act is codified at 42 U.S.C. §1396p(d)(4)(A) and is included as Appendix 22A to

this chapter. As a result of this legislation, it is now possible to avoid negative impact on

the disabled person’s eligibility for Medicaid and many other federally-funded disability

related benefit programs by directing settlement and judgment proceeds into properly

crafted, court-ordered, special-needs trusts (SNT).

Proper Selection of Management Devices

Guardianship/Conservatorship

These are the traditional vehicles for managing income, assets, and resources of persons

who experience disability. Unfortunately, assets held in a guardianship or conservatorship

belong to the ward and preclude eligibility for needs-tested benefit programs if they exceed

the prescribed limits. If the client is able to work and earn an amount which precludes

benefit eligibility, and is expected to be able to continue working to retirement age despite

the disability, placing settlement or judgment proceeds into a guardianship or conserva

torship may not result in harm to the client. Even so, the expense and time required to

maintain a guardianship or conservatorship are considerations that may make this option

unattractive for managing settlement or judgment proceeds. The need to seek court

approval for changes in investments, which greatly reduces the guardian/conservator’s

ability to respond to market changes, is also of concern.

While guardianship or conservatorship may not be the optimum method for managing

settlement or judgment proceeds, it can provide important protections for a disabled

person who has cognitive deficits. A guardian or conservator of the estate should be

appointed for such disabled adults to protect them from entering into contracts and other

financial abuses. Appointment of a guardian of the person may be important to ensure

adequate medical attention, for authority to give informed medical consents, and for

making residential and other personal arrangements for the disabled person.

Spendthrift/Support Trusts

This type of trust arrangement may be adequate for a disabled individual who does not

have ongoing medical needs, who is able to reside at least semiindependently, and who

is able to earn a wage that is adequate, or almost adequate, to allow self-support, especially

if employment benefits include medical insurance. The trust can be crafted to protect

against exploitation and against creditors. However, the drawback to a “support” trust is

that, if the disabled individual is unable to sustain long-term employment or suffers a

subsequent injury, the trust will effectively bar eligibility for SSI and Medicaid.

Special-Needs Supplemental Trusts

This is the type of trust which complies with the requirements of 42 U.S.C. §1396p(d)(4)(A)

of the 1993 Omnibus Budget Reconciliation Act and prevents the assets directed to the trust

from being considered available to the disabled beneficiary. This type of trust will not, by

itself, ensure eligibility for SSI and Medicaid collateral source benefits. The disabled bene

ficiary must still meet all of the disability criteria and all of the income, assets, and resources

to which the applicant holds title must fall within financial eligibility criteria. If the other

eligibility criteria are not met at the time such a trust is established, the special-needs

supplemental trust still provides all of the protections of a spendthrift support trust, while

protecting the beneficiary's possible future need and eligibility for collateral source benefits.

Structured Settlement Annuities

Structured settlement annuities can be an important and beneficial part of a settlement

achieved for a disabled person. A structured settlement annuity can be made payable

directly to a court-ordered trust that is established for the benefit of a disabled person.

Flexibility in the use of the funds and in responding to changing investment climates

is not possible with a structured settlement annuity so they must be very carefully

considered in advance. The Internal Revenue Code sections (IRC sections 104 and 130)

which authorize the use of a structured settlement annuity specifically provide that

they are nonassignable and should not be sold or borrowed against. Accordingly, it is

important that sufficient settlement or judgment proceeds be left liquid to meet unex

pected needs that may, and often do, arise. A good rule of thumb for the majority of

cases is that no more than one-third of the net settlement available to the client be used

to fund any such structure. To obtain the income tax advantage that ostensibly results

from a structured annuity settlement, the structure must typically be purchased by a

defendant. Any structure included as part of a settlement or judgment for the disabled

client should be designed to meet anticipated needs. For example, if the client has home

medical equipment that needs to be replaced every 5 years, that known need should

be a factor. If the client is expected to require major surgery which may not be covered

by medical insurance (or Medicaid, if eligibility is anticipated), that known need should

be a factor. If the client requires a wheelchair lift-equipped van for transportation and

it is expected that the vehicle will need to be replaced every 5 years, that known need

should be a factor.

Keep in mind that the rate of return on a structured settlement annuity is less than the

current taxable interest rate at the time of issuance of the annuity. A good rule of thumb

is that, if the trust assets can be invested with a rate of return that is 2% above the current

taxable interest rate, the tax advantage of a structured settlement annuity is nullified. In

addition, for individuals with substantial ongoing medical expenses, the tax deductibility

of the medical expenses will operate to negate the “tax-free” advantage of the annuity.

Maximization of income through careful investment becomes a paramount goal superced

ing any limited advantage generated by tax-free income. On the other hand, if there are

concerns about undue influence for inappropriate or unnecessary expenditures because of

family or other situations of the disabled person, a structured settlement annuity held in

a trust can provide enhanced conservation and protection to the beneficiary.

Selection and Format of Fiduciary/Investment Manager

Types of Trustees

The trustee is responsible for management and investment of the trust assets and, depend

ing upon the format of the trust agreement, is sometimes responsible for determining trust

disbursements. There are several types of entities which often serve as trustees to manage

special-needs and other kinds of trusts. Each type of entity offers advantages and disad

vantages, and a variety of factors must be considered in selecting the entity best suited

to a given trust arrangement. The three most commonly used entities are institutional

trustees, private trustees, and broker advisor/trustee affiliations.

Institutional Trustees

This term refers to banks and trust companies, which are traditionally the most commonly

designated professional trustees. Fees among bank and trust company trustees are fre

quently on the higher end of the spectrum, but can often be negotiated. It is often the case

that the fees for investment management services performed by bank trustees are not fully

disclosed when the bank is promoting its services. Be sure to ask if separate investment

fees result when the bank uses its own investment accounts or those of an affiliated

company. Using a bank or trust company as a trustee generally ensures competent, expe

rienced management that is familiar with the relevant state and federal legislation and

regulations controlling trust activities.

However, unless the specific institution has experience with special-needs trust man

agement, bank and trust company management goals may conflict with the beneficiary’s

needs. These institutions are most accustomed to administering trusts that contain clear

and unambiguous disbursement instructions. In special-needs trusts, all disbursements

are discretionary. The traditional bank trust management focus is to increase and enhance

the trust corpus, only making disbursements that are required. No disbursements are

required in a special-needs trust. As a result, before designating a bank or trust company

as trustee, it is vital to ascertain familiarity with special-needs trusts and the institution’s

understanding of its role under them. If the trust is placed with a bank or other professional

trustee, it is very important that the trust document clearly outline the duties and obliga

tions of the trustee, especially as they relate to expenditures that will preserve benefit

eligibility, yet still meet the disabled beneficiary’s needs.

Private Trustees

This term includes private individuals who may simply be related to, or friendly with,

the beneficiary, and professional persons with backgrounds that will assist them in trust

management. A significant advantage to naming a private trustee is increased responsive

ness to the beneficiary’s evolving situation and needs. Conversely, it is also a risk that the

private trustee could become unduly influenced by the beneficiary or the beneficiary’s

family. A private trustee is likely to serve at a comparatively low fee, but is likely to require

substantial legal and accounting assistance, at trust expense. A private trustee would

generally be required by the court to be bonded or insured, the cost of which would also

be at trust expense. Unless the private trustee has investment expertise, investment returns

are likely to be lower than would be seen in management by an institutional trustee. In

addition, unless the private trustee has a great deal of experience with public benefit

coordination or employs a benefit compliance manager, they are not likely to be familiar

with the special restrictions that apply to a special-needs trust.

Broker Advisor/Trustee Affiliations

Use of a specifically designated broker in conjunction with a professional trustee to manage

trusts is a recent development that has evolved to meet the unique demands of special

needs trusts. In this arrangement, a professional trustee (either an institutional or private

trustee) is named to “hold” and manage trust assets, while a broker or brokerage is

designated to manage trust investments. Brokers are usually better informed about various

markets and investment opportunities than are banks and trust companies, and invest

ment performance is often better than that of a bank or trust company when this arrange

ment is used. The broker/brokerage is prohibited by SEC regulations from acting as a

fiduciary, hence the two-part trustee arrangement. A drawback to this arrangement is that

some duplication of fees generally occurs. Careful negotiations prior to appointment of

the broker and professional trustee can minimize that drawback. Similarly the broker and

the trust company will need assistance to fully comply with ensuring that distributions

from the trust do not compromise benefit eligibility.

Trust Disbursement Committees

A trust disbursement committee is often designated in court-ordered special-needs trusts

to serve in conjunction with a financial trustee. The committees actually serve as cotrustees

with full fiduciary responsibility and liability for the decisions they are called upon to make.

These committees decide trust expenditures that are intended to benefit the disabled ben

eficiary by majority vote. They are usually comprised of three voting positions, one of which

can be held by an immediate family member or shared by the

parents of the disabled

beneficiary. Most courts will not approve a disbursement committee that is controlled by

the beneficiary's family in order to minimize opportunities for self-dealing. Appropriate

persons to fill two of the three voting positions might include nurses, physicians, counselors,

therapists, vocational or rehabilitation advisors, teachers, close family friends, and members

of the clergy. It is important that the entities filling the nonfamily committee positions be

able to act independently and not be under undue influence of any of the other parties.

The use of this type of committee usually increases not only the responsiveness, but

also the appropriateness of disbursements made for the disabled beneficiary over those

that might be authorized by a trustee alone. The committee members usually assign

different duties among themselves, with each voting position having or acquiring expertise

in specific and relevant areas such as familiarity with local service providers. The com

mittee often evolves into a highly effective case-management team that is able to advocate

for the beneficiary with third parties such as government agencies and maximize the

combined benefits of government and private programs and insurance in conjunction with

carefully selected trust disbursements. In addition, these "teams" often develop long-term

personal relationships with, and personal investment in, the beneficiary.

Family members usually serve on these committees without fee, particularly if those family

members received loss of consortium or other direct compensation for the beneficiary's

injuries. They are compensated for expenses. In situations where family committee members

are asked to perform a great deal of legwork such as seeking out residential arrangements,

interviewing aides, and so forth, fees for time spent in those specific projects may be appro

priate. Other committee members are usually compensated for their time and expenses. While

this may, at first glance, appear to be costly, it is often less expensive than paying trustee's

hourly fees for services rendered in investigating and determining trust expenditures.

Collateral Source Benefit Compliance Managers

These are individuals or organizations with expertise concerning government and private

benefit programs that provide services to persons who experience disabilities. Those

services can be vital in a special-needs trust arrangement if eligibility for Medicaid, SSI,

and a host of other programs is to be established or preserved. The statutes and regulations

concerning these programs undergo frequent change and reinterpretation. There are state

by-state variations on waiver and certain other programs. For example, giving a benefi

ciary a monthly cash allowance can have disastrous effect on his or her continuing benefit

eligibility. A collateral source benefit compliance manager can assist a trustee or trust

disbursement committee in selecting disbursements that allow maximum benefit and

flexibility for the beneficiary while avoiding serious consequences to continuing eligibility

for needs-based benefit programs.

Primary and Secondary Guardianship/Conservatorship Selection

While the proper drafting and implementation of a special-needs trust to manage settle

ment and judgment proceeds can minimize negative impact on the beneficiary’s program

eligibility, there remain a significant number of services that a trust, quite simply, has no

authority to provide. Any income or assets to which the beneficiary holds title (such as

monthly Supplemental Security Income benefit payments, or ownership of a home) are

outside the control of the trust. In addition, unless the beneficiary has a valid durable

power of attorney, only the beneficiary can make informed medical decisions for him or

herself. If the beneficiary has marginal cognitive capacity, he or she may go without

treatment simply because there is no one authorized to grant consent.

Guardianship and conservatorship statutes allow appointment of persons or entities

which can provide those services. While relevant statutes vary from state to state, a

guardian of the person generally can be granted court authority over almost all personal

decisions the disabled person could make if he or she were able. In some jurisdictions, a

guardian’s “substitute” consent to elective surgery

requires advance court approval. In

almost all jurisdictions, nonemergency sterilization procedures may only be authorized

by a guardian with advance court approval. For day-to-day personal needs such as

selecting a personal physician or dentist and minor procedures (stitches, root canals), a

guardian has general authority to grant consent. As to asset management, a guardian of

the estate or conservator can receive and manage the disabled person’s income, manage

personal assets, and negotiate fees and contracts with service providers (outside of the

trust). It is important, in situations where the guardian of the person and the guardian or

conservator of the estate are different entities, that they be able to work together for the

good of the disabled person.

Due Diligence

When representing an incapacitated client, the attorney is exposed to greater moral and

ethical considerations than when representing a nondisabled client. If the client is so

disabled as to benefit from a special-needs trust arrangement and the attorney is presenting

such an arrangement for consideration by the court, the attorney must exercise due

diligence in assisting in locating, evaluating, and selecting the trust management team.

Even if the recommendation for a special-needs trust and management team is made by

a guardian ad litem or next friend, the trust instrument and proposed team is usually

selected by counsel and the disabled client’s family and, thereafter, presented for the

guardian ad litem or next friend’s consideration. Key considerations include the following.

Disclosed and Undisclosed Fees

Trustee’s fee schedules are generally premised on the assumption they would have full

responsibility for all trust activities. Special-needs trusts often have disbursement activity

directed by a trust disbursement committee that is separate and apart from the trustee.

As a result, reductions from standard fees should be negotiated with trustees for special

needs trusts, whenever possible. In addition to the fees taken under the standard fee

schedules, most trustees provide supplemental services that are billed on an hourly or

other basis. Supplemental services might include preparation of tax returns, accounting

services, and investment services. It is important to obtain a full disclosure of specific

services that are covered by the proposed trustee’s fee schedule and what services are not,

what expenses are included and what are not, and what hourly fee rates are charged for

the staff members that will work on the trust account. What initially appears to be a

bargain fee schedule rate may result in very high fees if many basic services are billed

separately from the schedule.

When a broker/trustee arrangement is utilized, counsel should negotiate with both the

broker and the trustee to ensure that double charging for investment services is minimized.

Brokers are sometimes willing to discount their fees, while trustees may be more difficult

to convince to reduce their fees proportionate to the time they would have spent making

investment decisions. It is their position that they continue to bear liability for trust

investments so must be compensated for the risk. While this may be true, most broker/

trustee arrangements are between sister organizations and, if that is indeed the case,

counsel should argue that the risk is between the organizations and should not result in

fee doubling to the trust.

Insurance/Bonding

In evaluating prospective trustees, counsel should determine whether or not the prospec

tive trustee carries blanket bonding or fiduciary insurance. Obtaining approval of a trustee

which subsequently fails in its fiduciary duty to an incapacitated client’s trust can place

counsel in a position of liability. Some courts will require that the trustee be bonded or

insured, at least as to the trust. If the trustee does not carry appropriate insurance, the

cost of purchasing that coverage as to the trust is a factor that must be considered as a

cost of using that trustee. One caveat is that, in Texas, trustees of court-ordered trusts

cannot be required to purchase a bond. This requirement makes it almost mandatory to

use an FDIC or other fiduciary carrying blanket coverage as

a trustee in order to properly

protect the beneficiary.

If any significant portion of the settlement will be structured, it is wise for counsel to

at least inquire about obtaining an underlying guarantee on the structure. The Executive

Life Insurance Company failure about 14 years ago left a great many annuitants receiving

reduced annuity payments. The cost of an annuity from a small insurance company

combined with the cost of a guarantee from a larger insurance company is often less costly

than having the structure purchased from that larger company.

Experience with Type of Settlement Device

When comparing prospective trustees, experience with, and understanding of, special

needs trusts is often worth paying higher fees. Inexperienced trustees can generate a great

deal of excess fee in the process of familiarizing their staff with interpretation of the terms

and conditions of a special-needs trust. Costly errors, such as allowing inappropriate

expenditures that result in loss of benefit eligibility, are more likely to occur with an

inexperienced trustee. Remember, most members of trust disbursement committees are

initially inexperienced as to special-needs trust expenditures, themselves. An experienced

trustee can provide guidance if inappropriate expenditures are authorized, often avoiding

negative consequences. If a sole trustee is selected to manage a special-needs trust, expe

rience becomes even more important. Beneficiaries of special-needs trusts are often unable

to determine their own needs or the impact that disbursements will have on any benefits

they may receive, so cannot be relied upon to seek appropriate disbursements from the

trustee. A sole trustee of a special-needs trust must be proactive in remaining aware of

the beneficiary's ongoing situation and needs, and must also develop information on, and

contacts with, resources for meeting those needs. We have seen inexperienced trustees

happily invest and manage special-needs trusts for years, increasing the corpus, without

making any disbursements for the beneficiary because none had been requested.

Estate Planning Considerations

There are a number of estate planning issues that must be considered aside from estab

lishing an appropriate method for receipt and management of settlement or judgment

proceeds for the person who has experienced a traumatic brain injury. Areas that should

be reviewed are the estate plan for the disabled individual and estate plans for his or her

family members.

Estate Planning for the Brain Injury Survivor

Will/Power of Appointment

Whenever possible, the survivor of a traumatic brain injury should have a will. The injured

person should be carefully evaluated by medical and legal professionals to determine

whether or not he or she has testamentary capacity. If there is sufficient capacity, a will

should be drafted by appropriate counsel reflecting the injured person's wishes. It would

be wise to accumulate and retain evidence of testamentary capacity and, perhaps, even

to videotape the will's execution. That will would control all assets to which the injured

person holds title.

In addition, the will may control disposition of assets remaining in a court-ordered

special-needs trust established for the injured person after satisfaction of the statutory

Medicaid lien. Many of these trusts contain provisions directing distribution upon the

beneficiary's death to his or her heirs at law or pursuant to the beneficiary's will, if any.

A review of the trust's termination provisions should be evaluated. If the trust remainder

assets can pass pursuant to a will, it is important for the injured person to understand the

extent of assets his or her will can control before he or she decides on a distribution scheme.

In some instances, a court-ordered trust or local statutes may allow the beneficiary to

designate remainder trust beneficiaries through a power of appointment. It is unclear

whether the standard of capacity for execution of a power of appointment rises to the

level of testamentary capacity. If testamentary capacity is in doubt but marginally possible,

it may be wise to obtain a separate power of appointment reflecting the injured person's

distribution instructions. It would be important to accumulate and retain evidence of

capacity, again, even to the extent of videotaping the document execution.

If the injured person does not have capacity to execute a will, assets to which he or she

holds title will pass at his or her death in accordance with the laws of intestate succession

applicable to his or her state of residence.

Power of Attorney

A power of attorney is a formally written document granted by one individual (the

principal) to a second individual(s) who is designated as an attorney in fact (AIF). Each

state has statutes governing the creation and use of powers of attorney. First and foremost,

it is necessary to determine that the injured person has legal capacity to execute a power

of attorney.

Generally, it is possible, and sometimes advisable, to name more than one individual

or entity as the AIF, but it is always prudent to designate a substitute in the event the

primary AIF is unable to serve. A properly drafted power of attorney should specify the

authority that is to be shared or transferred from the principal to the AIF. In some states,

it may be possible to combine a delegation of authority over financial matters with

delegation of authority over personal and health care matters. A general power of attorney

typically grants authority from the principal to the AIF

upon execution of the document.

A durable power of attorney (sometimes called a springing power of attorney) becomes

effective upon the disability of the principal. In a combined general and durable power

of attorney, the authority of the AIF commences upon execution and continues through

disability until either written revocation by the principal or the principal's death.

Powers of attorney should be specifically drafted to meet the client's express wishes. In

a durable power of attorney, the client should select the criterion to be used in determining

when the disability comes into existence. The client should be counseled on the nature

and extent of authority that is, or will be, transferred to the AIF. Gifting, estate planning,

the creation or revocation of trusts, management of specific assets, real property transac

tions, and tax issues must be expressly addressed.

Again, it is critical to remember that the principal must be capable of understanding

the nature of the document and the extent of authority being transferred at the time the

document is executed in order for the power of attorney to be valid. The client should

also be counseled that the power is primarily an assistive device and offers only minimal

protection. The existence of even a durable power does not deprive the principal of the

right to make decisions on his or her own, up to and including the decision to revoke the

power. This may be true even after the criterion for

disability established in the document

have been met.

Estate Planning for the Brain Injury Survivor’s Family Members

Wills

The use of a carefully drafted will is essential in preparing estate plans for people who

have a family member who experiences disabilities. One must attempt to maintain the

disabled family member’s eligibility for the basic government services, both to maximize

the resources available to meet that disabled person’s needs and to ensure access to the

public service delivery system. This must be done with a recognition that those basic

government services are not going to be adequate to meet all of the disabled person’s needs.

In almost all cases, spouses, parents, grandparents, and other relatives should consider

making arrangements to the effect that the disabled person does not own or receive legal

title to their money, real estate, or other assets, whether transferred by will, inheritance,

or gift. This may be good advice even if the disabled person is “legally competent” and

only experiences physical or sensory disability. The disabled individual should not be

designated as a direct beneficiary of any life insurance or retirement programs.

A basic will is the cornerstone of the estate plan. Each family should consult an attorney

with training in estate planning who is also aware of the need to provide special planning

for the family member who experiences a disability. A special-needs trust will be utilized

as the basic planning mechanism and it must be recognized that this type of trust should

not contain the state lien reimbursement language that must appear in the litigation

settlement trust. Planning will need to consider personal, financial, federal estate tax

planning, and state inheritance tax issues relevant to the state in which the family resides.

Planning for disability is less state-specific because the most important benefit programs

for individuals with disabilities are federal in origin. The majority of disability-related

programs are based upon federal statutes, such as the Social Security Act, the Develop

mental Disabilities Act, vocational rehabilitation legislation, the Individuals with Disabil

ities Education Act, and the Americans with Disabilities Act. Many of these laws include

implicit or explicit preemption provisions of inconsistent state laws, or supersede state

provisions through federal funding requirements.

As part of the basic estate plan, the disabled family member should be specifically

acknowledged in the will and excluded from any direct inheritance. The exclusion should

be explicit. A will could state “I expressly leave nothing to my child, JOHN DOE, except

my love and affection, knowing he will be adequately provided for otherwise.” Any

bequest intended for the disabled family member, whether that family member is a spouse,

child, grandparent, or other relative, should be directed to a special-needs trust for that

person's benefit. That trust can either be included in the will as a "testamentary trust," or

created prior to death as a "living trust," which is more fully discussed below. If a living

trust is established, the will should then include "pour over" provisions directing the

funds intended for the disabled person's benefit to the trustee of the living trust. The pour

over language must specifically identify the living trust; for example, "The Smith Living

Trust for the Benefit of Johnnie Smith Under Agreement Dated 1/10/2002."

Living Trusts

Living irrevocable trusts are another planning option. These are most useful when money

or other assets are, or will be, set aside during the lifetime of the grantor (maker of the

gift). A "living trust" is created in a separate document and not included within a will.

In order to be valid, some asset must be placed into the name of the trust at, or shortly

after, the date of creation. The beneficiary of a living trust who is disabled cannot be given

any right to compel payments from the trust or terminate the trust, in whole or in part,

in his or her own favor. Where a living trust is used as a vehicle for tax-planned gifts, a

limited right of withdrawal, or "Crummey" power, is usually included. Care must be

taken in this regard as access to the gifts available through a Crummey power will

disqualify the trust beneficiary from needs-tested benefit programs for at least the period

during which the power remains open. For SSI and Medicaid, the disqualification period

could be for several months after the right of withdrawal expires. The grantor must weigh

the grantor's possible gift and estate tax benefit against the cost of the beneficiary's loss

of eligibility for needs-tested government benefit programs.

An increasingly popular option is the "Irrevocable Life Insurance Trust," or living trust

funded with life insurance. The use of insurance within an SNT is totally appropriate and

recognized as a proper financial planning tool in this field. It is especially important when

the special-needs beneficiary is likely to outlive his or her parents. In today's era of modern

medicine, we are seeing large numbers of even severely disabled or injured persons outlive

their adjusted life expectancies, sometimes many years beyond what was anticipated.

Funding a trust with life insurance generally provides excellent return on the investment,

with funds becoming available when they are most needed — after the loss of the care

and supervision of a parent.

Term insurance is an effective and inexpensive funding device for younger families to

place into a trust. Premium cost can be reasonable for a significant amount of coverage.

Whole life policies may also be used at a somewhat higher premium cost, but with the

added advantage of the accumulation of cash value in the policy. This builds an immediate

principle in the trust.

If the cost of premiums is an issue, a “second to die” policy, instead of term life, is

attractive. The “second to die” policies are guaranteed to pay upon the second insured

party’s death. There is no risk that the trust will not receive the policy proceeds so long

as the beneficiary outlives both parents. This is very appealing because it guarantees

future funding at low cost.

The purchase of any insurance should take place within the trust to avoid negative

estate tax consequences to the insured. Use of a Crummey power may be desirable as the

amount of the premium that may be gifted to the trust each year to fund the insurance

premiums will not usually be large enough to impact the beneficiary’s eligibility for needs

tested benefit programs. If a trust beneficiary who is granted a Crummey withdrawal

power to a current trust deposit meant for payment of insurance premiums is already

receiving SSI or Medicaid, access to the right of withdrawal will negatively impact ongo

ing benefits.

If a living life insurance trust is not desired, life insurance proceeds can also be directed

to testamentary trusts (trusts in wills). If this option is used, the proceeds should be

directed to the trustee of the “testamentary trust established in my Last Will and Testament

dated _____ or as hereafter amended, for the benefit of my disabled child/

spouse/grandchild, _____, to be held, managed, and distributed pursuant

to the terms and conditions of that testamentary trust." Life insurance proceeds should

not be directed to the disabled individual.

Special-Needs Trust Provisions

Whether a testamentary or living SNT model is chosen, there are certain critical provisions

that must be included within the trust language. The trust must be a discretionary sup

plemental spendthrift trust. It must be designed to protect the trust assets and income

from the claims of creditors, including the state. The assets in the trust will actually be

owned by the trust, and not by the disabled beneficiary. Hence, if the trust is properly

drafted, the trust assets cannot be considered to preclude the beneficiary's financial eligi

bility for local, state, and federal government benefit and service programs. The trust

should also provide a structure for the management of the assets on behalf of an individual

with disabilities who may lack the capacity to fully appreciate the complexities of invest

ment and management of substantial sums of money.

It is not the main purpose of an SNT to pay for the basic food, clothing, shelter, and

medical needs of the disabled person. The government benefit programs are intended to

cover those needs. The stated purpose of the trust might

read as follows: “Purpose: The express purpose of this trust is to provide for JOHN DOE extra and supplemental care, maintenance, support, and education in addition to, and over and above, the benefits JOHN DOE otherwise receives as a result of his handicap or disability from any local, state, or federal government, or from any other private agencies, any of which provide services or benefits to handicapped persons. It is the express purpose of the trustor to use the trust estate only to supplement other benefits received by the beneficiary. To this end, the trustee may provide such resources and experiences as will contribute to and make the beneficiary’s life as pleasant, comfortable, and happy as feasible. Nothing herein shall preclude the trustee from purchasing those services and items which promote the beneficiary’s happiness, welfare, and development, including, but not limited to, vacation and recreation trips away from places of residence, expenses for traveling companions if requested or necessary, entertainment expenses, supplemental medical and dental expenses, social services expenses, and transportation costs. This trust is to be considered as a discretionary, and not a basic support, trust. The trust estate shall not be used to provide basic food, clothing, and shelter nor be available to the beneficiary for conversion for such items, unless all local, state, and federal benefits to which the beneficiary is entitled as a result of disability have first been applied for those purposes or the trustee has determined that full or partial benefit eligibility is not in the beneficiaries best interest. This trust is to be irrevocable except as provided in Article __, entitled “Term,” set forth below.”

The trustee must be given complete discretion to determine when and under what

circumstances payments should be made on behalf of the disabled individual. The key to

financial eligibility for the government benefits will be the “availability” of the resources

to the disabled person. If the disabled individual has the ability to demand distribution

of the resources, as would be the case in a basic support trust or a trust that requires

annual distribution of income and principal, then the resources contained in the trust, or

to be distributed in that year, will count against the person for financial eligibility for

benefits. The primary question appears to be whether the disabled person can receive

state assistance without the state having any enforceable rights to contributions from the

trust. An example of a paragraph establishing full discretion is as follows: “Discretion: The trustee shall have absolute and unfettered discretion to determine when, and if, the beneficiary needs regular or extra supportive services and provisions as referred to in the paragraphs above. The trustee may make or withhold payment at any time and in any amount as the trustee deems appropriate in the exercise of his/her discretion. The exercise by the trustee of his/her discretion shall be conclusive and binding on all persons.”

Payments from the trust should be made directly to the individuals or companies who

provide goods or services to the disabled beneficiary. If the trust, or any other third party,

for that matter, makes payments of cash to the disabled individual or pays for basic food,

clothing, or shelter for the disabled individual, the cash or value of the item provided

must be reported to the benefit agencies. That amount will be deducted from the individ

ual’s level of benefits. Sample payment language might read as follows: “Payments: All payments from this trust which do go to the benefit of the beneficiary are to be direct payments to the person or persons who supply either goods or services to the beneficiary at the request of the trustee. However, the trustee may exercise discretion in allowing the beneficiary such periodic allowances for personal spending money as the trustee shall deem appropriate.”

One of the advantages of establishing a trust for an individual with disabilities is that

the person who creates the trust can determine to whom any assets remaining in the trust

will pass after the disabled person's death. It is important to designate a beneficiary who

will be entitled to take the remaining balance in the trust at the disabled person's death.

That secondary, or residual, beneficiary then has a legal interest in the trust, providing

additional protection from state claims for repayment that could be made against the

disabled beneficiary's interest.

A spendthrift provision is the traditional way to provide protection in a trust against

claims by the creditors of the beneficiary, in this case, the disabled individual. Such a

provision acknowledges that the disabled beneficiary has no legal interest in the trust until

disbursements are actually made on his or her behalf. Statute and common law on spend

thrift provisions may vary widely from state to state. Therefore, state-specific legal review

is necessary. Sample spendthrift language reads as follows: "Spendthrift: The beneficiary shall have no interest in either the principal or income of this trust. The assets of this trust shall in no way be assignable or alienable by or through any process whatsoever. The assets of the trust shall not be subject to garnishment, attachment, levy, or any other legal process of any court from any creditor of any beneficiary, nor shall the assets be an asset in any future bankruptcy of any beneficiary. Furthermore, because this trust is to be conserved and maintained for the special needs of the impaired beneficiary throughout his lifetime, no part of the corpus thereof, neither principal nor undistributed income, shall be construed as part of the beneficiary's 'estate' or be subject to the claims of voluntary or involuntary creditors for the provision of goods, care, and services, including residential care, by any public entity, office, department, or agency of the State of _____ or any other state, county, municipal, federal, or other governmental entity, department, or agency, except specifically provided for otherwise in this

instrument.”

Under most court decisions interpreting such trusts, the intent of the trustor is one of

the key deciding factors in implementing the trust. The trustee should have the ability to

determine when, if, and how payments are to be made on behalf of the disabled beneficiary.

It may even be well to go so far as to allow the trustee to deny payment for such basic

and elemental needs as food, housing, and clothing. A clear statement of the trustor’s

intent to supplement, and not supplant, other sources of income to the beneficiary, includ

ing local, state, and federal benefit programs, is vital. The drafter could even include a

provision that requires the principal of the trust to be distributed to a third party in the

event that the trust assets are used to disqualify the trust beneficiary from government

program eligibility. A sample statement of intent follows: “Trustor’s Intent: It is the intention of the trustor in executing this trust to provide benefits for the beneficiary without interfering with or reducing the benefits to which he or she is entitled under the social services agencies of the State of _____, its successor agencies, and/or any other state or federal agency or department, and to maximize the benefits to the beneficiary. Accordingly, regardless of any provisions in this instrument to the contrary, if, in the trustee’s opinion, a distribution called for herein would not achieve its full economic benefit as intended due to physical, emotional, legal, or other disabilities or reasons, the trustee may withhold such distribution or benefits or a portion thereof until such time as the trustee feels that the fully intended benefit would be accomplished by the distribution.”

Because trust distributions may subject the beneficiary to federal and other tax liability,

a provision allowing the trust to make distributions to cover that liability should be

included. “Taxes: The trustee shall pay any income tax liability of JOHN DOE which results from income received by the trust but properly reported on JOHN DOE’s income tax return, such amount to be specified in writing and delivered by JOHN DOE’s tax accountant or tax preparer to the trustee. The trustee shall rely conclusively on this amount. The funds used to pay any such tax liability shall be paid directly to the appropriate tax authority and shall not be available to JOHN DOE. Any such funds are not a resource of JOHN DOE and should not be treated as a distribution of income for purposes of Medicaid or SSI qualification.”

In some situations, disabled family members may lose eligibility for collateral source

benefits due to improvement in their health, employment which provides income over

the federal poverty standard, or other reasons. In those cases, the disabled person may

be left with insufficient assets and resources to pay rent or buy food. Thus, incorporating

language which recognizes this type of problem and provides a safety net for the disabled

family member is important. “POMS: Disbursements from the principal or income of the trust estate in accordance with the purpose provision above shall be made subject to the provisions of the Social Security Act, Regulations, and Programs Operations Manual System (POMS) in such a manner that distributions shall not be considered as income to the beneficiary under the definition of that term as provided therein, during any period of time when, in the judgment of the trustee, the beneficiary is, or should be, receiving means-tested local, state, or federal disability-related benefits which are funded in whole, or in part, with funds originating under the Social Security Act (42 U.S.C., as now or hereafter amended) or related funding sources, or to which the beneficiary is, or should be, categorically eligible as a result of the beneficiary’s receipt of Supplemental Security Income. During any period of time when JOHN DOE is, or should be, receiving such benefits and so long as distributions from this trust do not exceed the level of income which would allow preservation of

eligibility for such benefits under the Act, Regulations, and POMS, any such distributions shall be considered allowable by the trustee under the terms of this trust agreement. Should JOHN DOE not be eligible for such benefits or should the trustee determine that it is not in his best interest to seek or maintain such eligibility, this restriction on distributions shall not apply, provided that all distributions from this trust shall be for the sole benefit and in the best interest of JOHN DOE."

Summary

The suggestions made in this chapter should not be employed without the assistance of

an attorney who is intimately familiar with all the eligibility criteria applicable to all local,

state, and federal benefit programs available to individuals with disabilities. This is a new

and very helpful area of practice for individuals with disabilities and their families. It

allows us to provide extended services to maximize the benefits available to disabled

consumers while still providing for an enhanced quality of life through the coordination

of public benefits and private resources.

Appendix 22A

42 U.S.C. §1396p(d)(4)(A) 01/02/01

(4) This subsection shall not apply to any of the following trusts:

(A) A trust containing the assets of an individual under age 65 who is disabled [as defined in section 1382c(a)(3) of this title] and which is established for the benefit of such individual by a parent, grandparent, legal guardian of the individual, or a court if the State will receive all amounts remaining in the trust upon the death of such individual up to an amount equal to the total medical assistance paid on behalf of the individual under a State plan under this subchapter.

(B) A trust established in a State for the benefit of an

individual if — (i) the trust is composed only of pension, Social Security, and other income to the individual (and accumulated income in the trust), (ii) the State will receive all amounts remaining in the trust upon the death of such individual up to an amount equal to the total medical assistance paid on behalf of the individual under a State plan under this subchapter; and (iii) the State makes medical assistance available to individuals described in section 1396a(a)(10)(A)(ii)(V) of this title, but does not make such assistance available to individuals for nursing facility services under section 1396a(a)(10)(C) of this title.

(C) A trust containing the assets of an individual who is disabled (as defined in section 1382c(a)(3) of this title) that meets the following conditions: (i) The trust is established and managed by a nonprofit association. (ii) A separate account is maintained for each beneficiary of the trust, but, for purposes of investment and management of funds, the trust pools these accounts. (iii) Accounts in the trust are established solely for the benefit of individuals who are disabled (as defined in section 1382c(a)(3) of this title) by the parent, grandparent, or legal guardian of such individuals, by such individuals, or by a court. (iv) To the extent that amounts remaining in the beneficiary's account upon the death of the beneficiary are not retained by the trust, the trust pays to the State from such remaining amounts in the account an amount equal to the total amount of medical assistance paid on behalf of the beneficiary under the State plan under this subchapter.
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23

The Implications of Bioethical Principles in Traumatic Brain Injury Rehabilitation

Stephanie Hanson and Thomas Kerkhoff

CONTENTS

Brief Historical Perspective

Respect for Autonomy

Beneficence

Nonmaleficence

Justice

Conclusions

Preface

This chapter focuses on the application of the bioethical principles of respect for autonomy,

beneficence, nonmaleficence, and justice to the rehabilitation setting. This chapter is

divided into sections in which each principle is reviewed and discussed. In the section on

Respect for Autonomy, guidelines for standards for competency are proposed and specific

recommendations for acquiring informed consent with persons with traumatic brain injury

(TBI) are offered. In the Beneficence section, the concept of paternalism and when it is

justified in TBI rehabilitation are discussed. The examples of return to driving and restraint

use, as well as detailed commentary on family involvement, are used to demonstrate how

beneficence operates in the rehabilitation milieu and the responsibility of the rehabilitation

team to patient welfare. In the Nonmaleficence section, issues surrounding a patient’s right

to refuse treatment are reviewed and the complexities of the patient who is in a Minimally

Response State (MRS) are highlighted. Finally, in the Justice section, it is shown that justice

applies to different levels of rehabilitation, from the broad level of social policy to the level

of the individual practitioner. This chapter should be of interest to all rehabilitation

practitioners, as well as administrators who are responsible for clinical policy and proce

dure development, and/or implementation.

Introduction

We are living in times of momentous opportunity in the United States, and yet the rift

between rich and poor is widening with every generation. Over 40 million people currently

lack access to health care, and another 20 million are under-insured. 1 During the next 2

decades, we can realistically anticipate a dramatically increased need for rehabilitation in

response to the aging population. These powerful societal forces challenge us to mold our

current health care system into one robust enough to weather tests of its integrity, based

on accessibility, equitability, and respect for patients and families. The most rigorous tests

of a retooled health care system will come from the national community of consumers,

practitioners, economists, and bioethicists. As practitioners, we will be guided by the

changing social policy forces as well as our individual professional standards. Most ethics

codes governing the disciplines represented by rehabilitation dictate that professionals

respect patients' rights and welfare, fundamental aspects of the ethical principles of respect

for autonomy and beneficence. However, because traumatic

brain injury (TBI) can affect

the individual's cognitive, behavioral, emotional, and social functioning, the impact of

TBI compromises the patient's ability to fully participate in ethically-responsible behavior

with the treatment team. It is within this context that many of the commonly discussed

ethical dilemmas experienced by rehabilitation practitioners occur. In addition, organiza

tional and social policy pressures to meet the rehabilitation needs of patients with limited

resources have raised concerns regarding how much treatment is necessary, whether we

cause harm if we withdraw treatment, and who should receive what services (e.g., is it

ethical to use limited resources to treat someone for limited gain?), fundamental aspects

of the bioethical principles of justice and nonmaleficence. The rehabilitation continuum,

by its very nature, challenges the traditional application of basic bioethical principles such

as respect for autonomy, beneficence, nonmaleficence, and justice. In this chapter, we will

discuss these four bioethical principles as they relate to key issues in ethical practice in

the rehabilitation system, particularly for persons with traumatic brain injury. We also

hope to provide a sense of the current ethical-political debate regarding health care. We

begin by acknowledging our less than noble past.

Brief Historical Perspective

Given the complexities of the rehabilitation environment and the dramatic growth of

rehabilitation programs with limited regulation and dialogue about ethical standards, it

is not surprising to us that traumatic brain injury rehabilitation has a somewhat checkered

past regarding ethical practice. The significant proliferation of TBI rehabilitation programs

and organizations during the 1980s was followed by charges of fraud and provider abuse

in the early 1990s. 2 As a result of employee and consumer complaints, a congressional

subcommittee investigated and substantiated reports of unethical conduct including abuse

of patients' rights, inappropriate admissions and treatment, inappropriate billing to max

imize revenue, and a general disregard for patient care. The report concluded by indicating

that people with head injuries need legal and regulatory protection. 3 Both the National

Head Injury Foundation (now the Brain Injury Association of America) and Committee

on Accreditation of Rehabilitation Facilities (CARF) subsequently established ethical

guidelines for brain injury service providers and rehabilitation programs. 4,5 Similarly, in

1992, the Joint Commission on the Accreditation of Health Care Organizations (JCAHO)

significantly expanded its section on patients' rights in its manual for hospitals, covering

topics ranging from respectful care to rights of persons who are dying. 6

Concurrently, professional writing on ethical issues in rehabilitation increased substan

tially. Since the initial Hastings Center series on

rehabilitation ethics, there have been

several special editions on ethics in rehabilitation populations. 7–11 Overlapping themes

among these and other publications include competency and the decision-making capacity

of the patient (e.g., who makes rehabilitation treatment decisions), involvement of family

members in the rehabilitation program (e.g., roles in decision making and protecting

patient welfare), risk-taking behavior (e.g., what is the responsibility of the rehabilitation

team in protecting the patient), and resource allocation (e.g., justification for specific

services to specific patients). We must also recognize that there is a common set of assump

tions which we believe operate in the rehabilitation continuum of care. These assumptions

include, but are not limited to:

- A primary purpose of rehabilitation is to help patients maximize their level of functional independence.
- Competent patients would want to improve their function.
- The rehabilitation team protects patients' interests.
- Patients, when capable, should be involved in decisions affecting their well-being.
- When limited, resources should be allocated to those who can gain the most (functional) benefit.

These assumptions are based on an underlying value system that necessarily drives the

rehabilitation system milieu and, thus, the ethical practice of rehabilitation professionals.

We will incorporate these assumptions as we discuss the application of the bioethical

principles to TBI rehabilitation in the sections that follow.

Respect for Autonomy

At the core of Western morality is the basic belief in individual freedom. Respect for

autonomy is a reflection of this morality and is based on the constitutional right to privacy

and self-determination. Two fundamental components of autonomy are liberty, the right

to self-determination without interference or controlling influence from others; and agency,

the capacity to make decisions and intentionally act upon them. 12 Liberty generally

requires that the patient be able to make a decision without being coerced or manipulated.

For example, if a person with a TBI were threatened with physical restraints if he or she

did not cooperate with a particular treatment protocol, the decision to cooperate would

be nonautonomous because it is based on coercion (i.e., a credible threat difficult to ignore).

Similarly, manipulation can result in nonautonomous choice. For example, in order to

accomplish a specific outcome (such as a patient decision the provider desires), the pro

vider could limit or alter information that the person would have been able to process.

On the other hand, liberty should not be equated with the prohibition of provider input.

The opposite is true; as rehabilitation professionals, we have an obligation to provide our

patients with meaningful information to help them make informed decisions. Beauchamp

and Childress 12 also discussed the acceptability of persuasion; that is, “a person must come

to believe in something through the merit of reasons another advances.” They further

clarified their definition of persuasion as an influence by appeal to cognition and not

emotion, which could overwhelm the individual. The challenge for the health care pro

vider, then, is to determine the appropriate type and amount of information the patient

needs to make an autonomous choice without unduly burdening the patient. Unfortu

nately, guidelines are lacking regarding how much discussion is adequate for informed

decision making. 13

Brown discusses the concept of self in relation to focal brain injury and indicates that

autonomy depends on the completeness of one’s self-perception. 14 However, it is our

contention, as others have previously argued, that autonomy is not a dichotomous variable

(autonomous or nonautonomous). 12 Autonomy falls on a continuum from totally incapac

itated to fully autonomous. Indeed, the trend in our legal system in the past decade supports

this continuum, reflected in the potential for different levels and types of guardianship.

Making an autonomous choice and being an autonomous person are not equivalent.

This distinction is critical in discussing the autonomous actions of a person with TBI.

While some individuals with TBI may be nonautonomous, this does not mean they have

lost all ability to participate in decisions affecting their care. Autonomous choice requires

decision-making capacity but not autonomy as a person. As Phipps has stated, the reha

bilitation team must optimize “opportunities to engage persons with head trauma in

decisions affecting their care.” 15 Therefore, health care providers have an ethical obligation

to facilitate patient involvement. The challenges in doing so, however, are many. They

range from the patient lacking the cognitive capacity to make truly informed decisions to

concerns regarding coping with injury when full disclosure is offered. In the next two

sections, we will define and describe how to assess decision-making capacity and informed

consent, and comment on how rehabilitation professionals may strive for the optimization

described by Phipps.

Defining Competency to Make Decisions

Accurately evaluating the competency of individuals to make their own decisions is a

significant practical application of the concept of respect for autonomy held by clinicians.

There currently exists no single definition of competence. Jonsen et al. suggest that com

petence represents the legal authority to make personal choices. 16 Beauchamp and Chil

dress define competence simply as the “ability to perform a task.” 12 We believe both

components — decision making and action — can be relevant. For example, with the

appropriate information, an individual with a TBI may be

able to make decisions about

how to spend finances but not be able to execute manual calculations. The patient, there

fore, is competent to decide about money even though incompetent to manage the check

book. Conversely, that same individual may not be able to set up a safe home environment

but can safely move about within it once the structure is established. Thus, the person’s

action, but not the planning, is competent. We therefore offer the following definition of

competency for consideration: the capacity to make and/or carry out decisions regarding one’s

own care and livelihood.

While legal definitions vary across states, the concept of competence has evolved from

solely a unitary concept (i.e., competent or incompetent necessitating full guardianship)

to a multidimensional concept in which performance on specific functional skills is

assessed. The end result is that a patient may be deemed competent in certain areas of

daily life and not others. For example, a person with a TBI may be able to participate in

decision making regarding specific treatment activities but not be able to manage his or

her daily affairs because of the injuries sustained.

Although competence is technically a legal determination, the practical reality is that

rehabilitation professionals, especially physicians and psychologists, routinely engage in

evaluating a patient’s competency to make specific health care decisions and to contribute

to his or her overall treatment and discharge planning. Rosenthal and Lourie suggest that

competency questions with persons with TBI commonly center on competency to consent

to treatment, manage their own financial affairs, and make decisions about their care. 17

What is particularly challenging in assessing competency in individuals with TBI is

that competency can obviously change over time, sometimes even hour to hour. Clearly,

the evolving nature of TBI necessitates ongoing evaluation of the person’s level of com

petence to make decisions on specific tasks. The time frame in which this evaluation must

occur depends on the rapidity with which the individual’s functioning changes, the

permanence of the consequences of the decision, and the current task demands. It

behooves the rehabilitation team to establish clearly accepted standards upon which to

judge decision-making capacity, which will then influence the breadth and depth of

assessment tools required.

Standards for Competence

Similar to the definition of competence, no single set of standards exists that characterize

decision-making capacity. Drane and Braddock have argued that standards of competence

change as the potential risk relevant to the outcome increases, a concept referred to as the

sliding scale of competence. 13,18,19 We disagree with this contention as Beauchamp and

Childress have done. 12 The methods for assessing competence may change but not the

standards themselves. It does not matter whether the person with a TBI is participating

in range of motion, a behavioral management program, or requires shunt revision. In each

case, a decision must be based on understanding. The amount and depth of material

required to achieve understanding may vary significantly but not the importance of

understanding itself.

Several authors have suggested or reviewed the literature to provide applicable stan

dards as noted in Table 23.1. 12,20,21

Consensual, nonhierarchical elements we have adapted to rehabilitation include the

ability to:

- Attend to and comprehend relevant information regarding specific rehabilitation assessment, care or treatment, and outcome.

- Rationally weigh the information provided in light of one's own personal situation, including basic considerations of personal values and resources (i.e., physical, social, economic, and neurobehavioral).

- Freely choose and communicate a consistent choice among available options.

In selecting standards, Grisso and Appelbaum caution that "selection of a rigorous

standard for decision-making capacity risks depriving a substantial number of persons of

their rights to make decisions about their lives … If a less rigorous standard is selected,

however, the process would fail to identify some patients who should be protected from

the potential deleterious effects of their decision-making incapacities.” 20

In their research, Grisso and Appelbaum 20 found that different types of patients (those

with schizophrenia, depression, or ischemic heart disease) were labeled impaired, depend

ing upon the standards applied. In addition, when more than one measure was used to

determine capacity, the percent of patients identified as impaired increased. Therefore,

how one defines and assesses capacity can influence whether a patient is seen as competent

to make his or her own decisions. Decisions regarding the rehabilitation process are

fortuitously based on varying levels of complexity.

TABLE 23.1

Standards of Competence

Beauchamp and Childress (2001) Grisso and Appelbaum (1995) President’s Commission (1982)

Has the capacity to communicate

freely their wishes. Ability to express a choice. Ability to communicate and understand relevant information.

Has the capacity to understand the

material information. Ability to understand information relevant to the decision about treatment. Ability to reason and deliberate about one’s choices based on weighing alternatives and potential outcomes.

Has the capacity to make a

judgment about the information

in light of values. Ability to appreciate the significance of the disclosed information for one’s own situation. Possession of a stable set of values and goals.

Has the capacity to intend a certain

outcome. Ability to manipulate the information rationally that allows weighing options.

Competency Assessment

Because there is no unitary definition of competence, there clearly is no single assessment

tool for its determination. However, as Drane has noted, a competency assessment should

eliminate what we label here as false positives (i.e., identifying a competent person as

incompetent, preventing full participation in decisions) and false negatives (i.e., failing to

prevent an incompetent person from making harmful decisions). 19 Boyle has suggested

that the determination of decision-making capacity must relate to: (1) the individual

abilities of the patient, (2) the requirements of the task at hand, and (3) the consequences

likely to flow from the decision. 22 Beauchamp and Childress proposed three questions in

assessing competence: (1) Can the individual understand the treatment or procedure?, (2)

Can the individual deliberate on the risks and benefits?, and (3) Can the individual make

a decision based on the first two questions? If one or more of these answers is negative,

then the authors suggest questioning competence. 12

In the case of traumatic brain injury, competency assessment is more complicated

because of the perceptual dysfunctions many patients experience, the differential recovery

rates of skills related to decision making, and mitigating

factors, such as fatigue and

medications, that can negatively impact cognitive performance. Based on the assumption

that the patient is alert enough to attempt a specific assessment, we recommend that

assessment include measures of attention, memory, language, executive function, and

psychological function. These categories are supported by others working with individuals

with brain dysfunction as well. 23,24 (A review of individual tests is beyond the scope of

this chapter; we refer the reader to several sources for specific suggestions for adult and

pediatric neuropsychological assessment.) 23–29 Callahan and Hagglund have indicated that

competence in rehabilitation patients must be evaluated in a two-step process; a nomoth

etic approach in which the patient's core cognitive skills are assessed (e.g., memory,

executive function, etc.) followed by an idiographic analysis of required abilities specific

to the referral question. 23 We believe it is imperative to link the specific assessment areas

to the tasks at hand, a process referred to as functional assessment. As many rehabilitation

clinicians know, performance on standardized tests does not necessarily translate into

functional or consistent performance, in part because these tests were not designed to

predict everyday functioning. 30 (For a detailed discussion of functional assessment and

nonstandardized testing, the reader is referred to other authors.) 31–33

Attention

The person must be able to attend long enough to process the relevant information and to communicate a choice. Freedman et al. suggest patients capable of engaging in conversation for 1 minute meet a minimal attentional criterion.[34] Clinicians and, particularly, nonclinical personnel influential in care decisions sometimes erroneously consider a patient incompetent when resolution of attentional deficits unmasks adequate language and executive skills to make decisions. Attentional deficits should be rigorously assessed, given the rapidity with which they can sometimes improve (e.g., daily would be the bare minimum in the long-term care setting). The team should structure the assessment environment and the characteristics of the questions to facilitate attentional processing (e.g., calm, quiet, free of distractions, limited concrete material presented, etc.).[35,36]

Memory

The inability to recall material may preclude patients from being considered competent to participate in specific skills. For example, patients who cannot recall safety precautions may not be competent to cook even though they have the physical skills to do so. Whether memory plays a significant role in competency should correlate with the level of risk involved in the specific task demands. The first author worked with one individual who had virtually no recall for recent events but intact recall

for events prior to the TBI. Most

members of the rehabilitation team believed the patient would have to attend adult day

care because she did not appear competent secondary to poor recall. Through the use of

visual compensatory techniques, as well as a safety check-in system managed by others,

the woman was able to return to her home and stay alone during the day. This case

highlights the importance of understanding strengths in other cognitive and behavioral

domains as well as the effectiveness of compensatory techniques that might help an indi

vidual compensate for individual areas of weakness and thus improve functional capacity.

If someone shows a recall deficit, he or she must still demonstrate a consistent response

to meet the standards of competency proposed. Even though the patient may not recall

by the afternoon that a competency inquiry took place in the morning, if the patient

responds in the same manner across multiple testings, the response suggests a stable value

system and decision. Consistency of responding should ideally be assessed over more

than one day, if feasible in the practice setting, and through the use of questions with the

same meaning but not necessarily the exact wording. By introducing intervening material

before returning to the task at hand, perseverative responding that can be mistaken for

response consistency might be minimized. This approach might also help determine if

patients in posttraumatic amnesia can make specific decisions such as routine treatment

choices. If the patient responds differently and inconsistently, competency is unlikely. In

the case of a person at Rancho Level II or III, even though improving from a minimally

responsive state, he or she would typically not meet competency criteria for most tasks.

Language

Obtaining a consistent response is fundamental to decision-making capacity. Language

assessment permits team understanding of how to communicate with the patient and in

what modalities the individual with TBI shows reliable responding, if it exists. We have

experienced two types of competency errors by rehabilitation teams related to language.

First, patients have retained intact verbal skills and present, superficially, as competent

when they are not. In this scenario, patients often are pleasant and carry on general

conversation without difficulty, leading clinicians to overgeneralize patients' abilities. It

is important for clinicians to press for details, ask for concrete steps in task problem

solving, or request demonstrations of skills to help clarify whether the patient can truly

rationally consider consequences and resources, such as physical limits. Second, patients

with significant expressive aphasia are labeled incompetent to participate in care decisions

when, in fact, they are competent. Obviously, in this situation, the team must try to

circumvent the effects of aphasia and complement verbal communication with other

communication modalities (e.g., physical, pictorial, etc.). In addition, identifying other

factors, such as speed of processing, that directly impact auditory comprehension and

expression is critical to valid assessment. 37 Detailed assessment of language abilities, rather

than assumptions about skills, will help prevent false positives and negatives, such as

those described above, from perpetuating.

Executive Function

The importance of executive function, like memory, to competency assessment depends

on the task for which a competent decision is required. Judgment and planning that are

severely impaired become more problematic as the risk of harm to the patient increases

(e.g., patient chooses risk-taking behavior). For example, the individual with TBI who

denies deficits relevant to the use of dangerous equipment is at substantial risk of harm

to self and possibly others. In this type of situation, even though the patient has not been

declared legally incompetent, rehabilitation professionals take steps to minimize the risk,

typically by enlisting family assistance. One way in which the provider can assess the

reliability of the patient's reports regarding executive function is to ask the patient ques

tions about performance already well known to the provider. In addition, family input

regarding the patient's performance on tasks involving

executive function and recall can

be invaluable in terms of both application of skills, such as organization and planning in

the home setting, and changes from premorbid functioning.

Psychiatric Status

Psychiatric decompensation, as well as neuropsychological dysfunction, can characterize

incompetence. In one recent study, the authors reported lifetime prevalence rates of 3.4%

for schizophrenia and 11% for major depression in patients with TBI. 38 Although psychosis

and mood disorders can render a patient incompetent to make informed decisions, neither

automatically implies incompetence. For example, only severe depressive episodes are

likely to rise to the level that might support overriding a person’s right to decide, and

rehabilitation teams have a tendency to overstate the patient’s level of impairment. 23

Psychotic episodes in patients with TBI frequently are transient and can be the result of,

among other things, fatigue or medications, factors sometimes easily corrected.

In determining capacity, the rehabilitation milieu offers significant advantages over acute

care settings. Rehabilitation professionals are intimately familiar with functional assess

ments. Patients are seen by diverse health care professionals who have the opportunity

to observe the patient at varying times practicing functional tasks that require different

skills. In addition, familial input is integral to rehabilitation treatment planning and,

therefore, offers an additional critical resource for collecting information on the person's

capacity. In patients with compromised cognitive and behavioral function as a result of

TBI, multiple assessments across multiple situations are necessary to prevent overreaction to single

events. Neuropsychological testing, patient and family input, direct observation of patient

performance, and team input on skills underlying pertinent tasks are all important evi

dence of competency (or lack thereof). Determining the stability of the patient's perfor

mance becomes more likely in this milieu as well as determining any mitigating factors

contributing to reduced capacity. Haffey eloquently articulated the need to consider envi

ronmental contingencies, as well as the structure and presentation of material, when

assessing capacities in individuals with neurological impairment. 39 Other factors, such as

medications, fatigue, seizure activity, pain, and rehabilitation treatment changes, can con

tribute to reduced cognitive and behavioral function and, sometimes, can also be directly

manipulated to improve capacity. The significance of determining whether the patient has

the capacity to make decisions regarding his or her health care cannot be overemphasized.

The rehabilitation team is determining whether to limit a fundamental right of another

human being. The obligation to not only assess and reassess based on agreed upon

standards but also to minimize mitigating factors

potentially contributing to reduced

capacity are inherent in sound ethical practice in the rehabilitation setting.

Informed Consent

The legal doctrine of informed consent has been discussed in great detail. 40,41 The evolution

of case law has clearly established the necessity of obtaining informed consent for health

care procedures with very few exceptions (e.g., emergency care). Lack of obtaining

informed consent constitutes negligence on the part of the provider if the patient can show

he or she was directly harmed by this inaction and would not have granted consent if

properly informed. The rehabilitation professional, just like the acute care physician, is

obligated to involve the patient in decision making, including soliciting informed consent

for participation in, and continuation of, rehabilitation activities. Ideally, informed consent

represents shared decision making in which providers and patient agree on a rehabilitation

plan or activity as well as develop a therapeutic relationship. In this section, we will first

discuss the components of informed consent and then discuss the legitimacy of the consent

process in TBI rehabilitation.

Components of Informed Consent

Disclosure

Beauchamp and Childress have identified six key elements of informed consent — com

petence, disclosure, understanding, voluntariness, consent

(or refusal), and authoriza

tion. 12 Competence, as previously discussed, refers to the individual's capacity to consent

and incorporates the ability to evaluate information and rationally decide and communi

cate choices about one's health care. The second element, disclosure, has served as the

backbone for much of the civil litigation in this country in the past 40 years. The classic

Canterbury vs. Spence case, in which a physician was negligent for failing to disclose a

small risk of paralysis to a gentleman undergoing a laminectomy, highlights the impor

tance of adequate disclosure. 22 However, how much and what type of information need

to be disclosed has changed over time. Scott has indicated that almost all states require

five components of disclosure for consent to be legally informed. 41 These components are:

- Diagnosis and pertinent evaluative findings
- Nature of treatment and intervention recommended
- Material risks of serious harm or complications
- Expected benefits of treatment
- Reasonable alternatives to the proposed intervention

Other authors' recommendations for disclosure parallel Scott's, although Boyle adds pro

vider recommendations to the list. 16,22 Beauchamp and Childress present a somewhat

different, although not contradictory, list for consideration: 12

- Facts/descriptions the patient usually considers material in making a decision

- Information the professional believes is material
- Professional’s recommendation
- Purpose of seeking consent
- Nature and limits of consent

Professional ethics codes also shape the type of information rehabilitation professionals

are obligated to provide. Because informed consent is meant to be a shared process

between provider and patient, the written consent form should play only a minor role in

disclosure of information.

The courts are fairly evenly divided on the type of standard under which a health care

professional should be judged regarding whether disclosure has been sufficient enough

for a patient to make an informed decision. The two most commonly considered standards

are the professional practice standard and the reasonable person standard, although a third

standard, the subjective standard, may also have relevance to TBI rehabilitation. The pro

fessional practice standard embodies two primary assumptions: (1) the health care pro

vider possesses the expertise to determine relevant information to be disclosed and the

patient does not; and (2) the health care provider’s decision reflects the prevailing profes

sional practices and wisdom of the time. The professional practice standard appears to

have significant weight in TBI rehabilitation. For example, it has been common rehabili

tation practice to withhold information from patients who are not believed to be emotion

ally ready to process that information. Rehabilitation providers may choose not to disclose

the likelihood of poor outcome because of their belief that poor coping will result. The

problems inherent in this standard are significant, including the lack of prevailing customs

relevant to the decision needed, the de-emphasis on the patient’s right to be involved in

treatment decisions, and misassumptions regarding the patient’s interests and capabilities.

In addition, the general practice of the time may later prove to be incorrect. It was not too

long ago, for example, that invariant stages of coping were embraced as the “correct”

recovery process after the occurrence of a traumatic injury, and that patients who did not

become depressed, for example, were viewed as maladjusted.

The reasonable person standard was first raised in the Canterbury case and refers to

disclosure of information based on what a reasonable person would want to know if faced

with the same circumstances as the patient. Therefore, a health care provider who discloses

what he or she believes is in the best interest of the patient could still be liable if he or

she omitted information a reasonable person would consider material to the decision. The

application of this standard places the burden on the health care provider to know what

to disclose given no clear guidelines exist to define what is reasonable in the multitude

of health care decisions necessitating disclosure. While there seems to be limited direct

comment in the literature on what patients and families want to know regarding capacity

determination, some suggest factors patients and families consider important to their

empowerment are knowledge of basic information [of TBI] and ways to apply it to daily

life; regular knowledge updates and advice from health care providers, including discus

sions of realistic expectations; clear direction about improving quality of life; emotional

support; financial counseling; and information about community resources. 42,43

The third standard, the subjective standard, requires that the health care professional

provide information that is relevant to the particular patient. Therefore, the patient's rights

clearly take precedence over the rehabilitation professional's own evaluation of what is

in the patient's best interest. This standard, more than the other two, accounts for patient

values and sociocultural background but is vague about the amount of detail that would

meet the standard's intent.

We believe that, in rehabilitation, we walk a fine line of compromise among all three

standards. Because TBI manifests itself uniquely in each patient and family and because

rehabilitation treatment plans are individually tailored, much of what we disclose is

specific to what individual patients and families want to know, such as the social worker

providing specific resource information, the rehabilitation counselor discussing vocational

strategies for a specific work setting, or the occupational therapist recommending specific

hand exercises. However, there are limits to what we share with our patients at a given

time. For example, early in rehabilitation, we might not immediately confront patients

who deny their TBI because denial can serve as a protective coping mechanism against

the emotional impact of the severity of injuries sustained. We therefore set limits on what

we are willing to share at the individual level based on both professional knowledge (i.e.,

professional practice standard) and what is reasonable, given the nature of processing

deficits. In the example above, we have invoked the therapeutic privilege to withhold

information because we believe that information would be harmful.

Unlike acute care physicians seeking consent for invasive procedures, rehabilitation

professionals generally have not been the target of legal action for inappropriate disclo

sure. The importance of understanding the standards is to realize that there does exist

a legal obligation to provide information based on a particular state's value system,

which may or may not fit neatly within the context of what rehabilitation professionals

consider ethical practice. Let us reconsider the denial example. If the state used a rea

sonable person standard, and it is assumed that reasonable persons would want to know

that they have deficits associated with their TBI, a health care provider would be legally

obligated to provide this information. However, presentation of this material could easily

violate the ethical principle of nonmaleficence, or “do no harm,” if the patient decom

pensated. This example is simply used to illustrate that providers need to be aware of

their state’s standards and exert sound judgment regarding their own decision making

about what to disclose to patients and families who need to decide on rehabilitation

recommendations.

Understanding

While disclosing the right amount and type of information is important, there has been

a significant shift in emphasis in the last decade toward the relatively greater importance

of patient understanding to informed consent. This may seem like an obvious statement

today, but the traditional emphasis for consent in acute care was on provider disclosure

rather than on patient understanding. If providers had disclosed the central facts, they

had done their job. Obviously, this approach could be disastrous from an ethics point of

view in working with individuals with compromised brain function (e.g., treating and

billing without true consent, excessive provider authority, lack of consideration of patient’s

situation and welfare, etc.).

Disclosure should be adapted to facilitate patient

understanding, whereas the converse

is not true. The elements of disclosure listed in the previous section must be clearly

understood by the patient to achieve informed consent. Achieving understanding when

soliciting consent from patients with TBI requires special consideration of the many factors

that can impact processing and manipulating material. Even in persons without TBI,

understanding can be affected by a plethora of factors including cultural values, presen

tation mode, and amount and complexity of material. For example, McNeil et al. showed

that couching a consent form's statistics as survival vs. death statistics dramatically altered

the percent of research participants who would have selected a surgical procedure vs.

radiation for lung cancer treatment. 44 For persons with TBI, to obtain a true understanding

can be a bit like trying to assess their attention — only a little should be attempted at a

time. We recommend the following nonexhaustive list of strategies during disclosure to

solicit understanding if it is questionable:

- Assure a calm, familiar environment
- Minimize distractions and interruptions
- Vary the presentation mode of disclosure, if needed
- Use concrete, nonstressful examples linked to the patient's personal situation
- Limit the amount of material to be attended to and recalled at one time
- Ensure material is matched to the patient's educational

and social level

• Provide time for the patient and family to learn material based on their neuropsychological and emotional status

• Repeat information as needed

• Assess understanding via different patient demonstrations, if applicable (e.g., evidence of generalization of information presented, verbal or physical demonstrations, etc.)

• Enlist other team members' assistance and assess at an optimal time for the patient (e.g., when pain and fatigue are low, attention high, etc.)

• Reassess via direct additional questions or observation of the patient applying material provided (e.g., questions the patient asks, discussion of material with others, etc.)

It is also important to remember that understanding does not have to be 100% or match

the same level of quality the provider incorporated into the disclosure. We all filter material

based on our personal circumstances. Some information disclosed may carry no signifi

cance for the patient and family and will be discarded. Beauchamp and Childress have

suggested individuals achieve sufficient understanding if they have "acquired pertinent

information and have justified, relevant beliefs about the nature and consequences of their

actions." 12 They include diagnostic and prognostic information, the nature and purpose

of the intervention, benefits and risks, alternative actions, and recommendations in their

list of essential features patients need to understand.

When assessing understanding in rehabilitation, we believe the goal is to help the person

with TBI achieve an understanding of the minimal essential

criteria for the decision at

hand. When there are team disagreements about what is considered essential material,

we generally recommend applying the lowest common denominator of agreement among

the team, although the team may choose to defer to the expertise of an individual team

member when tasks seem discipline specific. Here, of course, team members need to

remember their own limits of professional competence.

One final point bears discussion in soliciting patient understanding. Understanding is

not only about whether the person has the cognitive capacity to process and comprehend

information but also whether the person believes the information is accurate. Beauchamp

and Childress have suggested that a false belief can invalidate consent and offer the

example of someone who is seriously ill who refuses treatment because she does not believe

she is ill. 12 Their example has parallels to individuals with TBI who believe they are

independent when they are not, and so refuse treatment. Critical questions that bear asking

are (1) Does the belief limit an understanding of the tasks involved? and (2) Can the belief

be modified with knowledge? In TBI, the false belief is not created by ignorance; it is

created by a response to physical damage. Perhaps, then, we can argue that even though

the patient may understand the task, the refusal is based on lack of self-awareness created

by the TBI, either physically or psychologically.

Therefore, the refusal is not informed

because the patient has not reacquired the capacity to evaluate pertinent information.

Voluntariness

Voluntariness is embedded in the concept of liberty previously discussed in the chapter.

In order for consent to be voluntary, it must be given without coercion or significant

controlling influences and only after adequate understanding of essential data. Boyle

indicates that “fully voluntary choice is an ideal.” 22 There exists no pure voluntariness in

persons with TBI whose cognitive or emotional functioning has been compromised. Vol

untariness is a matter of degree and is influenced not only by positive and negative

feedback by others, but also by the same controlling factors that can mitigate understand

ing (e.g., medications, fatigue, mood disorders, cognitive dysfunction, etc.). Consent can

be offered without it being voluntary. Rehabilitation professionals must be particularly

sensitive to their power over patients and to not cross the ethical line from persuasion to

coercion in soliciting consent. While coercion is sometimes necessary when incompetent

rehabilitation patients put their own or others’ safety in jeopardy, it is unacceptable in

routine decision making.

Consent

Consent represents the outcome of the cognitive process of weighing the various alterna

tives embedded in a particular decision. While consent implies the patient agrees to care,

as we have noted in other work, this component of informed decision making refers

equally to informed refusal. 45 The provider’s acceptance of a patient’s decision to disagree

is as fundamental to sound ethical practice as the acceptance of a patient’s concurring

choice. Clinicians most often question competence when patients refuse treatment seem

ingly important to achieving rehabilitation goals. 46 Patients do not necessarily refuse

treatment because they lack understanding; religious values, strongly held beliefs and

The rehabilitation professional has a duty to sort out differing values and informed choices

from the effects of the brain injury. In doing so, we suggest the following:

- Consider the level of confidence the provider has that the patient understood the material relevant to the decision; if questionable, reeducate and reevaluate.

- Evaluate the consistency of the patient’s decision with previously held values or cultural mores reported by the family.

- Minimize the impact of situational variables on consent outcome (e.g., consider if stress, medications, and treatments unrelated to the decision are stable, etc.).

- Reaffirm consent to ensure the provider understood the nature of the patient’s decision and that the patient showed stability in the decision.

As noted in the discussion on decision-making capacity, consent should be stable.

Although the patient and family have the right to withdraw consent, the provider should

at least solicit a basic rationale for this withdrawal to

rule out confounding variables

clouding the patient’s decision making.

Authorization

The final component of informed consent represents the transferring of authority from

the patient to the health care team to offer services. It is not enough to agree to an

assessment, treatment procedure, or program, the patient must recognize he or she is

authorizing someone else to carry out an agreed-upon action. In essence, the patient is

transferring right of care to another. While the consent form has a legitimate, albeit small,

role in the informed consent process, authorization is more clearly informed through

team dialogue with the individual with TBI. It is within the context of effective commu

nication that the team determines if the patient truly understands that he or she is not

only concurring with the program but is allowing the team to proceed with specific

interventions.

Authorization necessarily implies the person has the legal right to authorize treatment.

This may include the patient or the patient’s surrogate. Patients who are unconscious,

patients who have psychiatric disorders with active delusional, hallucinatory, or severe

depressive features, patients declared incompetent by the courts to make health care

decisions, and minors typically have surrogates. A minor is defined by state statute and

commonly includes exceptions that provide the minor with the legal standing to authorize

care. Examples include minors who are married or emancipated and minors who are

pregnant when decisions relate to the health care of their fetus or themselves. Other

exceptions include decisions regarding sexual activity and substance abuse or mental

health treatment. However, as the Committee on Bioethics of the American Academy of

Pediatrics (AAP) has argued, even if patients do not have the legal authority to determine

their health care, they should still participate in decisions consistent with their

developmental level. 47 The committee has offered suggestions for age-related involvement

in health care decisions (e.g., discuss psychotropic medications for attention deficit disor

der with a third grader as well as the parents).

Assent is the term used when referring to the process of acquiring the patient’s opinion

to undertake health care procedures when the patient does not have the legal authority

to provide consent. The AAP Bioethics Committee recommends that assent include: (1)

helping the patient achieve a developmentally appropriate awareness of the nature of his

or her condition; (2) telling the patient what to expect from assessment and treatment; (3)

clinically assessing the patient’s understanding of relevant information and influences

affecting responding; and (4) soliciting patient’s expression of willingness to receive care.

The authors caution that, if a decision will not be altered by considering the patient's

opinion, then assent is superfluous and the patient should be told the decision and

rationale for it. 47

The Application of Informed Consent to Rehabilitation

Some authors have suggested that informed consent cannot be easily applied to rehabil

itation because the informed consent doctrine was not developed with the rehabilitation

setting in mind. 46,48 Informed consent was developed in acute care in which single proce

dures or care needs with limited scope were considered. The rehabilitation milieu differs

from acute care in that rehabilitation involves an interdisciplinary team, active patient

involvement in care, potentially long lengths of treatment across different types of settings,

and an emphasis on care and quality of life rather than on cure and length of life (although

these latter two are also valued). Caplan has suggested that "models of informed consent

based on episodic interactions with specific health care providers may be of little utility

in understanding the moral framework within which care is provided to those with chronic

impairments … ." 46 He further states that there is an assumption that the patient-provider

relationship is "discrete, finite, and episodic … " and that patients are free to seek or refuse

services. Caplan suggests that patients admitted to rehabilitation are not afforded the same

opportunity to accept or reject treatment and that

treatment refusals are sometimes over

ridden or ignored. Unfortunately, one parallel between acute care and rehabilitation that

does have some empirical support is that health care providers in neither setting are

acquiring informed consent when they should be. Consider the following findings. Auer

swald et al. conducted an epidemiological investigation to determine solicitation of con

sent to medical/surgical procedures with older adults who developed delirium during

their hospitalization. 49 They found no documentation of assessment of decision-making

capacity and found documentation of consent in only 19% of cases. Documentation of

disclosure of potential risks was only 35%, and a surrogate was not utilized in 53% of

cases in which the patient had substantial cognitive impairment impacting decision

making capacity (documented via researcher evaluation of cognition). Conversely, a sur

rogate was used in 4% of cases in which the patient's mental status was considered normal,

suggesting inappropriate employment of a surrogate. 49 Fowles and Fox surveyed brain

injury facilities to determine consent practices. Seventy percent (70%) of facilities that

responded (N = 71) were classified as rehabilitation facilities, most treating patients at

Rancho Level IV and above, with a mean length of time in program of 102 days. Restrictive

procedures, such as pharmacologic interventions, physical restraints, and behavioral con

tracts, were used by the majority of facilities. However, only 22% (N = 14/64) of facilities

indicated they required additional consent for neurobehavioral interventions once patients

provided general consent to rehabilitation services. Forty-eight facilities (75%) indicated

reassessing competency to consent to rehabilitation. However, the authors reported the

mean length of time to reassessment was 53 days, suggesting reassessment only once. 50

We believe there are several reasons consent may be lacking in rehabilitation. First,

clinicians do not give enough consideration to consent. There is some indirect support for

this through Tarvydas and Shaw's work. Their survey of rehabilitation team members

found that the most frequently cited ethical concerns were inadequate training to render

required services (i.e., suggesting potential lack of knowledge for proper disclosure) and

inappropriate prognostic statements (e.g., inaccuracy in disclosure). They also found that

one of the most distressing ethical issues was inadequate consideration of medical con

traindications to rehabilitation treatment (e.g., soliciting consent for treatment that may

not be appropriate or valid). 51 Tarvydas and Cottone have pointed out that professionals

untrained in ethics rely more on personal experience and, thus, are more likely to engage

biases and prejudiced thinking. 52 This could impact a rehabilitation professional's decision

to assess capacity, for example. In addition, rehabilitation professionals may exert the

professional practice standard upon admission, choosing rehabilitation on behalf of the

patient who does not yet possess the knowledge or skill to judge the merits of the program.

Fowles and Fox have noted that patients are often considered de facto competent and,

therefore, consent is accepted without necessarily conducting a proper evaluation to

determine the validity of that consent. 50

Second, there has been some commentary in the literature that quality of care has become

less important than cost reduction in brain injury rehabilitation. 17 Managed care has

impacted rehabilitation in such a manner that efficiency is prioritized over quality care

and that, in this environment, clinical competence is diminished. 53 Thus, rehabilitation

providers are not able to dedicate the time necessary to monitor informed consent or to

maintain reasonable admission standards, which should include informed consent proce

dures. Time pressures may create the perception that consent procedures are impossible

to implement successfully. Third, less invasive procedures have been shown to correlate

with failure to obtain consent. 49 Because rehabilitation is viewed as an environment of

limited risk and obvious benefit, a weak standard of consent has been in operation. 50 This

is consistent with the practice of acquiring general consent but nothing further.

Soliciting Patient Consent

While each of the above three ideas may offer some insight into why consent is not

obtained, the lack of solicitation of consent is still unacceptable. Although it can be chal

lenging to assess consent with individuals with TBI, the difficulties encountered do not

free us from our moral and legal obligation to obtain consent from our patients. However,

it need not be as cumbersome as it might first appear. Acquiring informed consent does

not have to be narrowly implemented. Acute care models do not require consent for every

procedure upon a patient being admitted to a hospital or clinic. Routine care is provided

under the auspices of general consent. We believe this approach can be applied to reha

bilitation despite the differences in length or intensity of treatment, and we suggest the

following guidelines:

- Consent should be obtained by the individual legally recognized to provide that consent. If this person is not the patient, then patient assent should also be solicited, if appropriate, based on neurological status and task simplicity (usually by Rancho Level III or IV).

- Patients should be encouraged to discuss consent decisions with family members who will be involved in their rehabilitation.

- Consent, upon admission, should cover routine, nonrestrictive assessments and therapies (e.g., exercise programs, provision of resource information, mental status assessments, physical exam, etc.). This statement is made with one strong caution, however. The consent process must reflect the breadth of rehabilitation specialties. All rehabilitation team members are strongly encouraged to review the general rehabilitation admission form for inclusion and accuracy of their primary roles. If needed, organizations should support efforts to reconstruct initial consent procedures, as we had to do in an outpatient TBI

setting in which the first author worked.

• Consent should include specific discussion regarding how information will be used and to whom it will be disclosed.

• Admission consent should not cover invasive or restrictive procedures except as general descriptions.

• Additional consent for restrictive procedures is necessary to preserve the patient's self-determination given these procedures imply a reduction in personal autonomy. Restrictive procedures such as physical and pharmacological restraints have a clear initiation point and, therefore, also have a discrete point at which consent should be solicited. If a patient is suddenly out of control, necessitating action prior to consent, the provider should be able to justify this position by invoking therapeutic privilege to prevent harm to the patient. However, there is no justification for continuing restrictive procedures once the immediate crisis is managed, which, in our experience, is usually no more than a few hours. Consent for therapeutic continuance must be sought.

• If the patient initially requires a surrogate decision maker, a protocol for reassessment of the patient's decision-making capacity should be established at admission. This protocol should include frequency of reassessment, which will depend on the severity and type of impairments and anticipated recovery curve based on prevailing empirical knowledge and clinical judgment, disciplines involved, and standards for capacity.

• If a program significantly changes (e.g., addition/deletion of a therapy), affirmation of consent to the changes reflects sound ethical judgment.

As Scofield has noted, increasing patient decision making can increase commitment to

the rehabilitation plan and the overall therapeutic relationship. 54 Ultimately, it is hoped

that, through this relationship, the patient will maximally benefit from rehabilitation,

increasing overall independence and improving quality of life.

Beneficence

Miller states that the goals of rehabilitation are “maintaining, enhancing, restoring, and

compensating for disabling conditions, promoting the highest quality of life, and integrat

ing the patient into his/her family, community, or vocation.” 55 Rosenthal and Lourie

believe that respect for autonomy is the ultimate rehabilitation goal. 17 However, Banja has

noted that rehabilitation professionals commonly hear complaints from patients and fam

ilies regarding their lack of inclusion in rehabilitation planning. 56 Martone described her

experience as a parent of an individual with TBI and indicated that, as surrogates, she

and her spouse were not included in decisions. She urges that families be part of the

team. 57 If maximizing patients’ independence is a core rehabilitation value, then why do

so many patients and families indicate their autonomy is not respected? In our opinion,

the principles of beneficence and justice play critical roles.

The principle of beneficence is deeply rooted in both ethics codes of professional conduct

and general medical practice. That is, strong beliefs in helping others and promoting

patient welfare have resulted in patient safety being prioritized over respect for patient

choice, further complicated by an increasing litigious society and limited resources with

which to comprehensively address patients’ needs. TBI rehabilitation, in particular, chal

lenges the professional to balance individual freedom with

patient safety. In this section,

we will discuss the principle of beneficence, especially as it relates to the risk-taking

behavior of patients with TBI and to the rehabilitation professional's role in protecting the

person's safety while balancing respect for autonomy. The role of the family in rehabili

tation will also be addressed. Justice will be discussed later in the chapter.

Our Moral Obligation to Assist Others

Beneficence can be viewed on a continuum from preventing or removing harm (e.g.,

preventing persons with TBI from injuring themselves) to facilitating good or promoting

a person's welfare (e.g., offering a rehabilitation plan that helps ameliorate or compensate

for deficits). It is based on one human being's duty to assist another in need. Beneficence

usually requires specific action on the part of the provider, which includes weighing all

available options to facilitate maximal benefit to the patient. Pellegrino 58 has suggested

that professional medical codes are based on a three-tiered system: observance of laws,

observance of rights and fulfillment of duty, and the practice of virtue. Pellegrino indicates

law operates as the minimal level of acceptable behavior; however, it may not necessarily

rise to an acceptable level of sound ethical practice. Respecting the rights of others and

fulfilling one's duty raises the standards of conduct and includes beneficent obligations

beyond what law mandates. A truly virtuous person, however,

chooses actions that are

good even when personal sacrifice is required. 58 This third tier is consistent with the

principle of general beneficence, a societal moral duty. Beauchamp and Childress 12 suggest

we have a moral obligation to act when

• An individual is at risk for significant loss or damage to a major interest.

• Our action is needed to prevent the loss/damage.

• Our action is likely to be successful.

• Our action does not place us at significant risk (e.g., personal, financial, etc.).

• The other person's benefits outweigh potential harm/costs to us.

As noted in the beginning of the chapter, rehabilitation presumes a beneficent relation

ship; that is, we agree to admit patients into our care because we believe they will benefit

from the rehabilitation program we offer. While this acceptance does not necessarily

require the level of virtue discussed by Pellegrino, 58 it is consistent with Pellegrino's second

tier. We have an obligation to act in such a manner that promotes our patient's welfare,

commonly defined in rehabilitation as maximizing the patient's independence. Herein lies

the classic ethical dilemma underpinning much of rehabilitation practice — how does one

balance respect for autonomy with beneficence? There, also, is a Catch 22 for many patients

— in order to maximize their independence, patients require a certain degree of depen

dence on others, typically the family. In addition, what is in the patient's best interest

must now be considered in the context of what is in the organization's best interest to

remain solvent. Key challenges include determining under what circumstances each

principle should drive decisions and what level of intervention is appropriate. Banja

clearly supports an autonomy-based model and suggests that patients should "enjoy an

authentic semblance of personal and individual liberty despite participating in a thera

peutic program supervised by a rehabilitation professional." 56

Justifiable Paternalism

Paternalism is the term applied to health care provider actions that override respect for

patient autonomy. The provider makes a care decision on behalf of the patient based on

health care knowledge and training. It implies three possible outcomes: (1) the provider

overrides patients' or surrogates' expressed decisions; (2) the provider does not provide

patients with information or service, even when requested; or (3) the provider fails to

solicit involvement in decision making. Examples of paternalistic actions in TBI rehabili

tation include: (1) not disclosing prognostic information; (2) terminating, initiating, or

modifying care, particularly pharmacological or behavioral, without patient knowledge

or consent; (3) limiting treatment options from which the patient selects; and (4) denying

specific equipment or ceasing treatment despite patient or family requests to the contrary.

There has been significant literature debating the topic of when paternalism is justified.

Common conditions suggested from a review of the literature by Beauchamp and Chil

dress include: (1) the negatives prevented/benefits gained outweigh loss of independence

and invasion of privacy; (2) the person's condition seriously limits ability for autonomous

choice; (3) the intervention is universally justified; and (4) the person provides consent or

would consent, if rational. 12 These criteria are consistent with the widely held rehabilitation

assumption that patients would choose the rehabilitation intervention if capable of doing

so. In a widely cited article, Caplan has suggested that rehabilitation operates on a time

continuum — at first, justifiable paternalistic action by the provider is acceptable as the

patient and family learn about and cope with the initial impact of injury on their lives. 46

Over time, however, paternalistic actions increasingly yield to the rights of patients and

families to make their own health care choices. This educational model was later reinforced

by Scofield. 54 The educational model is adaptive because it allows for the evolving capac

ities of the patient and acknowledges the developing relationship between the patient and

rehabilitation team over time. It does not represent a license for rehabilitation professionals

to be generally paternalistic, but it does allow providers to override or ignore patient

requests based on the presumption that the eventual benefit will be increased autonomy.

This is consistent with Scofield’s assertion that beneficence and respect for autonomy are

not mutually exclusive. The model also allows for greater use of persuasion than might

be expected in an acute care setting. However, Beauchamp and Childress indicate that

justifiable paternalism really hinges on the level of harm or benefit, and Banja argues that

the burden falls on the rehabilitation provider to demonstrate that risk is excessive. 12,56

Risk is the probability that the patient will incur some type of harm (to self or others)

based on a particular course of action. Risks, of course, can occur in multiple domains,

including physical, psychological, social, vocational, financial, and legal. Risk assessment

in the rehabilitation setting requires both general and specific skills, including sound

clinical judgment, a clear understanding of the patient’s clinical presentation, and a

thorough understanding of common patterns of behavioral dyscontrol resulting in

increased risk of harm. The health care provider must judge not only how likely he or

she believes specific harm will come from risk but also the magnitude of harm. Benefits

require similar consideration (i.e., likelihood and magnitude of benefit) if the provider is

considering overriding patient autonomy for some benefit. In essence, then, as we in

rehabilitation weigh paternalistic actions, we need to

address the risks, benefits, our

confidence in our predictions, the fundamental rights of individuals, and our responsi

bility as professionals to make sound ethical decisions. Unfortunately, there are no clear

rules at the individual level upon which to make these judgments, and clinicians tend to

be over-confident in their predictions. 59 In other work, we, as well as other authors, have

offered steps to guide the ethical decision-making process. 60,61 However, these steps serve

only as general guideposts. In the next section, we will specifically discuss three common

situations arising in TBI rehabilitation that create ethical dilemmas: family involvement,

driving, and use of restraints.

Family Involvement

If family* involvement were to be considered from a strictly legalistic point of view, we,

in rehabilitation, would be extremely limited in our ability to succeed with our patients.

It is within the context of family consideration that we believe western morality and law

are narrowly defined. Regardless of whether a patient is competent to make decisions,

the role of the family is critical to the rehabilitation agenda. Families (who are not always

legally recognized as decision makers) provide the rest of the rehabilitation team with

perhaps the most important framework with which to understand the patient and create

functional treatment plans. We rely on families, as much as the patient, to grasp historical

Phipps comment on the importance of understanding the family’s narratives as they

connect the patient’s past to the present and provide a broader understanding of who the

patient is. 62 In addition, we depend on families to help patients make sound decisions

and to create a safe environment (e.g., physically, interpersonally, financially) in which

patients can reacquire skills and compensate for deficits. Finally, families not only provide

emotional support, but they “take part in the patient’s narrative self-discovery that helps

her to reconnect with her values and give them meaning as expressed in choices.” 63

Although not specific to TBI, Kuczewski, 63 has eloquently described an interpretive model

of the informed consent process in which families help the patient reconnect and construct

new values. This seems particularly applicable to the TBI rehabilitation process in which

the patient’s self-awareness may be compromised. As Rosenthal and Lourie have implied,

TBI rehabilitation often results in the emergence of a new self. 17 Conversely, however,

rehabilitation professionals are caught in a very interesting dynamic with families because

families not only serve as the caregivers in TBI rehabilitation, they also are learning to

cope with the impact of TBI. Most rehabilitation professionals practicing in the field long

enough have worked with families for whom the demands of caregiving exceed what can

be managed. Those families are burdened by the pressure of

the third tier — the moral

obligation of self-sacrifice — without having the internal and external resources to suc

ceed. 58,64,65 That is not to suggest that all families become dysfunctional; research has shown

otherwise. 66 Research also has shown that even families with limited emotional resources

can benefit from interventions, such as psychotherapy, education, support groups, and

advocacy, in both the acute and postacute period. 64,66 We are simply recognizing that it is

the family and not simply the patient that will be redefined in the rehabilitation process

and the lifelong process of adaptation to disability. Not only do treatment decisions have

immediate and direct impact on families (e.g., delivery of care, home modifications, costs,

etc.), over time, they can have positive and negative implications for evolving relationships

as well as overall family health. 64,67 Families can experience qualitatively changed rela

tionships as a result of brain injury. For example, marital distress and divorce rates have

been reported to rise beyond the first year postinjury; siblings of children with severe TBI

* We use the term family broadly to include caregivers not necessarily related by blood or marriage.

sometimes exhibit increased behavioral problems. On the other hand, the same authors

suggest some marriages improve and siblings get actively involved in care. 66,68

We believe the uniqueness of providing rehabilitation care and coping with disability

gives families rights (access to information, involvement in decisions) not immediately

apparent in a legalistic model of health care practice even though we still are bound by

legal statutes. We therefore suggest a compromise that echoes Caplan's educational model.

Although the importance of the family's role might not change, as the patient's autonomy

increases, providers need to weigh the patient's desires more heavily than the family's as

it relates to the patient's health care choices. Patients do not give up their right to choose

simply because they are accepted into a rehabilitation program. However, this is not the

same as minimizing the family's input. In fact, in rehabilitation, it is common for families

to play an active role in rehabilitation care. Hardwig suggests families have the right to

be involved in any decision directly affecting them. 69 We also believe families have a right

to be involved but concur with Kuczewski that patients who have generally functional

families include family considerations in their deliberations when families are directly

impacted by these decisions (although the person with TBI may need assistance in com

prehending the information and the family and patient may need assistance in reconciling

differences). 63 The family clearly can play a pivotal role in assisting the patient to make

autonomous choices. 70 However, in our current cultural climate and until better models

exist for balancing the benefits and risks to both patients and families directly affected by

disability, the legal protection needs to lie with the patient who, generally, is at greater

risk for neglect or abuse than is the family.

Thus, the principle of beneficence can arguably be applied in at least three circumstances.

First, it can be applied in the context of clear risk and potential harm, which justifies

provider solicitation of family input on behalf of the patient when the patient objects to

beneficent intervention. Second, family involvement can be limited if it is interfering with

the patient's progression in functional skill development because the patient's welfare is

no longer prioritized. However, in these situations, family involvement can sometimes be

refocused towards educational meetings, discharge plans, household modifications,

accessing community resources, etc. Finally, beneficence supports soliciting family

involvement when the patient does not yet have the capacity to understand the conse

quences of decisions even if the patient has not been declared legally incompetent. Cal

lahan has suggested that legal sanction may not even be wise in recognizing the family's

obligation to their loved one. 71 While the benefits might not seem immediate, some

research supports the contention that appropriate family involvement directly affects long

term patient outcome for persons with disabilities. 64,72

Prevention of Driving

The decision to prevent a patient from driving is based, at

least in part, on the principle

of beneficence, particularly when we decide to involve the family in our prevention plan.

Consider the following case: A 21-year-old patient at Rancho Level VII will be discharged in 3 days after a month-long stay for a TBI as the result of a car accident. The patient is adamant about driving even though a predriving evaluation indicated poor self-awareness, impulsivity, and visual-perceptual problems. The rehabilitation team's response has been consistent; the deficits preclude clearance to drive. The patient states that he plans to drive and requests that we not mention this decision to the family.

As a rehabilitation team, the choice to enlist the family's help to prevent the patient

from driving is relatively straightforward, although not necessarily legally sanctioned.

That is, if the patient does not show self-awareness of the dangers, from a rehabilitation

point of view, he or she is not making an informed decision. However, the choice to enlist

the family is based on beneficence (safety), not autonomy (lack of capacity). While we

cannot predict with certainty the actual harm, we do have both general and specific

information to guide our decision. We know, for example, that the Number 1 cause of

brain injuries is motor vehicle accidents, that seizure activity precludes driving, that

performance on certain tests (such as Trail Making) is correlated with successful return to

driving, and that the very young and very old have a greater number of accidents. We

can combine this general information with our understanding of the patient's neurobe

havioral presentation to document justification for

recommending infringement on the

patient’s right to self-determination. In this case, the patient lacked the ability to truly

protect his own safety interests. The patient must possess the ability to protect his or her own

welfare even if choosing not to. For some skills, such as driving, the patient’s lack of self

awareness, plus other deficits, creates a probable risk of harm that may be prevented

through provider actions, and these actions (e.g., demonstrating driving risk to family via

simulations and education regarding deficits to enlist their support, encouraging family

to take keys, disabling essential equipment, etc.) do not involve substantial risk to the

provider. Therefore, the basic criteria for justifiable paternalism are met. If the provider

chose not to act, he or she could be considered negligent because of the special relationship

rehabilitation professionals have to protect their patients. 73

The rehabilitation team chooses to support actions that prevent driving even though

the individual still possesses the legal right to drive. Driving is an example where reha

bilitation and the law intersect in a manner that is not always productive for the patient’s

safety. Although there are state-based procedures through the Department of Motor Vehi

cles (DMV) for removing a driver’s license after a change in health status, these procedures

are often cumbersome, ambiguous to access, and not reflective of the changing status of

individuals with TBI. Clearly, rehabilitation professionals can contribute to social policy

in this arena. For example, several years ago, we partnered with rehabilitation facilities

and worked with key representatives from the Department of Motor Vehicles in one state

to place a rehabilitation professional on the medical review board that considers fitness

to drive in individuals with changed health status. Second, we worked to streamline the

paperwork process for submitting review requests. (Physicians had reported to us that

the paperwork was too cumbersome to complete.) Our success was clearly based on broad

based cooperation of the major rehabilitation sites to influence the DMV, and the DMV's

willingness to seriously review their procedures. The more important point, however, is

that, even at the clinical level, we can play an important advocacy role that supports the

welfare of our patients. If practicing in a state without reporting procedures, ambiguous

procedures, or lack of representation by rehabilitation personnel on medical review panels,

rehabilitation professionals can have a significant impact on improving general processes.

On the other hand, because the standard for admission for expert testimony has recently

changed to proven scientific reliability, significant research needs to be done to bolster

evaluative data predicting successful return to driving in individuals with TBI. 73 Because

driving is fundamental to American culture, restricting driving privileges needlessly could

be considered maleficent.

Use of Restraints

Persons with TBI, particularly in early stages of recovery and at Rancho Levels II, III, or

IV, commonly demonstrate agitation, confusion, and lack of behavioral control that can

place themselves, family members, and rehabilitation staff at risk for injury. Both phar

macological and physical restraints have been used as treatment strategies to control these

types of symptoms under the principle of beneficence. However, these types of interven

tions are not without their own risks, such as falls and physical problems from immobi

lization when using physical restraints, and slowing of cognitive recovery and uncertainty

regarding drug interactions with chemical restraints. 74 In addition, restraints can prove

counterproductive to their primary purpose by directly increasing agitation. 75,76 Inherent

in the JCAHO standards for use of restraints are the following components:

- Provide patient/family education regarding restraint use.
- Document efforts to reduce restraint use.
- Follow the organization’s established clinical protocol for restraint implementation and discontinuation.
- Protect the patient’s rights, dignity, and safety during restraint use.
- Ensure staff competence in using/discontinuing restraints. 77

These standards serve to protect both the patient’s right to self-determination (e.g.,

documenting efforts to decrease use) as well as to protect his or her welfare (e.g., following

clinical protocols) and are buttressed by significant case law. 74 The rehabilitation team

must carefully balance the risks and benefits of restraint use to determine the reasonable

ness of implementation. In considering the reasonableness of selecting restraints, the

rehabilitation team should consider both the immediacy and magnitude of the potential

danger, the antecedents and consequences to the behavior considered problematic, and

the underlying rationale for choosing the restraints as the method of control. As illustrated

in Table 23.2, we argue that justification for restraints under a beneficent model of decision

making is clearly present only under Condition IV (i.e., high potential for occurrence in

immediate future and high magnitude of harm).

We firmly believe, however, that Condition IV does not provide a rationale for a uni

versally acceptable practice of restraint use when risk is present. There are obviously other

options for managing unsafe behavior that should be carefully weighed. Behavioral man

agement programs, electronic bracelets, and special beds are just three examples. 75,78,79 In

one study, researchers were successful in managing problematic behaviors, such as phys

ical aggression and inappropriate sexual behavior, 2 years post-injury through behavioral

interventions. 80 Consider the following case: Mr. Archer is a 56-year-old gentleman who sustained a TBI as the

result of a fall from a hunting stand. He was recently transferred from an inpatient rehabilitation program to a skilled nursing facility for continuation of therapy. Because he has fallen out of his wheelchair the past two evenings and seems to be getting increasingly agitated at night, he has been placed in soft Posey restraints in his wheelchair in the evening and in his bed at night. TABLE 23.2 Decisional Matrix for Restraint Use Low Magnitude of Harm High Magnitude of Harm Low Immediacy of Potential Harm No Restraints I No Restraints II High Immediacy of Potential Harm No Restraints III Possible Restraints IV

In this case, the immediacy is high but the magnitude of harm justifying restriction is

unclear. So, too, is whether any other intervention has been attempted or any accommo

dation made for adapting to the new facility. It must also be addressed whether the

restraints are being used as a substitution for staff monitoring, something Cope has

previously discussed as a significant ethical issue in restraint use. 74 The restraints, in this

case, might have been placed under the guise of beneficence (i.e., not wanting harm to

come to the patient), but the underlying motive actually might have been to address a

staffing or organizational need. That is, restraints might have been used as a cost-cutting

measure. 74 A decision based on this rationale clearly is not beneficent. It should also be

noted that hospital behavioral restraint standards (i.e., restraints applied for any reason

other than medical healing) require clinical review every 15 minutes, which may prove

more time consuming than simply monitoring the patient. 81

Determining the type of intervention for unsafe behavior requires a thorough under

standing of the antecedents and consequences of that behavior (e.g., what triggers and

sustains the behavior). This type of understanding may allow the team to then address

specific factors contributing to the problematic behavior without restraints, or in combi

nation with decreased restraint use. Lodge describes a multimodal approach with an

individual with a large left frontal contusion and history of previous TBI and alcohol

abuse. 25 The patient’s severe agitation endangered the staff and himself. Although both

pharmacological and physical restraints were initially used, the team developed a system

in which they charted the antecedents, behavior, and consequences, which then allowed

them to design a program of behavioral management, interpersonal interaction, education,

and controlled activity that resulted in decreased need for restraints. 75 This case highlights

the point that, unless the provider is in imminent and severe danger, he or she cannot

make an ethically reasonable decision regarding restraint use without determining

whether potentially modifiable precipitants exist. Similarly, restraints, once implemented,

require appropriate monitoring to determine efficacy supporting continued paternalistic

use. The importance of monitoring and determining mitigating factors, such as agitation

and confusion, are included in the 2002 CARF facility standards. 4 Excessive use of

restraints potentially violates the bioethical principle of nonmaleficence.

Nonmaleficence

The bioethical principle of nonmaleficence, or “do no harm,” is applicable to at least four

circumstances related to traumatic brain injury — coma, persistent vegetative state, min

imally responsive state, and the competent individual who believes his or her quality of

life has diminished to a point that life is not worth living. The concept of nonmaleficence

generally has been developed in consideration of all but the individual in a minimally

responsive state (MRS), perhaps the most challenging in TBI rehabilitation from an ethical

point of view. After briefly reviewing the general concept of nonmaleficence, we will

provide comments on the person who is minimally responsive.

The Concept of Harm and the Right to Refuse Treatment

Nonmaleficence is sometimes considered on a continuum with beneficence: do no harm,

prevent harm, remove harm, and facilitate good. To harm someone means to negatively

impact another’s significant interests such that he or she is disadvantaged in some way.

Beauchamp and Childress suggest the following general rules are supported by non

maleficence:

- Do not kill.
- Do not cause pain or suffering.
- Do not incapacitate.
- Do not cause offense.

- Do not deprive others of the goods in life. 12

In rehabilitation, just as in acute medical practice, it can be challenging to stipulate

guidelines regarding the level of responsibility the provider has to lower and avoid risk

of harm to the patient. Legally, health care providers can be found negligent if they have

or had a duty to a patient and, as a result of a breach of that duty, the patient is harmed.

Health care providers are not necessarily negligent if someone has been harmed as a result

of reasonable standards of care.

Much of the literature and case law regarding nonmaleficence has been based on

withholding or ceasing treatment in individuals with a terminal illness or those in a

persistent vegetative state (PVS) in which the patient has lost cortical but not all brain

stem function (i.e., awake but unaware). While the United States Supreme Court has not

directly sanctioned physician-assisted suicide (i.e., provider gives patients the means to

end their lives), it has clearly upheld the individual's right to terminate life-sustaining

measures. The Quinlan case established a legal precedent for proxy decision making and,

in the Cruzan case, Justice O'Connor implied that there does exist a constitutional right

to proxy to protect one's liberty to refuse treatment. 82,83 Therefore, either through the due

process clause of the Fourteenth Amendment (i.e., protected liberty) or the patient's

general right to refuse treatment, the courts have

generally supported a patient’s request

to terminate life support if the surrogate adequately demonstrated that the decision

reflected the patient’s wishes. Although the State’s interest in individual rights is in

preserving life, the State’s position weakens as the burdens begin to outweigh the benefits.

In the case of a competent person, the courts have become consistent in recognizing the

person’s right to end his or her own life. 84 The Patient Self-Determination Act of 1990 also

was established to protect a person’s right to refuse treatment. This act requires health

care facilities to inform patients in writing about their right to refuse treatment and to

provide advanced directives. 85

Surrogate Decision Making

Surrogate decision making, while theoretically designed to protect the patient’s wishes,

can be problematic. Surrogates are individuals who make health care decisions on behalf

of the patient when he or she is incapacitated. Most states have prioritized surrogacy

authority, to be applied when the patient has not designated a surrogate. A common

hierarchy is: guardian, spouse, adult child, parent, and sibling. The surrogate is responsible

for both protecting the patient’s welfare and representing the patient’s expressed wishes

regarding health care. There are two commonly applied standards in proxy decision

making: substituted judgment and best interests. In the case of substituted judgment, the

surrogate’s responsibility is to honor the patient’s previously expressed wishes or prefer

ences. The best interests standard is applied when the patient’s wishes are unknown. Key

difficulties with substituted judgment include that the surrogate may: (1) extrapolate too

far beyond what the patient expressed, (2) misunderstand and, thus, misrepresent what

the patient meant, or (3) impose or confuse their own values with the patient’s. Although

living wills can sometimes be brought to bear, they are often too general or ambiguous

to be helpful. 86 Dresser and Robertson provide excellent commentary on additional con

cerns about substituted judgment. 87

Application of the best interests standard is also problematic. The surrogate is supposed

to make a decision based on what a reasonable person would want in order to maximize

quality of life, maintain current function, and relieve suffering. Like group statistical data,

the best interests standard does not necessarily fit at the level of the individual. In addition,

there may be biases at work such as devaluing a person with a disability that create

misinterpretations when determining potential quality of life and predicting the future

value of life (e.g., burden/cost of care, etc.). Although not specific to TBI, some research

has shown that almost one-third of surrogates do not necessarily know or represent what

patients would want. 82,88

Minimally Responsive State (MRS)

Making informed decisions as a surrogate can be particularly complex when the patient

is minimally conscious — that is, not considered competent but has some capacity for

meaningful, simple response and may be making gradual gains (although patients can

plateau in a MRS). Patients who are minimally responsive can be confused with patients

in a vegetative state because of the presence of reflexive responding, eye opening, and

lack of complex behavior. It is imperative that the rehabilitation team repeatedly evaluate

patients who are minimally responsive to determine consistency of response and to assist

with diagnosis, and thus, surrogate-based decisions, especially those as grave as termi

nation of life-sustaining measures. Whyte 89 offers concrete recommendations for assess

ment, and Canedo et al. 90 offer a critical review of popular assessment tools. They suggest

clinical findings may be underrepresented, which could contribute to inappropriate ter

mination of treatment. The role of the rehabilitation professional in educating families of

patients who are minimally responsive cannot be overstated. Even professionals some

times confuse the meaning of patient responses (both positive and negative) at this level

of function. Clearly, families with no previous experience with TBI can be confused and

overwhelmed. Family reactions can range from grandiose expectations (e.g., my loved

one will awaken) to a loss of hope and misrepresentation of factors contributing to the

patient's presentation (e.g., my loved one is deeply depressed as a result of injury). 89

Whyte recommends moving from general to specific issues regarding the brain injury

when educating families. In addition, the rehabilitation team should consider sharing

data used to monitor the patient's responsiveness, which may assist families in assimi

lating what is happening. In essence, final decisions regarding continuation of rehabili

tation to stimulate increased consciousness often rest not with the rehabilitation team but

with the surrogate and, potentially, the legal system, particularly when family conflict

exists regarding whether to terminate care. We do believe, however, that the rehabilitation

team has an ethical duty to attempt to clearly diagnose and monitor patient responding,

ensure the surrogate is well informed and that barriers to understanding have been

identified and minimized or removed, that clear documentation regarding treatment

decisions and education is completed, and that support for consensual decision making

among family members is provided.

The difficulty of appropriate decision making is highlighted by the legal case of Michael

Martin, who was minimally responsive after sustaining a severe TBI. The Michigan

Supreme Court overruled the lower court's decision to honor the patient's wish to die if

he were a “vegetable,” which the patient’s wife contended Mr. Martin had repeatedly

expressed to her premorbidly, but which Mr. Martin’s parent and sibling challenged. As

discussed by Banja, the court indicated the evidence regarding Mr. Martin’s wishes was

not specific enough to apply to his situation. 91 It is our contention that the interest in

preserving life generally outweighs the interest in relieving burden if the patient has

ambiguous or no advanced directives, is making progress, and may reach a point when

participation in the decision becomes possible. The difference between PVS and MRS is

significant in weighing legal decisions based on the presumption of permanent loss of

function and, thus, no reasonable chance for improved quality of life. It seems that a

reasonable time period should be allowed to assess whether the patient has plateaued in

the minimally responsive state or exhibits further recovery impacting quality of life. This

position, of course, reflects our own value, which is deeply embedded in rehabilitation.

That is, the patient, if capable of deciding, would want to continue rehabilitation if progress

is being made. However, if the patient stopped making gains, then quality of life issues

might justify termination of artificial nutrition and hydration. Childs and Cranford offer

a compelling dialogue reflecting contrasting views on quality-of-life and termination of

life-sustaining measures for patients who are minimally responsive. 92 Unfortunately, we

have yet to determine what is reasonable, beyond which family burden and patient's

quality of life take precedence. For people in a vegetative state as a result of trauma, one

set of authors suggested the person's status becomes permanent after 1 year. They indi

cated that one third of patients in a vegetative state at 3 months postinjury will show

some improvement by 1 year and only 20% of these patients will be severely disabled. 93

Other research is exploring ways to predict early emergence from a vegetative state. 94 We

would anticipate the data for MRS would be stronger and, thus, might suggest life-ending

decisions could be deferred within a timeframe of less than 1 year. However, we really

do not have the data to decide, and even if we did, determining quality of life and when

it is appropriate to usurp the surrogate's authority remain very thorny issues. If we chose

to deny the surrogate's representation of the patient's wishes to terminate life-extending

measures, then who bears the cost?

This leads to the final bioethical principle: justice. There is no small challenge in pre

senting issues related to justice in a manner that spans varied domains of clinical appli

cation. Therefore, we will begin with a discussion of broad theories and social policy

issues and end at the level of the treatment interface and the individual rehabilitation

professional.

Justice There is neither a social consensus nor a paramount theory of justice at the present time, so we should expect public policies to oscillate … 1

Introduction to the Concept of Justice

Beauchamp and Walters remind us that, in the United States, there is no constitutional

right to health care. 1 However, if such a right were to be recognized by society, it would

presumably be based upon the principle of justice, rather than on charity, compassion, or

benevolence. The utilitarian perspective argues that the principle of utility (usefulness)

must define the validity of a right to health care. Egalitarians attempt to derive the right

from a principle of equality (fair and equal opportunity). In contrast, libertarians deny any

welfare rights, including a right to health care. Each of these positions will be addressed

later, but suffice it to say that the issue of the citizenry being deserving of some adequate

minimum of health care is hotly debated.

Gaining some sense of the meaning of varying concepts of justice is therefore necessary

before we can arrive at our goal of applying this principle to the practice of rehabilitation.

Bersoff defines justice in terms of the professional's "obligation to treat equitably those

whom they serve and, perhaps, the superordinate responsibility to respect the worth and

dignity of each individual." 95 Upton writes that justice is a matter of people receiving

what is due them, the rectification of previous acts of injustice, and the fair distribution

of goods. 96 Similarly, Beauchamp and Walters conceive of justice as an obligation to give

persons what they are owed, what they deserve, or what they can legitimately claim. 1

Beauchamp and Childress state that justice is interrelated with principles like nonmalef

icence and beneficence. 12 They also state that concepts like fairness and entitlement have

been used to explicate justice — fair, equitable, and appropriate treatment in light of what

is due or owed to an individual. This, in turn, relates to the idea of distributive justice which

encompasses the allotment of diverse benefits and burdens (e.g., property, taxes, resources,

privileges and opportunities, etc.) and is determined by justified norms that structure the

terms of social cooperation.

For example, consider current government-funded health care systems established to

assist certain classes (i.e., elderly, poor, armed service veterans). Justice demands that

services be available and allotted fairly to all members of those classes. However, such

systems unjustly deny access to equally needy people outside the identified classes (e.g.,

persons with brain injuries, spinal cord injuries, workers without health insurance, etc.).

In order to control for such conflicts, justice should be motivated by need; without an

identified need, persons will be harmed or at least detrimentally affected. Assuming a

need has been identified, distributive justice is then validated by the following principles:

- To each person an equal share
- To each person according to need
- To each person according to effort
- To each person according to contribution
- To each person according to merit
- To each person according to free-market exchanges 12

The challenge created by these potentially conflicting principles is to achieve balance

when making decisions. However, tradition, convention, moral and legal principles, and

public policy all impact such decisions, rarely making the process easy. 15,97

Theories of Justice

Several theories of justice are worth consideration in light of the absence of a single

consensual construct. They are: Utilitarianism, Libertarianism, Communitarianism, and Egal

itarianism. Each serves to broaden the parameters of our understanding. Utilitarianism

embodies the idea that the standard of justice is evaluated against the concept of utility.

Utility is the maximization of the overall social good. This theory is based on the philos

ophies of Jeremy Bentham and John Stuart Mill, where justice represents the most stringent

form of utility. Any rights conferred upon the individual are contingent upon social

arrangements that establish enforceable rights and that maximize the net social utility

(usefulness), the meaning of which is ever changing. Proponents of this theory have been

criticized for lack of sufficient attention to the distribution of benefits and burdens inde

pendent of aggregate welfare, the result of which is inequitable distribution (e.g., denying

access to the sickest and most vulnerable populations).

Libertarianism, associated with the writings of Robert Nozick, holds that a just society

protects the rights of property and liberty, allowing people to improve their circumstances

and protect their health based on their own initiative, free of morally prohibited and

coercive taxation. 99 Justice is linked to procedures rather than outcome; therefore, no

individual entitlement to health care exists. There are only three procedural principles:

acquisition of property, transfer of property, and rectification of an injustice. Libertarians

do not object to utilitarian patterns of distributing health care resources as long as the

distribution system is freely chosen by its participants. This theory supports privatization

models of health care access.

The theory of Communitarianism, espoused by E. Emanuel, states that what is due

individuals and groups depends upon pluralistic community-derived standards. 100,101

Responsibility of the individual and the community is bidirectional. Justice is often sub

ordinate to solidarity of the individual within the community. Therefore, the health care system

needs to benefit both the individual and the community. This theory could envision

thousands of community health programs of citizen-members

who join in small federa

tions, with participation vouchers and consensually-defined benefits.

Egalitarianism, commonly linked to J. Rawls and Norman Daniels, supports equal dis

tribution of certain goods like health care, but this distribution does not extend to all

possible social benefits. 102-104 Justice is not inherited. It is based in freedom inherent in

secular moral communities and in securing consent of community participants. A foun

dation principle within Egalitarianism is “fair equality of opportunity” — that is, everyone

should have equal opportunity to pursue the range of life plans they could reasonably

hope to accomplish given their talents and skills. Society’s obligation, therefore, is to

reduce or eliminate barriers to opportunity. In this system of thought, disease and disabil

ity are undeserved restrictions on opportunities to realize basic goals. The implication for

health care is that patients have equal access to adequate, but not maximal, level of care.

The level of access depends on available social resources and the public process of decision

making. Egalitarianism leaves open the option for citizens to privately purchase more

comprehensive levels of care.

Several other interesting concepts and challenges linked to varying theories of justice

demonstrate the complexities involved in developing a just health care system. As an

example, consider Englehardt’s natural lottery and social

lottery. 105 The natural lottery

assumes that all people are exposed to the vicissitudes of nature. Some individuals are

born healthy and live full lives free of disease and suffering. Others are born with con

genital or genetic diseases or disabilities, or are injured. As a result, some individuals die

early in life. The natural lottery creates inequalities and disadvantages with no straight

forward secular moral obligation to aid those in need of health care services.

The social lottery is more complex because some individuals prosper and others languish

(good and bad fortune). Some individuals toil, delay gratification, accumulate wealth, and

leave inheritances — thereby, their resources are conveyed to another. Conversely, through

malevolent actions of others, some citizens will be disadvantaged. A benevolent state tries

to protect, force restitution, or charitably assist those who are disadvantaged. However,

restitution is owed by the injurer, not society. Any redistribution of personal resources to

provide care for those injured by others would require strong societal buy-in regarding

fairness. Englehardt relies upon the principle of permission (consent) regarding decisions

affecting the distribution of resources. He contends that health care policy is a challenge

for the egalitarian because of the dramatic character of the inequalities it faces (natural

and social lotteries). His maxim regarding just health care allocation is: “Give to those

who need or desire health care that which they, you, or others are willing to pay for or

provide gratis." 105

Several authors have explored the right to a "decent minimum or adequate level of

care" to allow access to fundamental health care resources. 12,45,103,104 Equitable access can

be accomplished through a two-tiered system of health care in which a public-funded sector

affords universal basic services, while a voluntary private sector provides for other needs

and desires. This position presents a compromise for all four theoretical positions regard

ing justice and the allocation of health resources. However, a question arises regarding

forfeiting the right to health care by engaging in risk-taking behavior (e.g., tobacco use,

unprotected sex, etc.). This question could be addressed by assessing a risk-penalty to

insurance. However, keeping healthy individuals healthy longer actually costs more than

covering services of risk-takers who are more likely to suffer an early death.

Resource Allocation

No discussion of health care resources could occur without reference to allocation strate

gies. For our purposes, rationing (allowance, allotment) is considered a form of allocation

based on externally determined priorities. To the extent that these priorities reflect equi

table distribution and the ability to pay for additional goods, such an allocation rationale

is justifiable. Englehardt considers two classes of

allocation: macroallocation, which encom

passes funds expended, goods made available, and distribution scheme, and microalloca

tion, which refers to who will receive particular scarce resources. 105 Decisions need to be

made at both the policy (macroallocation) and implementation (microallocation) levels

before a workable health care system can meet society's needs.

Daniels puts the concept of allocation and system design to a test of reason by posing

critical questions:

- What kinds of health care will exist in a given society?
- Who will receive services, and on what basis?
- Who will deliver those services?
- How will the burdens of financing them be distributed?
- How will the power and control of those services be distributed? 103,104

The answers to these questions are fundamental to the process of devising a realistic

health care system. In addition, they demand knowledge of existing service delivery

resources, the will of the populace, funding alternatives, and, importantly, limitations in

each of these domains.

Beauchamp and Childress contend that critical knowledge regarding allocation can be

obtained by attending to several concepts. 12 The first is the Social Budget. Expenditures on

valid goods, like education, defense, housing, and health care, imply competition for limited

resources. Moral decisions regarding what to pay for necessarily reflect the values, prefer

ences, and priorities of the entire society. Health resources within the Health Budget (i.e.,

occupational safety, prevention, environmental protection, consumer protection, food/drug

control) are more than medical resources. Therefore, equitable access to medical care is not

the most effective strategy for balancing opportunities for health. Finally, the Health Care

Budget must address society's priorities, particularly prevention vs. treatment. Statistics can

be used to argue rather convincingly that prevention is more cost-effective than treatment,

especially in rescue situations, e.g., organ transplantation and TBI survival. 12

Are "killer" diseases like cancer more fundable than widespread crippling diseases like

arthritis that affect more people? This kind of question illustrates society's traditional bias

toward saving identified lives and the personal relationship we expect with our health

care providers, rather than funding impersonal statistical gains by prevention. Indeed, the

tool of cost-effectiveness analysis, routinely employed by health care economists, is now

criticized as being too limited in scope. More attention to societal values is urged in

developing new metrics of health care outcomes. 106 However, at the treatment interface,

where managed care organization (MCO) allocation rules often come into play, Orentlicher

and others warn of the dangers inherent in bedside allocation to the individual

patient. 107–109 There are obviously contentious global issues to be resolved that are beyond

the scope of this chapter.

On the national scene, the Oregon Health Plan represents a pioneering approach to

actively managing health care provision and public financial resources. 12 The plan has

prioritized allocation of Medicaid-administered health insurance coverage to uninsured

state residents below the poverty line. Legislated in 1989 and implemented in 1994, the

plan is based upon the principle of a decent minimum of health care. Judgments about

priority rankings of authorized treatments were initially based on data about quality of

well-being after treatment and cost-effectiveness analysis (CEA). Then, the CEA was

abandoned in favor of citizens' values obtained via community meetings. The finalized

list of 709 ranked treatments was based on clinical effectiveness of the treatments and social

value. Care was initially extended to all persons eligible for Medicaid. Cost overruns caused

"means tests" to be employed to cull the roster. While access to services was expanded,

some moderately incapacitating procedures fell below the cut-off for coverage on the

priority list. The critical question has become: How high can the cut-off be set and still

qualify as meeting decent minimum standards? Additionally, the plan has experienced

consistent budget shortfalls. Nonetheless, the experience in Oregon has spurred furious

national debate about methodologies for setting priorities. No one theoretical camp has

succeeded in dominating these discussions.

We now return to our original position, that of opportunity. When will a visionary

federal government craft a viable, equitable health care system that adequately reflects

society's needs while protecting limited resources? The societal pressures over the next 2

decades will demand a response, and as we have highlighted above, policy options are

being considered. But what about rehabilitation, with its high cost, lengthy course of

treatment, need for ongoing support services in perpetuity, and outcomes often measured

in terms of abstract concepts like well-being and quality of life? The next section of this

chapter focuses on the principle of justice within the domain of rehabilitation.

Justice Applied to Rehabilitation

Costly health care services like rehabilitation represent a fly in the ointment of economi

cally-driven notions of health care like Managed Care. Managed Care clearly prioritizes

cost containment. This kind of approach most effectively focuses upon the extremes of

the health care continuum — reinforcing efficacious prevention, early treatment and cure,

and avoiding or limiting injudicious end-of-life treatment.[110,111] In those arenas, MCOs

have engineered significant changes that have boosted health care efficiency. However,

rehabilitation rests squarely in the middle of the continuum, neither offering cure nor

accepting death as an outcome. Instead, we facilitate the natural course of healing and

offer remediative or compensatory strategies, a process that is often subtotal. Sometimes,

the need for rehabilitative services spans an individual's lifetime. It is not surprising that

the implementation of the Prospective Payment System (PPS) was delayed for rehabilita

tion until early 2002, given its unique position within the health care continuum.

The economics of chronic rehabilitative care represent a complex burden upon the

nation's limited health care and financial resources. Indeed, the "business" of health care

is fraught with gain/profit-maximizing strategies that do not appropriately fit conditions

of finite resource access. In a 1997 study, Chan et al. demonstrated that recently opened

for-profit rehabilitation hospitals adopted these kinds of business approaches in response

to Medicare's newly implemented cost containment regulations. 112 In that study, the hos

pitals manipulated their lengths of stay and case-mix to optimize reimbursement. In a

follow-up study, Chan and Ciol analyzed their data with a focus on changes in discharge

disposition in response to the altered Medicare rules. 113 They found a significant increase

in rehabilitation hospitals' patient discharge rates to skilled nursing facilities (SNF) after

the rule changes. They linked this increase to financial incentives to maximize reimburse

ment available within the new Medicare rules. The authors cautioned the Health Care

Finance Administration about the unintended effects of economic incentives on the dis

charge planning process. Malec's research-based assertion that "beliefs will determine

behavior" describes the business arena into which rehabilitation has reluctantly

emerged. 114 If economic contingencies prevail in determining the "image" of rehabilitation,

the service organizations will adapt to those rules, behaving predictably within that

context. The superordinate ethical principle of dignity and respect for the individual with

a disability will be diminished within such a system of care. 115 Can we morally afford to

move away from patient-centered rehabilitative care?

Despite cogent arguments put forth by DeJong and Batavia in 1989 supporting a duty

to allocate health care resources to those individuals with TBI, the response of the state

run health care systems has been slow to evolve in that direction. 116 Reynolds et al. have

called for national guidelines for allocating resources to serve individuals with TBI. 115 They

caution that, without overarching guidelines, service onset is often delayed, greatly

increasing care costs. In states that have created agencies to assist with case management

and payer-of-last-resort funding of TBI services, both funding sources and budgets are

limited. 117 Budget-necessitated restrictions on access have been imposed (i.e., qualifications

specify only traumatic brain injury, case load caps, and wait lists). The challenge facing

such state TBI agencies is complicated by the breadth of needs their clients have as they

return to the community and the social/institutional barriers that make satisfying those

needs difficult. 118 Nonetheless, in the absence of national guidelines, state agencies have

formed a national organization (National Association of State Head Injury Administrators

[NASHIA]) to assist with program development across all interested states. It is hoped

that this organization can spearhead a national consensus regarding equitable service

delivery to special populations.

Thus, broad issues exist pertaining to justice in rehabilitation. These issues focus upon

the development of service delivery programs representing societal values, equitable

service allotment, and evaluation of treatment efficacy via outcomes. These issues were

outlined by Banja in 1994 and remain pertinent today. 119 The call for outcomes research

in rehabilitation has been loud and clear, yet the complexity of evaluating objective and

measurable consequences of neurorehabilitation in the contexts of the individual, com

munity, and state and national environments is daunting. As data from large multicenter

studies, such as the National Institute for Disability and Rehabilitation Research “Model

Systems,” are aggregated and melded with moral questions posed by ethicists, perhaps

the design of a validated and justified system of rehabilitative care will emerge within a

larger national health care scheme. 1,12,103,105 In any event, we must now turn from the

sometimes dizzying panorama of the national health scene to our daily professional lives

in rehabilitation.

Tarvydas and Cottone proposed a four-level concept for the application of ethical prin

ciples in the clinical environment of rehabilitation. 52 These levels include: policy, organiza

tion/facility, the rehabilitation team, and the individual practitioner. We will now apply the

principle of justice to these levels to demonstrate how ethical decision making spans the

spectrum, literally impacting all aspects of the daily commerce of rehabilitation.

The Level of Policy

A study conducted by the United States General Accounting Office (GAO) concluded that

difficulties in obtaining appropriate services experienced by individuals with brain injuries

related to two factors: lack of physical (visible) deformity or disability, and lack of an

effective advocacy system to procure resources. 120 Indeed, costly rehabilitation services for

individuals with cognitive impairment are considered by some to be a luxury. 121 Conse

quently, funding priorities are often geared toward disabling conditions with more obvious

disabilities. Federal and state resource utilization policy needs to reflect the outcome of

public debate on issues pertinent to brain injury, as urged by the fair opportunity rule. 122

Further, extending such a public debate to address the shoring-up of support infrastructure

required for quality care in chronic conditions is encouraged. Specifically, the needs of

family caregivers and community support agencies targeting behavioral impairment have

been emphasized. 80,68

Finally, Cervilli and Banja have argued for a revamping of the relationship between

rehabilitation service providers and health insurance companies. 123 This redefined rela

tionship attempts to circumvent sometimes contentious interactions between clinicians

and insurance case managers by emphasizing veracity (appropriate information sharing)

and fidelity (fulfilling obligations in good faith) as underpinning consumer contracts. While

we, as rehabilitation professionals, believe that our services are essential for the health

and well-being of our patients, we are morally required to demonstrate the efficacy of our

services before public resources can be justly expended. As rehabilitation outcome data

(including elements of both functional performance and patient satisfaction) begin to

consistently drive efficacy-based program development, we will provide the grounds upon

which health care policy discussions can move forward in addressing the myriad needs

of individuals with cognitive, physical, and emotional disabilities.

The Level of the Organization/Facility

It is at the level of the rehabilitation organization or facility that national and state policies

are implemented. While accrediting bodies like CARF and JCAHO heavily influence the

breadth of policy development in rehabilitation institutions, the dynamic process does not

stop there. A subtle feedback loop exists. These accrediting bodies constantly look for new

opportunities to strengthen the delivery of health and rehabilitation services. A prime

source of innovation in this evolutionary process is the field of clinical practice. “Best

Practices,” as identified by public peer accolades, often form the basis for new rehabilita

tion accreditation initiatives in both CARF and JCAHO. These exemplars of effectiveness

and efficiency derive from the creative minds of rehabilitation professionals striving to

offer their consumers the highest quality services possible. Therefore, organizations and

facilities that embrace the creative process in offering their rehabilitation services will

ultimately benefit the general field of rehabilitation.

Taking a lead from this position, we suggest that resource allocation models might well

be developed and field-tested in vivo. 124 Gathering efficacy/outcome data can help fuel

and guide the national debate on the topic of allocation. Malec and Basford offer some

structure to this position in their encouragement for outcome studies to include economic

self-sufficiency and social integration into outcome

algorithms. 125 This emphasis focuses

upon important social values related to independence and solidarity within the community.

Along the lines of social values, our rehabilitation colleagues working in the United

Kingdom’s collective health care system are simultaneously calling for strengthening and

providing coordination of support systems for family caregivers, a need echoed in our

country. 64 This call is bolstered by the fact that families often serve as surrogate decision

makers for individuals with severe brain injury. 126 Indeed, systems of rehabilitation can

function as the proving grounds for innovative resource allocation schemes that directly

derive from their consumer constituency. This proactive approach places increased control

over the destiny of rehabilitation within the grasp of the service providers.

The Level of the Rehabilitation Team

The rehabilitation team is the operative entity delivering the multifaceted service termed

rehabilitation. At its best, the team functions seamlessly, coordinating disparate services

with ease and effectiveness. Collegial communication and partial submerging of profes

sional identities must be fostered and continually reinforced to support the process of

rehabilitation. This “fertilization” of team cohesiveness is not typically provided by indi

viduals external to the team. Instead, it emerges from the team itself, a self-propagating

force that strengthens when the team functions optimally.

To the extent that team members

commit to the team process, rehabilitation flourishes.

Ethical practice, therefore, emanates from the members of the team. Each member brings

her or his own practice code to the table, but the team itself, because of its unity of purpose,

also incorporates ethical principles into its everyday function. Autonomy is expressed in

the participation of the patient in the goal setting and achievement process. Care is dem

onstrated in the mission of the team — that of providing quality rehabilitation services

specifically designed to meet the patient’s needs. Beneficence serves as the raison d'etre of

collective treatment efforts. Justice focuses team interventions upon efficient delivery sys

tems and effective outcomes. Rehabilitation teams actively allocate a scarce health care

resource — professional time — whenever multiple patients are scheduled for treatment.

Intervention intensity is prioritized and equitably distributed according to need in order to

offer the broadest possible benefit to the most consumers in the time allotted. Since the

realization of the necessity for cost controls and the inception of managed care, the team

has had to adjust the most in accommodating the concept of a decent minimum of care. For

a profession that grew from the philosophical position of “more is better,” this has been

a bitter, but necessary, pill to swallow. It is in this values shift, spurred by emphasis on

outcomes research, that the team has moved farther from

society’s continuing belief that

more treatment equates to more recovery. Thus, an optimally functioning rehabilitation

team emulates a working model of an ethical health service delivery system.

However, the rehabilitation team must also divide its attention between the patient and

the family in order to optimize its effectiveness. Indeed, the preeminent role families play

in the rehabilitation process creates a unique set of responsibilities. We have already

discussed the necessary function of advocacy in securing adequate care resources for

individuals with brain injuries. Inpatient rehabilitation programs often serve as training

grounds for family members learning about effective advocacy. As consumers of rehabil

itation services, family members enjoy special credibility within the political system. In a

very real sense, consumers speak with a louder voice than health care providers when

policy matters are being considered. To the extent that teams foster acquisition of this

skill, the field of rehabilitation will benefit at the level of federal and state policy.

Caplan et al. have cogently cautioned that teams often relate with families paternalisti

cally. This criticism stems not from callous disregard for the family, but from the press of

time that influences all aspects of the team process. 7 Heavily involving families at all levels

of decision making is time-intensive and, on the surface, inefficient. Outpatient programs

have more opportunity to realize this optimal participative role for families because people

with TBI often reside with family members. Even more importantly, securing patient input

regarding who will serve as proxy helps to increase compliance with the proxy decisions. 127

This is only possible in some cases after sufficient recovery has occurred to allow such

To exclude families from the decision-making process regarding their loved one pro

vokes ethical criticism. This is especially true if the team recommends chronic care when

progress slows. Family members often perceive this kind of communication from the team

as abandonment. To the extent this kind of decision is perceived by family members as

denying hope, the necessary partnership between team and family is diminished. One

result of the family perceiving reduced decision-making control is that they may raise

ethical questions of justice, such as claims of inadequate care, financially motivated treat

ment decisions, and unilateral and paternalistic team dictums that do not respect family

wishes. 62 These are weighty issues that require active team discussion in order to preserve

optimal team function.

The Level of the Individual Rehabilitation Professional

We ultimately arrive at the final common pathway for applying ethics in everyday practice:

the rehabilitation professional. As we have noted above, each rehabilitation team member

commits to fostering the team process. However, this

commitment does not stem from a

position of dependency upon the team. Instead, it springs from two important sources —

the individual's training in ethical decision making, and disciplinary practice codes and

standards. Thomasma and Pisaneschi recognized several decades ago that lack of training

in ethics contributes to bias and prejudice that infects rehabilitation decisions. 128 In other

work, we have recommended an ethics training model for professional students. 129 Most

state health care professional boards have included testing regarding ethics as part of the

criteria for licensure, but ethical practice requires lifelong commitment to continuing

education. It is the professional's responsibility to engage in the evolving ethics debate

and to determine its applications to clinical practice. Fortunately, as the addition of this

chapter to the second edition of this text indicates, ethics has appeared on the radar screens

of rehabilitation professionals and is not likely to diminish in intensity.

Equitable treatment of individuals with cognitive impairments requires information

process sometimes makes communication of that critical information difficult, if not

impossible, as previously discussed. Blanket assumptions about decisional capacity in the

circumstance of cognitive impairment have given way to methodologies for detailed

investigations of that capacity. 39 However, even though the components necessary to give

informed consent or assent are well documented, clinical research continues to discover

inadequate assessment and documentation of this capacity.[49] Taking the time to be thor

ough, a virtue of the health care professional in the past, appears to detract from produc

tivity demanded in our current staffing models.[108] Nonetheless, we can base our treatment

expectations on ethical principles to self-diagnose shortcomings in our delivery system as

we explore new ways to provide efficient service. It is this dialectic process that validates

active, daily use of ethical principles in our practice of rehabilitation.

The issue of treatment efficacy remains to be discussed. Rehabilitation professionals rely

upon an armamentarium of quality services that are both efficient in application and effective

in outcome. These services produce objective and measurable improvements in our con

sumers. The act of employing efficacious treatments represents an application of the ethical

principles of care, beneficence, and justice. Yet, as Malec has eloquently argued,[114] treatment

efficacy can be a thorny problem with personal values and beliefs influencing our profes

sional judgment. Do we assess efficacy in the testimony of consumers or other profession

als? Do we value a particular treatment because it meets the emotional needs of our patients,

even though its performance-enhancing effectiveness is scientifically unproven? Do we

accept a treatment as valid on the basis of one scientific study with positive results or must

we await replication? Indeed, the literature in rehabilitation has evolved along disparate

pathways, ranging from testimonials through single-case observational studies to controlled,

double-blind group research. Each of the rehabilitation disciplines trains students in aca

demic programs that vary significantly in scientific and clinical emphases. Malec's article

about personal values and beliefs brings us back to the issue of assessing efficacy with

increased awareness of potential biases we may bring to decision making.

The example of cognitive rehabilitation illustrates the evolution that has occurred in our

maturing field. Research in the late 1980s and early 1990s focused upon specific compo

nents of the complex domains we attempt to address during cognitive rehabilitation.

Matthews and colleagues discovered that there was no demonstrable efficacy in treating

memory when primary neural circuits responsible for memory were destroyed. 130

Schachter and Glisky found that domain-specific learning and recall remediation could

be carried out despite severe, but subtotal, neural destruction. 131 This work supported

Goldstein's contention that partially functional neural structures could utilize compensa

tory strategies to perform tasks. 132 This domain-specific approach to cognitive rehabilita

tion was expanded by other researchers to include attentional training, increasing speed

of processing, and enhancing visuospatial abilities. 133–135

However, it was not until the mid to late 1990s, when Cicerone et al. critically reviewed this

growing literature, that a validating methodology for assessing efficacy was published. 136,137

His group applied existing criteria of scientific rigor in research design to the cognitive

rehabilitation research literature and used these criteria to make judgments about treatment

efficacy. The findings were both exciting and sobering. For example, the use of cognitive

rehabilitation procedures in strengthening visuospatial and attentional skill sets passed the

most rigorous scientific scrutiny whereas other approaches fell short of this most desirable

form of efficacy validation. Importantly, recommendations were made to strengthen the

design of outcome studies that would allow additional results to be evaluated under these

stringent criteria, thereby fostering development of more robust rehabilitation treatments.

The individual rehabilitation practitioner has the responsibility, under the principle of

justice, to equitably employ the most valid and reliable methods of therapeutic intervention

available. Fortunately, the field of rehabilitation has advanced to a point where a cadre of

rehabilitation researchers, supported by federal and private foundation grant funds, is

beginning to utilize research tools to provide the practitioner with high-confidence applied

clinical information (e.g., NIDRR-funded TBI Model Systems Program). That information

can then be used at the level of the treatment interface.

The final step in validation comes

when outcome data collected in various rehabilitation programs are evaluated, and this

feedback provided to the researchers, who incorporate it into new research designs, com

pleting the feedback loop.

Conclusions

It is our hope that this chapter has provided information that will enable the application

of ethical principles to both the national debate on health care and to the everyday practice

of rehabilitation. Of course, many issues were left uncovered such as the use of parapro

fessionals in clinical practice and ethical issues in research. The issues that were presented

clearly continue to be part of the national ethics debate on what is fair, equitable, and

respectful in the delivery of rehabilitation services. While it can be tempting to gloss over

ethical principles as being abstractions too removed from practice to be meaningful or to

think of ethical principles simply in terms of discipline codes requiring adherence to

prevent sanction, we must not miss the opportunity to use ethical principles for their

aspirational and practical value in guiding our daily actions as rehabilitation profession

als. 138 Ethics, utilized in creating aspirational, organizational, and professional goals, in

providing a foundation for advocacy in policy development, and in guiding clinical

decision making, promote moral outcomes in our efforts to assist those with TBI. Ethics

help us highlight the nobility of our health care profession and to effectively contribute

to evolving rehabilitation practice. We hope this chapter represents a small contribution

in that evolution.

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24

Discharge Planning in Traumatic Brain Injury Rehabilitation

Mark J. Ashley and Susan M. Ashley

CONTENTS

Introduction

The process of discharge planning varies with the setting in which it is undertaken, the

amount of information that is available to the discharge planner, and resources that may

be available for ongoing care for the individual. Since 1990, the overall length of stay

(LOS) for acute hospitalization and for hospital-based rehabilitation has decreased mark

edly for persons with traumatic brain injury (TBI). 1,2 Overall, hospitalization rates for TBI

had decreased by 50% from 1993 to 1996. Kreutzer et al. reported acute care LOS averaged

between 22 to 29 days between 1990 and 1994, and decreased to less than 20 days in 1995,

and an average of 16 days in 1996. Average LOS for acute rehabilitation hospitalization

decreased from 47.74 days in 1990 to 29.49 days in 1996. The authors attribute these

changes to concurrently occurring changes in overall delivery of medical services resulting

from the impact of managed care. It seems reasonable, nonetheless, to conclude that earlier

discharges from shorter LOS are likely to complicate the discharge planner’s job.

It is difficult to approach the subject of discharge planning with a single view due to

the different levels of treatment from which discharge planning must occur, that is, acute

hospitalization, hospital-based rehabilitation, or various postacute rehabilitation settings.

The purpose of this chapter is twofold: to offer a broadened view of discharge planning

that extends years beyond injury and to provide insights into the nature of the long-term

problems encountered, with methods of addressing those problems.

All too often, discharge planning looks at the immediate discharge environment follow

ing a treatment setting. While this is quite important, such an approach does not tend to

prepare the person or the caregivers for the longer term. Additionally, the medical model

tends to focus upon medical issues, with less attention paid to issues of life satisfaction. 3

Regardless of the level of disability following injury and the cessation of treatment, life

satisfaction for the injured person and the caregivers should be a major consideration of

any assessment of outcome. Ultimately, the degree to which sequelae of TBI are resolved

during rehabilitation will bear substantially on level of life satisfaction achieved by the

injured person.

Since relatively little attention is paid to the arena of life satisfaction in discharge

planning, many of the issues in this chapter will bear directly or indirectly on this topic.

People survive traumatic brain injury. The question ought to be how well they and their

caregivers survive the immense trauma inflicted by the injury itself and the absolute

upheaval of life that often follows. To that end, discharge planners should work to identify

not only the next immediate care or treatment setting, but they should also work with

their treatment team and community resources to pull together educational materials and

resources that will address the issues that follow in this chapter. The intent should be to

address both the immediate and long-term needs of persons with traumatic brain injury

and their caregivers.

As the field of TBI rehabilitation has matured over the last 25 years, it has become

increasingly possible to consider new aspects of outcome. Outcome has traditionally

encompassed self-care skills, independent living skills, and return to work. As will be

demonstrated, the importance of vocational skills cannot be overstated, though there is

no dependable nor reliable means of securing well-designed vocational rehabilitation

services for persons who have sustained traumatic brain injury. 4,5

Most discharges from treatment occur as events planned and agreed-upon among all

parties. A special circumstance is encountered, however, when an individual with TBI

makes a choice to stop treatment in a manner that is often referred to as against medical

advice. In these instances, many ethical questions arise that must be addressed by the

treatment team, the discharge planner, and caregivers. 6 The treatment team and caregivers

may face the decision of recommending competency hearings in order to attempt to

continue to provide recommended treatment. Simply put, a person’s refusal to willingly

follow treatment advice cannot become a reason to proceed to discharge. Banja et al. submit

that clinicians have an ethical responsibility to attempt to convince people of the need for

continued treatment in language they can comprehend and may also have a responsibility

to recommend competency proceedings. Should competency proceedings be undertaken,

it is incumbent upon the treatment team to provide clear, objective, and convincing

evidence that relates to people’s ability to care for themselves, obtain and maintain

employment, know what to do in an emergency, and be aware of and practice safe sexual

precautions. Banja et al. point out that many people with TBI can present relatively well

to an adjudicator who is unfamiliar with brain injury. Thus, the treatment team must be

prepared with hard facts and objective data.

Discharge disposition may also be heavily influenced by the type of funding available

to the injured person. Chan et al. 7 reviewed 1,271 cases of moderate to severe TBI and the

frequency with which individuals were placed in skilled nursing facilities (SNFs) or reha

bilitation facilities. Those not included in the study were people with Medicare or self

insurance coverage, people who were discharged to home or transferred to another facility,

people who left against medical advice, and people who were incarcerated. It was clear

that people with Medicaid coverage were more likely to have been injured by assault and

had longer LOS. People with Medicaid coverage were much more likely to be discharged

to a SNF than to a rehabilitation setting. People with fee-for-service insurance coverage

had shorter acute LOS and were most likely to be transferred to rehabilitation settings.

People with HMO coverage had a higher percentage of referral to SNFs, though the

difference did not reach statistical significance. The implications for recovery of function

are not entirely clear for those people less likely to be transferred to a rehabilitation setting,

though research with a stroke population showed a clear advantage in outcome for those

people who received rehabilitative treatment. 8 Discharge disposition may also be impacted

by whether a Physical Medicine and Rehabilitation specialist has been involved in the case,

either for treatment or consultation. Wrigley 9 reviewed the discharge disposition for 756

people with TBI and found a significant difference in disposition related to the presence

or absence of the specialist. The study also showed direct and indirect injury severity

indicators, marital status, and age impacted likelihood of referral to rehabilitation settings.

The impact of age was such that older people were more likely to be referred.

Much of the discussion in this chapter will involve postdischarge caregivers, their needs,

concerns, and education. The ethical implications of relegating the care of a person with

TBI to what is, usually, a lay population without adequate financial, clinical, educational,

or other resource will not be a focus of this chapter. In fact, it is highly doubtful that one

could reasonably conclude that sufficient resource is allocated to people with TBI and

their caregivers in general. This chapter will approach the issues from the perspective of

what can be done within current limitations of the managed care environment.

Early Problem Identification during Follow-Up

The sequelae of TBI can be many and varied, with relatively little congruency between

any two injured persons. In fact, it is only with the perspective gained by rehabilitative

experience with large numbers of persons who have survived TBI that one gains a view

of the wide variety of these sequelae, successful and unsuccessful approaches to them,

and some commonalities that can be found in sub-groups of the whole population. Con

sequently, it is this experience that illustrates the importance of regularly scheduled follow

up contact with persons and their caregivers to identify problems before they become

complicated or develop into insurmountable obstacles requiring major changes in the

person’s life. Such follow-up should be conducted in the days and weeks immediately

following discharge and in the months and years that follow.

Job coaching, as an example, has come to be widely recognized as a successful means

of accomplishing return to work. 10–12 The job coach functions to train the individual, assure

that the assigned work is completed, identify barriers to success, and find requisite solu

tions for those identified barriers. The concept of early problem identification is equally

valid when applied to the broader picture of the person’s family, social, academic, and/

or vocational experience postdischarge. Properly educated caregivers can sometimes be

quite successful in setting up more effective discharge scenarios and maintaining them;

however, they must be able and willing to participate in the early identification of problem

areas and have access to resources for ideas on management of those problems. Ideally,

the discharge planner has been able to provide good educational preparation of relevant

potential barriers that specific caregivers might encounter for their family member, as well

as act as an ongoing resource for the person and caregiver. In fact, the entire rehabilitation

team can often be helpful in answering questions caregivers may encounter postdischarge.

The discharge planner can act as an interface to the team or facilitate more direct contact.

Measures such as educational lectures, resource centers, Web sites, educational materials,

continued consultation for ideas, and problem-solving following discharge can all con

tribute to the ongoing education of persons and their caregivers.

As problems develop postdischarge — and they do — they often proceed to develop

greater complications than necessary only because their significance is either not recog

nized early on, their cause or endpoint may not be recognized, or a reasonable solution

to the problem cannot be identified by the people involved. Discharge planning should

include the preparation of a Caregiver Manual (Appendix 24A) which seeks to address

the known areas of concern for an injured person, as well as the more likely long-term

complications that may be encountered, and methods for either avoiding those complica

tions or methods to address them when they occur. Likewise, consultation should be

conducted with postdischarge treaters to ensure that these individuals are properly briefed

on the specifics of the case, that adequate records have been transmitted, and that an

invitation for ongoing consultation by the discharging team has been offered. This accom

plishes both a continuity of care and treatment approach

and provides the postdischarge

treater(s) with some depth of experience that they, as individual treaters outside a com

prehensive rehabilitation milieu, may be lacking.

Avoiding Reinjury

The literature is fairly clear about the additive nature of injury to the brain seen with

repetitive traumas. 13 Likewise, the literature is clear regarding the susceptibility of persons

to reinjury following a first or second TBI. 14 As a hallmark of success of rehabilitation and

in a desire to increase overall life satisfaction, normalization of routine and activities is

generally viewed rather positively. Return to some aspects of life, however, may be con

traindicated following traumatic brain injury.

In general, the person’s desired social, vocational, and recreational pursuits must be

considered with regard to balancing the level of risk for reinjury with the need to be

productive and meaningfully engaged in life. There is no clear-cut, easy approach to

admonition regarding such matters. For example, it may or may not be advisable to limit

an individual’s use of a bicycle. While it is clear that such use should always be done with

a helmet, some persons will have visual field, vestibular, or other physical deficits which

make reinjury far more likely. Others may find that bicycle use is a sole method for

transportation to engage in other life activities. In many cases, the best that can be accom

plished is a careful review of the intended vocational and recreational activities for the

potential of reinjury. Subsequent identification of high risk activities should be made for

the person, the family, and the employer with a discussion of the risks and benefits of

engaging in each activity. Sexual activity, dating, job safety, and return to risky recreational

pursuits, such as motor-cross, skiing, or snowboarding, are only some examples of issues

that will arise over the longer term to be considered.

These discussions need to begin early in the rehabilitation process as they often represent

major shifts in activities from which life satisfaction derives. People often have some diffi

culty adjusting to the idea that their lives will be affected over the long term. 15–17 It is often

beneficial if they can be helped to view these changes as educated choices they are making

to alter their lifestyles as a reasonable response to a major event in their lives, as opposed

to changes that are imposed by well-meaning healthcare providers and/or family members,

or by the injury itself. In some cases, persons with acquired brain injury (ABI) have signif

icant difficulty in understanding the nature of changes in their abilities. 18,19 They may persist

with expectations that can no longer be justified based upon their actual capabilities. Early

identification of such discrepancies must be undertaken in the rehabilitative process, aggres

sively addressed in treatment, and reflected in the discharge planning. 20

Activities and Activity Levels

Human beings are prepared from a very early age to become productive in later life. That

productivity is expressed, ever increasingly, through vocational endeavors, though this

is often preceded by educational preparation of one sort or another. Productivity in later

life is a major source of interpersonal interaction and socialization. Those activities and

facets of life that contribute to life satisfaction are largely contained within, or derived

from, the pursuit of avocational and vocational interests and the subsequent social inter

play that occurs.

Perhaps the harshest reality following traumatic brain injury for those persons unfor

tunate enough to be left with significant residual deficits is the lack of access to those

events and affairs in life which represent the pinnacle achievements of our adulthood and

all that we are prepared to participate in lifelong. Loss of the ability to work can have

demoralizing effects. 21 Social isolation and the resultant depression that often accompanies

arise largely from an inability to access avocational or vocational activities meaningfully

and independently following TBI. 3,22 In fact, in the United States, there is not a real societal

push to provide for return to such activities. Funding for rehabilitation into these activities

is not sufficient nor appropriate, 23 with the possible exception of the workers' compensa

tion system in some states. Even workers' compensation

systems may frequently fail to

adequately undertake vocational rehabilitation with this population.

The discharge planner must encourage the treatment team, injured person, caregivers,

and funding source to recognize the rich therapeutic and life satisfaction benefits associ

ated with immediate and long-term actualization of active and meaningful engagement

in living. The client must be prepared to complete as many activities of daily living (ADLs)

as possible and as independently as possible before discharge. The discharge environment

should encourage the injured person’s participation in ADL completion and foster con

tinued growth in areas of difficulty on a day-to-day basis. All too often, however, persons

are not left to dress themselves or feed themselves because to complete these activities to

the level of independence that they may be capable of requires too much time. Caregivers

may be pressed for time or patience and choose to complete the task for the injured person.

Some caregivers watch the injured person struggle to complete a given series of tasks and

conclude that the frustration is so great as to be emotionally painful for the person or

themselves. Sometimes these caregivers can “love too much,” attempting to reduce frus

tration by eliminating the task altogether or completing it for the person. The problem is

that people respond to the level of environmental expectation. Caregivers who complete

basic activities for the individual inadvertently strip the person of a righteous sense of

individuality and independence while unwittingly perpetuating, perhaps, an unnecessary

level of dependence. The key is to educate caregivers and injured persons alike to identify

reasonable levels of environmental support and expectation so as to create an environment

that is hospitable, yet one which fosters continued improvement.

Discharge planning should include a detailed and comprehensive resource analysis of

available venues for meaningful engagement in the real world. Though this may be

premature at a given level of treatment, engaging in this pursuit with an injured person

and/or the caregivers can provide them with insight into the long-term nature of the

problems before them and teach them to undertake the resource analysis on an ongoing

basis. The resource analysis should include options for volunteer activity, return to school,

or return to work, as well as information about more immediate care and treatment needs,

such as pharmacy location, current and future professional contact information, durable

medical equipment suppliers, and support groups. The process should review the proper

timing of return to school or work to avoid premature return to either of these activities.

The emotional trauma of failure in either of these environments can be considerable and

great care should be undertaken to affect a properly-timed return to these activities. It is

often helpful to identify family and friends' vocational and avocational interests as poten

tial sources of assistance early in the vocational rehabilitation process.

Likewise, the discharge planner must provide the injured person and caregivers with

information as to how to best bring about a return to school or work. Unfortunately, most

state-funded vocational rehabilitation programs are woefully inadequate for this popula

tion. 5 This should include education about the laws which may govern the return and

proper preparation for the return, both of the injured person and the people in the return

environment. The discharge planner should prepare a list of resources that are available

to help in returning to school or work. These may include specific persons within, or who

can consult with, a school district, departments for students with special needs at a

community college or university setting, or state-sponsored vocational rehabilitation ser

vice information. Chapter 18 provides an excellent discussion of issues relative to returning

to school. Some cities may have active support groups which assist persons in resource

identification, return to work, adjustment to disability, day care, and assisted living.

Return to work is usually best when it is accomplished on a protracted and gradual

basis. The employer of injury should be reserved as a final placement. It is usually best

to preserve this placement, reserving it for the last

vocational placement. Since vocational

rehabilitation following brain injury is actually more akin to vocational therapy, return to

work may require involvement in several less demanding positions which are intentionally

limited in their scope and have specific purposes of reestablishing basic worker charac

teristics and gradually increasing the level of task complexity and responsibility to be

carried by the injured worker. It is incumbent upon the discharge planner to properly

prepare the injured person and caregivers with information that allows them to undertake

this process with or without professional assistance. Equally important is the caregivers'

preparation to recognize a return to work that is premature or poorly timed. A more

detailed discussion of return to work can be found in Chapter 16.

Family Systems

The statistics regarding survival of family systems following return of a person with TBI

to the home are impressive. Families report increased depression, decreased ability to

express feelings, decreased time and energy for social or recreational activity, and a

tendency toward exercising increased control following severe TBI. 24 Lezak 25 has suggested

that the emotional disturbances and disorders of executive function in the family member

with TBI contribute distinctively to family burden. Education, counseling, and emotional

support are recommended for families. Lezak's observations

were substantiated by a study

that systematically examined family system outcome following brain injury. 26 Distressed

family functioning across all domains was identified by family members. The return of a

person with TBI to the home is first met with great pleasure. Lezak 27 identified six stages

of families' reactions once the stresses of having the injured family member at home are

experienced. Pleasure is replaced by bewilderment and anxiety as the families' energy

dwindles. Optimism diminishes and guilt, depression, despair, and mourning follow the

bewilderment. Families undergo a reorganization and, finally, an emotional disengage

ment. 27 Separation, divorce, behavioral problem development in children, or departure

from the home by nearly adult children or siblings are all expected consequences. Emo

tional responses vary somewhat by position in the family. Mothers, fathers, and siblings

appear to react differently to the stresses of TBI within the family. 28–32 First, parents report

increased global marital distress, reduced expression of affection, and a feeling of less

spousal understanding in families where children between 15 and 24 years of age suffer

TBI. 30 Mothers report greater dissatisfaction with spousal support than fathers. 30,32 Mothers

are more likely to be under a physician's care than fathers, are more likely to be using

psychotropic medications, and tend to express negative emotion more than their hus

bands. 30 Rosenberg 31 studied spousal reaction following mild head injury. Half of the wives

reported a high degree of negative impact in their relationships due to changes following

TBI. Lyth-Frantz 32 compared marital relationship impact between couples with a child

with TBI and couples with a child without disabling conditions. The effect of TBI was to

decrease marital satisfaction, decrease satisfaction with parent-child relationships, pro

duce greater family emeshment, create a perception that the family's fate was a function

of circumstances beyond the family's control, and decrease interest and involvement in

intellectual, cultural, and physically-oriented recreation. Next, siblings report that family

stress is the greatest problem encountered following TBI in another sibling 29 and show

significant signs of emotional distress. 28 Coping strategies used by siblings are suppression

of frustrations, 29 wishful thinking, avoidance, and self-blame. 28 The emotional trauma

inflicted upon a family is tremendous and predisposes most families to disruption of the

family system, sometimes with devastating consequence like marital separation or divorce,

development of behavioral problems in noninjured siblings, and challenges to the par

ent-child bonds between parents and noninjured siblings.

Members of a family can generally be expected to survive the immediate and long-term

consequences experienced when a family member is injured. However, the quality of that

survival should be actively discussed and planned. Families function in complicated

patterns of individual and group behaviors and settle into a manner of living that becomes

more or less the norm for that group. As catastrophic injury and disability enter the picture,

the customary rhythm of a family is severely disrupted.[24,25] The family resources of time,

attention, financial resources, and energy tend to become focused on the injured family

member, sometimes to the near exclusion of all other needs. This phenomenon has been

partially described as a command performance wherein a family member meets unbelievable

physical and emotional demands on a protracted daily basis, seemingly without regard

for his/her own needs, health, and welfare. While such a "crisis" mode of operation can

be useful for short periods of time, a diagnosis of traumatic brain injury usually heralds

the family embarkation upon a prolonged change in their way of living.

Families are rarely ready to hear the need to care for themselves, feeling as though such

a response would be unwise, risky, selfish, or all of these. They are, likewise, not prepared

to hear that their family member is either perilously close to death, as in the early stages

of moderate to severe injuries, and that, should they survive, they should begin to plan

for such huge changes in their lives. Given the very short time frames associated with

acute hospitalization, the discharge planner may be reluctant to contribute to the stresses

of an already overwhelmed family. This dilemma contributes to the lack of preparedness

most families report.

In the early stages of rehabilitation, families are sometimes reluctant to believe outcome

prognostications that may be provided, viewing them as inaccurate and pessimistic. Many

families report having been told that their family member may die, and if they did not

die, that they may be severely disabled. These comments are often interpreted as being

told their family member was going to die or that they would be severely disabled for

the rest of their lives. The result is a loss of credibility suffered by treaters down the line,

through no one’s fault, but circumstance alone. Such misperceptions may be avoided by

active pursuit of a planned educational format by the treatment team that covers a number

of topics regarding the nature of injuries sustained, their treatment, and both near- and

long-term issues for caregivers.

In these early stages of rehabilitation, families respond best to access to information

about their specific family member’s condition and possible future care requirements.

McMordie et al. 33 found a high sense of hopelessness communicated by professionals to

families and injured people, as reported in postdischarge surveys. Provision of a range of

possible outcomes is easier to accept for many families and probably most accurate. This

approach engenders a desire for more information about which outcome might be best

achieved and how. McMordie et al. also found the greatest consumer dissatisfaction with

information provision, specifically information about available resources, long-term out

come, and personality change following TBI. Resource centers which provide families and

injured persons with detailed information that is easy to understand and readily available

can be most helpful. McPherson et al. 34 support these assertions in their finding that

families interviewed just 6 weeks after discharge from acute rehabilitation indicated their

primary need was more information, though these needs were not spontaneously pre

sented. Instead, their need for information required prompting to be made known.

Likewise, counseling from either experienced staff or other family members can be

helpful in preparing families for the challenges that lie ahead. An analogy to racing can be

useful, comparing the coming weeks, months, and years to a marathon, rather than a sprint

of a few days or weeks. Of course, treaters are often reluctant to engage in such discussions

for fear of unnecessarily removing the element of hope from the picture for patients and/

or their families. Great sensitivity is required in the pursuit of information provision,

education, and preparation while continuing to encourage realistic levels of hope.

Families must be encouraged to both plan and actively return to normalized patterns

of family living. The initial disruption of such patterns can develop into a new norm for

families if allowed to continue unchallenged. Families may need assistance in learning to

discuss their concerns and fears. While this may be expected of younger family members,

facilitated discussions with adult family members and friends can be exceedingly helpful

for those participating directly and in modeling how to conduct such discussions with

children, siblings, extended family, and friends in the future. In fact, families should be

directed to talk openly about their concerns and fears, especially facilitating these discus

sions between couples, parents and children, and family members and friends. This should

include factual information about injuries sustained, treatments provided, future treatment

needs, and preparation for future stages in recovery and return home. Families need to

be educated about the various treatment facilities that may be available locally, regionally,

and nationally. They should be made aware of the various levels of care frequently

encountered, including acute care, acute rehabilitation, subacute care, residential and

outpatient postacute services, home and community treatment, and assisted living

services. They should be provided with all the treatment options and explanation as to

which will be available to them based upon financial constraints individual to their

situation. While some of these services may not be

appropriate or even available, the

discussion will help the family to understand, from a slightly different perspective, the

challenges they will be facing. This information can be provided in the form of informa

tional pamphlets, counseling sessions, or other educational formats.

Families may need assistance in identification of assumptions within the family that

may bias services that an injured person receives. Topics such as cost, geography, expertise

of treaters, and objective comparison of various treatment options can be helpful. Treaters

must recognize the need to investigate treatment options available locally, regionally, and

nationally and balance this with the somewhat parochial tendencies professionals gravitate

toward with reference to beliefs regarding their own competencies and those available at

other treatment settings. Many professionals believe they are able to provide for their

patient’s needs adequately, but this belief may inadvertently portend a blinding to other

more specialized or expert services available. This is particularly poignant for treaters at

the acute and acute rehabilitative treatment level. As length of stay has decreased for acute

hospitalization and acute rehabilitation services, 1,2 professionals must familiarize them

selves with the multitude of postacute treatment options available today and actively

advocate for their patient’s access to these highly specialized models of treatment.

Parents of injured children naturally rally around the injured child, all too often subju

gating the needs of siblings and themselves. This approach may be acceptable on a very

short-term basis; however, it should not be encouraged on a protracted basis. An aunt,

uncle, family friend, or grandparent usually cannot supplant a parent for children. Parents

should be encouraged and assisted in frank, age-appropriate discussions with siblings

about the injury and the future. Of course, care must be taken to consider the emotional

health and readiness of each child on a case-by-case basis, but generally speaking, children

deal best with factual information. Additionally, the family will be challenged as never

before to deal with high levels and ranges of emotion and may be unprepared to recognize

key differences in coping strategies exercised by different people in the family circle.

Failure of family members to recognize and deal appropriately with such differences in

coping strategies can lead to tremendous misunderstandings and misgivings. As has been

evidenced in numerous families, such misperceptions have actually contributed to dete

rioration and, sometimes, dissolution of family structures.

Families will need information on the importance of establishing and using a structured

routine once the injured person returns home. Ironically, structure leads to freedom. The

injured person will need as much external assistance as possible in organizing the envi

ronment and events. Predictable routines will aid in organization of the return home for

all parties and will enhance the redevelopment of self-care skills, in particular. Some

families function well with such direction since they functioned in a structured fashion

prior to injury. Other families, however, may not have functioned in such a way and may

need a fair amount of help in learning to do so. Families need to understand the importance

of a regular schedule for waking/sleeping, medications, meals, hydration, exercise, and

completion of activities of daily living. An approach which is haphazard not only causes

confusion but also brings risk associated with missed medications, meals, fluids, or rest.

Likewise, since rehabilitation maximized repetition, complete participation in activities of

daily living to the fullest extent possible by the injured person will bring about the fastest

return of these skills.

Last, caregivers should be advised regarding the provision of feedback and conse

quences for inappropriate behaviors they may encounter. Sometimes, families are at a loss

as to whether feedback should be provided for asocial behaviors. While feedback can be

overdone, generally, it is best for the family to be taught to deliver appropriate feedback

and consequences for asocial behaviors. They should be taught how to deliver conse

quences immediately after the behaviors occur. If a behavior analyst or psychologist is

available, such programming should begin in the treatment setting with instruction given

to caregivers on continuation of the programming following discharge. A more detailed

discussion of behavioral interventions can be found in Chapter 14.

Caregiver Concerns

Reduced and restricted lengths of stay have resulted in placement of persons with TBI

in the home setting far earlier than is, perhaps, best for the individual, in some cases.

The burden placed upon caregivers cannot be overstated. Caregivers are faced with a

myriad of potential medical complications that may not have been adequately identified

during hospitalization or may not have been manifest during that time. Most homes are

not built with the anticipation of dealing with the needs of a person with physical

handicaps, and, in a similar vein, most families are not equipped to deal with the

pervasive demands created by a person with medical, physical, cognitive, communica

tive, and/or behavioral problems.

Studies indicate that depression, anxiety, anger, fatigue, mood disturbance, and family

dissatisfaction are frequently encountered by the injured person and by caregivers alike. 35

These complaints are reported by many levels of involvement by caregivers, extending

well beyond the primary caregiver to secondary and tertiary caregivers. The primary

caregiver is most often a woman, usually a wife or mother.

35,36 In a population studied

where the mean age of the person with TBI was 28 years, 64% of caregivers were the

parent of the injured person and 25% were the spouse. 36 The mean age of the caregiver

was 44 years, suggesting a fairly long future of management of such responsibilities.

Seventy percent (70%) of the caregivers lived in the same residence as the injured person.

Measures of life satisfaction demonstrate a progression as chronicity increases. In the

first year after injury, employment was associated with life satisfaction while age, marital

status, social integration, and depressed mood were not. However, in year 2 postinjury,

employment, social integration, and depressed mood were associated with life satisfac

tion. 37 This progression may be due to recognition of the permanence of sequelae of the

brain injury as time progresses. Given the findings on the relationship between quality of

life and employment, it appears that persons with TBI who are able to become gainfully

employed or productive on a day-to-day basis experience greater life satisfaction. 37,38

Caregivers should be prepared for their responsibilities to both endure over a long

period of time as well as their burden of care to increase over time, especially so as severity

of injury increases. 39,40 Brooks et al. 39 found that the ten most frequently encountered

problems reported by relatives remained either stable or increased, in the majority, from

1 year postinjury to 5 years postinjury (Table 24.1). In fact, the largest increase in frequency

of reporting was in the area of disturbed behavior at 5 years. Threats or gestures of violence

increased from 15% at year 1 to 54% at year 5. Twenty percent (20%) of relatives reported

their family member to have been physically violent, involving actual assault at year 5,

an increase from 10% at 1 year postinjury.

Caregivers may need to take on the role of nurse, therapist, educator, counselor, vocational

rehabilitation counselor, social worker, case manager, and life care planner in addition to their

other responsibilities. Holland and Shigaki 41 point out that education of a caregiver early in

the acute treatment phase may be limited in its efficiency due to the disruption of the

continuum of recovery that can be encountered due to a lack of rehabilitation programming

continuity from acute rehabilitation through community reentry. These authors suggest a

three-phase approach to provision of educational materials to caregivers, according to the

phase of recovery of their family member. The authors suggest that a resource listing of

published educational material and local care resources be provided, over time, to caregivers

and the authors provide a listing of such bibliographic resources for the reader. 41 DePompei

and Williams 42 outline a family-centered counseling approach that is useful during rehabili

tation. Acorn 43 developed a guide for community-based family education and support groups

to provide education regarding TBI and its sequelae, enable families to identify community

resources, and build support networks among families with TBI.

Children of brain-injured adults present unique challenges for the discharge planner.

The caregiver will often have responsibility for both the person with brain injury and his/

her children. Uysal et al. 44 studied the changes befalling families with a parent with a

brain injury and children and found that parenting techniques changed following brain

injury. Parents with TBI reported they were less nurturing and less involved with their

children. They were also less focused on goal setting, encouragement of skill development,

and promotion of work values. Spousal reports added their counterparts were less affec

tionate and less accepting toward the children. Children reported that both parents were

less demanding from the perspective of discipline.

Seizure Hygiene

The overall incidence of posttraumatic epilepsy (PTE) is estimated at about 5% for all

persons with nonmissile head injury. 45 The incidence of PTE following moderate head

injury is 1.6% and, following severe head injury, is 11.6%. 46 Overall incidence for PTE has

been noted to be as high as 25 and up to 35% for persons comatose for 3 or more weeks. 47

In the 1980s, seizure prophylaxis was somewhat common in the United States, while in

Europe, the more prevalent approach was that of the “free

first fit.” Anticonvulsant

coverage was provided in the United States to attempt to prevent the first seizure, while

in Europe, such coverage was provided after evidence of a first seizure. A landmark study

by Temkin et al. 48 demonstrated no real long-term benefit associated with prophylaxis TABLE 24.1 The Ten Problems Most Frequently Reported by Relatives at 5 Years (N = 42) Problem Percent Relatives Reporting 1 year 5 years Personality change Slowness Poor memory Irritability Bad temper Tiredness Depression Rapid mood change Tension and anxiety Threats of violence 60 65 67 67 64 69 51 57 57 15 74 67 67 64 64 62 57 57 57 54 Source: Brooks, N. et al., The five year outcome of severe blunt head injury: A relative’s view, J. Neurol. Neurosurg. Psychiatry, 49(7), 765, 1986. With permission.

coverage and, as a result, this practice in the United States has slowly decreased. In fact,

a more considered approach to prophylaxis is generally followed, taking into account the

nature of the injury and the likelihood of PTE associated with that type of injury.

Posttraumatic epilepsy can first occur many years postinjury. 49,50 It is important to advise

persons with TBI and their families about their relative risk for the development of seizures

and factors that are within their control that may impact the nature of a given seizure

disorder. Families should be educated as to what constitutes seizure activity. Grand mal

seizures are easily recognized, while partial motor seizures may be less recognizable.

Clearly, complex partial seizures are least recognizable, though they constitute a surpris

ingly high percentage of seizure prevalence following acquired brain injury. 51 Complex

partial seizure disorders are difficult to diagnose and may be misinterpreted as psychiatric

conditions by caregivers and professionals alike.

Medication compliance represents a primary area of concern. The person must under

stand the medication regimen that has been prescribed. This includes the importance of

compliance with the timing of medication administration and understanding whether and

when a missed dosage can be made up. For example, missed dosages of Dilantin or

Phenobarbital, though best taken at prescribed times, can be taken at any time in the same

24-hour period that the missing dosage is prescribed. Tegretol, on the other hand, cannot

be handled in a like manner. Education must be provided as to the specific characteristics

and options of a given anticonvulsant coverage.

Likewise, it is important for persons and their families to understand whether an

anticonvulsant can be abruptly stopped. The cessation of medication may be due to a

prescription lapse, unavailability of the medication due to travel, forgetfulness, incarcer

ation, or a directive from an uninformed health care provider, family member, or friend,

or the injured person simply stops the medication. Some anticonvulsants and antispas

modics require a tapering, so that seizures are not actually precipitated.

It is also wise to educate regarding sleep, rest, and stress. Many persons with seizure

disorders experience increases in the frequency of seizure

activity with increased fatigue

and stress. Education regarding monitoring of drug levels during periods of diarrhea or

constipation can be important for the person with a relatively fragile seizure disorder as

drug absorption can be impacted by such conditions.

Information regarding maintenance of adequate hydration should be provided. People

who live in arid climates, who may travel extended distances by airplane, or engage in

outdoor activities such as hiking, backpacking, or river trips should be advised to carefully

monitor noncaffeinated and nonalcoholic fluid intake, both by noting the quantity per day

and the frequency and nature of urination. Education regarding the diuretic effect of

alcohol and caffeine should be provided.

Lastly, some anticonvulsants may interact with other drugs, either increasing or decreas

ing the other drug’s effectiveness, or increasing or decreasing the serum levels of the

anticonvulsant coverage. 52 Specific information about these drug interactions must be

provided to the person and his/her family so they may monitor future prescription use

for potential interactions. While this is a role that is best filled by the health care provider

and/or a pharmacy, these individuals may be unable to fill this role due to lack of

information or lack of access to the person’s complete medical history.

Depression

Depression has become identified as a significant long-term complication by numerous

authors. 35,53–55 Studies which look out 3 to 7 years postinjury point to depression as a major

complaint by both injured persons and their caregivers. 53–55 The advent of the SSRI class

of antidepressants has been an important development in the treatment of persons with

traumatic brain injury. 56 This particular class of drugs appears to be tolerated well, in

general, and has a low complication rate.

The etiology of depression appears to be twofold: biochemical and situational. Social

isolation is considerable and arises from diminished real-world interaction. This diminu

tion can be traced, in part, to a lack of avocational or vocational involvement, together

with frequently impaired interpersonal skills. 57,58 Both contribute to substantial social

isolation. Most persons with TBI are quite able to recognize the differences in their lives

comparing pre- and postinjury status. As a continual issue on a day-to-day basis, and in

the absence of meaningful involvement in the regular work-a-day world, feelings of

isolation, frustration, and depression are commonly reported. Discharge planners should

educate injured persons and their caregivers to participate in fitness and aerobic exercise

routines that have been medically approved to assist with fatigue and depression. It is

wise to educate regarding the symptoms of depression. This should include agitated

depression, panic attacks, and anxiety.

The discharge planner can address this issue by education and encouragement to estab

lish meaningful involvement to the person’s capability postdischarge. Likewise, the dis

charge planner can make the injured person and the caregivers aware of counseling

services, church or community support groups which may operate recreational, avoca

tional, or vocational activities, and the value of use of antidepressant medications in

consultation with their physician. There must be a careful tie-in to development and

maintenance of appropriate activity levels and meaningful involvement in both the home

and community.

Many people with TBI report frustration at the loss of choices and control in their lives

postinjury. Aware caregivers can provide an increasing array of choice and control in daily

decision making, gradually turning more and more control over to the injured person as

he/she is able to accept it. Since this is an ongoing and continually changing process,

caregivers need to understand the need to be vigilant and reexamine choice/control issues

on a regular basis. Families sometimes attempt to exert maximal control after a family

member is catastrophically injured, 24 perhaps in an attempt to limit their exposure to future

disastrous events. Some gain control over other aspects of life previously managed by the

injured person (e.g., finances) and are reluctant to give

up or share that control. Still others

sense a need to exert control to prevent a person with impaired judgment from becoming

financially, legally, emotionally, sexually, or socially encumbered beyond his/her capabil

ity. The need to protect stands in opposition, in some cases, to the pursuit of life satisfaction

and participation in age-appropriate activities. The interaction of risk with freedom of

choice and balancing rights to self-determination, life satisfaction, and safety should be

actively discussed on an ongoing basis.

These matters can become quite complicated and most families are best assisted by

professional counseling. Discharge planners are well advised to make contact with mental

health professionals in an injured person’s home area that are experienced with TBI and

can offer occasional assistance and counseling on an as-needed basis.

Sleep

Sleep disturbance is a relatively common complication following TBI. Sleep disturbance

can be manifest in three primary problems: (1) sleep apnea/hypopnea, (2) periodic limb

movement disorder (PLMD), and (3) hypersomnolence (excessive daytime sleepiness).

Interruption of sleep is a fairly common complaint following TBI and may be related to

routine, diet, psychological issues, or sleep hygiene. Education should be provided regard

ing each of these impacts to the injured person and his/her caregivers as they may be

most easily addressed. More complicated issues, such as sleep apnea/hypopnea, PLMD,

and hypersomnolence, may require medical interventions. It is beyond the scope of this

chapter to thoroughly review sleep disorders. Rather, the intent is to review some of the

more common issues that may be encountered following TBI.

In the general population, the prevalence of sleep apnea/hypopnea is estimated to be

between 2 and 4%. 59 PLMD is estimated to occur in 5% of the population 40,60 and hyper

somnolence occurs in 0.3 to 13% of the general population, depending upon definitions

used. 61,62 By contrast, sleep apnea/hypopnea has been evidenced in 11.3% of persons with

TBI, PLMD in 25.4%, and hypersomnia in 29.6% 63 in a study of 71 consecutively enrolled

persons admitted to a postacute residential rehabilitation program. An interesting finding

in this study was that persons with hypersomnolence were often unable to perceive their

hypersomnolence and the researchers suggested routine sleep laboratory evaluation. Cas

triotta and Lai 64 studied ten persons with TBI who reported hypersomnolence. These

individuals averaged 110 months postinjury. Treatable sleep disturbances consisting of

obstructive sleep apnea, upper airway resistance syndrome, central sleep apnea, and/or

narcolepsy were found in all ten cases. Three individuals had a preinjury history of

hypersomnia and, of these three, two actually sustained TBI from motor vehicle collisions

while driving, with the suspicion that they may have fallen asleep at the wheel.

Finally, in a study of 184 persons who complained of excessive daytime sleepiness after

head or neck injury, multiple sleep latency testing showed mean sleep onset time of less

than 5 minutes in 28% of the subjects and less than 10 minutes in 82%. 65 Awareness of

hypersomnolence did not correlate with the objective findings. Sleep-disordered breathing

occurred in 32% of the persons studied.

Sleep has been associated with cognitive function, behavioral functioning, and psycho

logical health. 63,66–68 Likewise, sleep apnea has been associated with motor vehicle

collisions 69,70 and unintentional injuries. 71 These data reflect potential contributory factors

to an initial TBI, as well as to likelihood of reinjury, either due to trauma or chronic

hypoxemic events.

The discharge planner should provide education regarding signs and symptoms asso

ciated with sleep disturbances, as well as information regarding diagnosis and treatment

in cases where these issues have not been thoroughly investigated prior to discharge.

Crisis Management

Few families can be expected to be prepared to manage the various types of crises that

arise for persons with TBI and their caregivers. Such crises can include financial, social,

medical, and legal matters. In general, it can be quite

helpful to attempt to prepare injured

persons and their caregivers by collecting information they may need in the event of

certain situations arising.

The injured person should be provided a succinct medical history that can be conveyed

to emergency personnel as needed. Likewise, this information should be provided to

healthcare providers who will continue to care for the injured person upon returning

home. A list of past treaters and their contact information can be quite helpful.

The discharge planner should see that discussions have been held with the injured

person and the caregivers regarding treatment authorization requirements, advanced

directives, and durable power of attorney for healthcare arrangements. Obtaining durable

power of attorney agreements can be expensive and, as a result, may not be undertaken.

Likewise, guardianship or conservatorship proceedings can be expensive and less likely

to be undertaken. Information should be provided to caregivers concerning experienced

legal resources within their vicinity and the advantages and disadvantages associated

with advanced directives, durable power of attorney for healthcare arrangements, and

competency proceedings.

Home Adaptations

It is most likely that an individual’s home will require some sort of modification to assist

in the management of the injured person. Fortunately, there are a number of inexpensive

and reliable electronic means to address some difficulties encountered following TBI.

Impairments of smell and taste represent a common area of concern. Smoke, natural

gas, and CO 2 detectors are available at fairly low cost, though, as battery operated devices,

pose a challenge for the memory-impaired in their proper maintenance. Caregivers need

instruction in establishing a food labeling procedure for storage of food in that spoiled

food cannot be detected with impaired smell, taste or, in some cases, vision or judgment.

Clearly labeled food which indicates a “do not use after” date can be helpful.

Visual and balance impairments may necessitate the introduction of additional lighting

to bedroom, hallway, closet, and bathroom areas. Many persons after TBI have balance

which relies heavily upon visual input as vestibular and proprioceptive inputs are dimin

ished. 72 Consequently, low light conditions increase the likelihood of a loss of balance and

fall, increasing the risk of reinjury.

Accessibility must be considered for the physically-challenged individual. This includes

access and egress from the living environment and moving around within the environment

safely. Access and egress should be considered from the perspective of ramping, as well

as time required to egress from various areas of the home. Locks on doors may need to

be modified so as to allow the person with dexterity problems easy operation in the event

of an emergency. It is necessary to consider door-way widths, bathroom fixture access,

hot water temperature control, transfer bars or equipment, height and elevation angle of

the bed, and placement, height, and sturdiness of furniture. Kitchen safety can be

addressed by consideration of electrical disabling of large appliances at the circuit breaker

box and placement of a lock on the access door to the circuit breaker box. Stove tops,

ideally, should have the controls at the front of the cooking surface. It may be necessary

to place nonbreakable dishes in lower cupboards for easier access, as well as frequently

used foodstuffs.

Persons with oral dysarthria, balance impairments, seizure disorders, or other serious

health conditions should be advised to obtain a Medical Alert bracelet which will allow

public safety officials a means of independent verification of a condition. This can be

crucial in obtaining needed medical attention and also in avoiding inappropriate incar

ceration under the mistaken impression of public intoxication.

Consideration should be given to the utilization of portable telephone equipment in the

home, with back-up fixed equipment. The portable phone should have an extended-life

battery capability and a loud, continuously sounding page/find feature due to memory

difficulties that may make finding the portable phone difficult. Placement of multiple

phones should be considered for the physically-challenged person. Phones are available

with very large buttons for easy dialing for the visually- or physically-challenged person.

Likewise, phones which allow for light indicators for incoming calls and volume adjust

ments can be useful for the hearing impaired. Lastly, an easily operated answering machine

can be helpful in managing communications.

Systems are available which allow for telephonic alerts to be delivered in the event of

an emergency. The system operates when a remote medallion worn by the user is activated.

This can be useful for people with balance problems, seizure disorders, etc. The system

contacts either a service or a user-defined contact to relay the emergency message.

Bathrooms should be equipped with grab bars around the shower/tub and toilet areas.

Hand-held shower wands can be helpful for the physically-challenged person. Bath

benches, which are nonslip, and nonslip floor coverings for the shower/tub area and

adjacent flooring should be considered. It may be necessary to remove glass shower door

fixtures, both for access and safety in the event of a loss of balance. Ground fault interrupt

electrical receptacles should be installed in the vicinity of water, such as in bathrooms

and kitchens.

Remote electrical control devices can be helpful in

managing the environment. These

include remotes for common equipment like televisions and radio/stereo units, but can

also be purchased to control lighting and other electrical appliances. Such units are referred

to as BSR or X-10 units and function by transmission of a signal through existing electrical

wiring to specially installed light switches or electrical outlets.

In general, home evaluations are conducted by occupational and/or physical therapy

staff members. These individuals are quite skilled in conducting these evaluations. It can

be useful to have a community resource catalog available to caregivers that lists vendors

of equipment and services.

Some individuals own weapons and keep these in their living environments. The exist

ence of weapons in the home should be explored and recommendation for their manage

ment made. Safety becomes an issue not only for the physically- or judgment-impaired

person, but also for the depressed person.

The Internet continues to evolve and offer increased access to services. Shopping for

many items can be safely conducted via the Internet and social contact can likewise be

enhanced. Of course, the Internet is also a place of vulnerability for social and financial

matters. E-mail contact with an established list of friends and professionals can be quite

useful. Chat rooms can be risky and difficult to participate in. Resources such as useful

Websites or services, identified in advance for the injured person and the caregiver, can

be provided.

Financial Planning

Families need help in preparing for the loss of income usually associated with traumatic

brain injury. Osberg et al. 73 reviewed missed work days and financial consequences for

parents of traumatically brain-injured children. Table 24.2 shows the percentage of families

reporting various problems at 1- and 6-month postdischarge intervals sorted by severity

of injury. A high percentage of parents reported a loss of work time and injury-caused

financial problems.

In a long-term outcome survey conducted of over 300 families averaging 7 years

postinjury, the mean reduction in monthly earnings for the injured person was over $1000

per month. 53 On a family basis, mean monthly income reduction 7 years postinjury was

over $400, suggesting that other family members had either obtained employment or

sought higher wages, perhaps in response to the loss of an income. It should be noted

that virtually all persons in this study had insurance of one sort or another which

provided funding for their rehabilitation. This is important in that some of these indi

viduals were covered by either liability or workers' compensation coverage, both of which

are likely to provide some income on a long-term basis.

This is obviously not the case

for persons without such coverage. The income loss may be markedly higher for people

without these coverages.

Families should be encouraged to immediately review their budgets and spending

plans. Larger purchases should be reconsidered or postponed. Re-financing, consolida

tion, or restructuring of family debt may become important. Again, most families are

overwhelmed with the changes in their day-to-day reality and will not have considered

these long-term issues. The discharge planner can create a resource list of lenders willing

to assist with debt restructuring, refinancing, consumer education, etc. In some instances,

families may have other income resources they can call upon to assist with short-term

financial needs as they adjust to a lower income as a family unit. These can be found in

retirement funds, whole-life insurance policies, and supplemental disability policies. TABLE 24.2 Percentage of Families Agreeing or Strongly Agreeing by Injury Severity Score Injury Severity Mild (n = 36) Moderate (n = 30) Severe (n = 14) One Month Postdischarge Financial Problems The injury is causing financial problems*** Additional income is needed** 17 11 27 17 79 50 Work Problems Time is lost from work I am cutting down the hours I work* I stopped working because of child’s injury* 36 17 3 47 30 17 57 57 29 Six Months Postdischarge Financial Problems The injury is causing financial problems** Additional income is needed** 14 6 20 10 57 43 Work Problems Time is lost from work** I am cutting down the hours I work*** I stopped working because of child’s injury** 22 0 0 27 7 10 71 57 29 *p < 0.05; **p < 0.01; ***p < 0.001. Note: Examples of how to read this table. Among the 36 children with mild injuries, 17% of families reported the injury is causing financial problems, vs. 27% among the 30 families of children with moderate injuries, and 79% of the 14 families

of children with severe injuries. The three asterisks indicate that the percentage differences across the three severity groups are significant at the 0.001 level. Source: Osberg, et al., Brain Inj., 11(1), 11–24, 1997; Taylor & Francis, Ltd. [http:// www.tandf.co.uk/journals]. With permission.

Families may need to consider the sale of certain assets to both generate income and to

reduce indebtedness.

End-of-life issues are difficult for many families to discuss and plan for, either with or

without TBI. Yet, the financial consequences of death can be considerable. Estate planning

can identify useful tools to assist a family to plan for the death of caregivers. Simple review

of a family's likely net worth will determine whether formal tools such as trusts might be

helpful in reducing tax consequences and preserving maximal funding for the injured

family member. Life insurance policies, both individual and second-to-die policies, may

be warranted to help in provision of some funding for care. It can be helpful for parents

to discuss their intentions for the use of proceeds from their estate upon their death with

noninjured siblings, especially if a decision is made to reserve those proceeds primarily

or entirely for the injured family member. As families age, different estate planning

approaches may be appropriate. For example, a family with several young children may

be inclined to plan estate distributions for the benefit of all the children. However, as

children become adults who are providing for themselves, the family may change its

direction of estate proceeds to benefit those who are unable to provide for themselves.

Lastly, the discharge planner should provide information and/or application forms

necessary for SSI, SSDI, and/or Financial Aid to Dependent Children. More information

on this topic can be found in Chapter 22.

Additional Rehabilitation Timing

Some persons with TBI recover over a period of time that is fairly concise and confined

in duration. Others, however, seem to experience recovery in a less time-contiguous

fashion. Still others may experience a fairly good period of recovery and success following

discharge, only to experience postdischarge complications which cause the individual to

regress to a lesser level of functioning. A return to rehabilitation services can sometimes

be useful in furthering the recovery of an individual or in reestablishing a previously

attained level of function. Many studies report functionally significant improvements and

reduced disability levels achieved during later application of rehabilitation services. 74–80

One study reviewed five cases of long-term institutionalized (SNFs) persons with TBI. 81

Each of the people was discharged from rehabilitation to either adult family homes or to

group home care. These studies conclude that, in individuals with moderate to severe

brain injury, substantial functional and neurobehavioral impairment can be reasonably

expected to achieve statistically significant functional improvements following application

of “late” rehabilitation. The literature, however, does not provide a thorough review of

the characteristics of those persons who respond well to late rehabilitation, at least not

enough to provide a clear delineation of that group from one that will not benefit.

The propriety of additional rehabilitation depends upon the reasons for a lack of progress

in earlier rehabilitation attempts or the reasons for deterioration from previously achieved

levels of functioning. Brain injury is not a degenerative diagnosis. Regression or deterio

ration observed following brain injury can be traced to either a medical, psychological/

emotional, or environmental etiology. The key is to accurately identify which of these may

be active as reasons for a decline in function and determine whether they can be reversed

or changed. One example might be the identification of iatrogenic complications associated

with inappropriate pharmacological intervention. Another might be a change in a family

system where an undue amount of overdependence was fostered for many years, only to

require further intervention when the responsible family member or caregiver was no

longer available or able to provide care. This might occur in the sudden death of a parent

or a decline in health of a caregiver due to advancing age. Again, regularly scheduled

follow-up contact may allow identification of such situations and allow the discharge

planner to proactively advocate for additional rehabilitative services.

Summary

The world of health care has changed tremendously in the last 2 decades. Shorter lengths

of stay and decreasing financial resources have increased the level of acuity with which

people are discharged from treatment settings and level of disability with which people

are returned to home environments. Ongoing care and treatment is relegated, many times,

to the injured person and his/her caregivers. The burden for discharge planning cannot

fall to a single individual on a treatment team, but rather must be dealt with by the entire

team and, institutionally, by the resources developed and made available by the treating

facility. Whether viewed as a part of patient care, advocacy, or community service, the

creation of resource and information centers and materials provides a vital service to

persons with TBI and their families. Caregivers must be encouraged to maintain contact

with previous care providers and to actively manage and participate in follow-up activities.

The responsibilities carried by discharge planners are immense and the information

suggested herein materially adds to an already overwhelming workload. A checklist is

provided in Appendix 24B to assist the discharge planner in both approaching and

organizing a discharge for a person with TBI and as an outline for services that the

discharge planner might encourage to be developed, institutionally, to support excellence

in discharge planning.

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Appendix 24A: Family Manual Outline

NAME:

DATE OF BIRTH:

DATE OF INJURY:

INJURY (in layman's terms):

LOCATION OF INJURY:

GENERAL APPROACH: (Discuss (1) what has been used in therapy for activity of daily living completion, (2) what to expect that the client needs for assistance, (3) specific areas of deficit and how they affect performance, (4) behaviors exhibited, and (5) what tasks are priority and must be completed and which should be encouraged.)

BEHAVIOR: (Make note of all behaviors including but not limited to physical aggression, angry language, exiting, stealing, self-abuse, nonparticipation, sexually aberrant behvior, and property abuse. This section should also include how to provide reinforcement and what approach to use to gain participation and compliance.)

AMBULATION STATUS: (Include level of independence with ambulation, what type of assistive device is needed and the type of supervision required.)

SPEECH:

VISION:

ADAPTIVE EQUIPMENT:

ACTIVITIES OF DAILY LIVING:

A. Hygiene and Grooming (Include information on showering ability, oral care, combing hair, make-up, etc., with how much assistance needed.)

B. Dressing (Include how much assistance is needed and any adaptive equipment.)

C. Toileting (Note level of independence, including limitations.)

D. Medication (Who should be responsible, times, any special instructions.)

E. Meal Preparation (Include level of assistance needed for all meals.)

F. Eating (Include level of help needed, type of diet, any special dietary needs or restrictions.)

G. Bedtime/Wake-Up/Alarm Clock (Structure should be maintained as much as possible to maintain abilities. Include techniques used to gain compliance.)

H. Laundry (How often and what assistance is needed.)

I. Dishes (Note assistance level needed.)

J. Mail Retrieval, if appropriate.

K. Time Management (Note level of ability.)

L. Travel (Include how the client will be transported with level of assistance needed.)

M. Grocery Shopping (List help needed for shopping list, money, food storage, etc.)

N. Money Management (Note level of involvement and who is responsible.)

OUTINGS/LEISURE ACTIVITIES: (Include type of activities the client can and likes to participate in. Set expectations for the outing if behavior exists.)

DAILY ROUTINE (Outline a typical day for weekdays and weekends, including any help needed such as a checklist.)

VOCATIONAL/AVOCATIONAL INVOLVEMENT (Include responsible parties, level of participation, supervision needed, etc.)

NURSING/MEDICAL ISSUES (Include current medications, any specific care issues or restrictions, allergies, etc.)

THERAPEUTIC HOME PROGRAMS (List activities from the therapists that the client can do at home. Outline the goal and procedure for the activity using pictures, videos, etc.)

Appendix 24B: Discharge Planning Checklist

NAME: _____ Date of Estimated Discharge: _____

GUARDIAN/CONSERVATOR: _____ DISCHARGE ADDRESS: _____

_____
_____

_____
_____

1) LIVING ACCOMMODATIONS: A) Apt. _____ Home _____ Rented _____ Owned _____ Group Home/Assisted Living _____ Other

2) SUPERVISION/CARE GIVER NEEDS A) Hours Required Weekday Weekend 1) a.m. _____ _____ 2) p.m. _____ _____ 3) O/N _____ _____ B) Type 1) Family _____ 2) Agency _____ 3) Nursing _____ C) Respite Alternatives: _____

3) COMMUNITY RESOURCE ANALYSIS: A) School Options B) Work Options 1) Volunteer 2) Day treatment 3) Sheltered employment 4) Competitive employment 5) Department of Rehabilitation C) Transportation D) Shopping E) Hospitals/Urgent Care/Emergency Services F) Banks G) Religious Information

4) MEDICAL: A) Medical History: (Include medical

precautions and concerns as well as past treaters with contact information.)

5) BEHAVIOR: A) Type: Physical
_____

6) CLIENT/FAMILY EDUCATION: Provide information in the following arenas: A) Seizures B) Drug interactions C) Long-term effects of TBI 1) Second impact syndrome 2) Depression 3) Alcohol/drugs 4) Sleep hygiene 5) Hydration 6) Bowel/bladder D) Community support systems E) Treatment authorizations 1) Advance directives 2) Durable power of attorney for heath care F) Therapeutic home programs G) Guardianship/conservatorship, if needed H) Public assistance, if needed I) Behavior interaction/approach

7) FINANCIAL PLANNING: A) Family Budget Review 1) Restructure debt 2) Use of retirement, life insurance for short-term needs B) Public Assistance 1) SSI 2) SSDI 3) Medicaid/Medicare 4) State specific benefits, i.e., victims of violent crimes, Regional Center, lowincome housing, disabled phone and electric rates, Easter Seals, CCS, service organizations

8) ADDITIONAL RECOMMENDATIONS:

Completed by:
_____
Date:_____

Client Signature/Reviewed with:
_____

Print Name:
_____ Date:
_____