Clinical Atlas of Polysomnography

Ravi Gupta | S. R. Pandi-Perumal | Ahmed S. BaHammam

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CLINICAL ATLAS OF POLYSOMNOGRAPHY

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CLINICAL ATLAS OF POLYSOMNOGRAPHY

By

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The front cover illustration was created by using the Starry Night (original was an oil on canvas by the Dutch post-impressionist painter Vincent van Gogh, 1889) with a superimposed picture of a polysomnographic tracing.
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DEDICATION

To our families . . .

for their abundant support, patience,
understanding, and everlasting love and affection.

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ABOUT THE AUTHORS

Ravi Gupta, MD, PhD, MAMS, Certified Sleep Physician (World Sleep Federation), is presently working as Professor in the Department of Psychiatry & Sleep Clinic, Himalayan Institute of Medical Sciences, Dehradun, India. He has contributed chapters to various high profile academic volumes. He has also authored a book “Psychiatry for Beginners,” and has more than 100 published articles in various peer-reviewed journals to his credit. He has received numerous awards and fellowships, including the Young Psychiatrist Award from the Indian Psychiatric Society (2008), fellowships from the World Psychiatric Association (2008) and from the Japanese Society of Psychiatry and Neurology (2009), and membership of the Indian Academy of Medical Sciences, New Delhi (2015) to name a few. In 2010, he received a Mini-Fellowship from the American Academy of Sleep Medicine. This fellowship provided him a chance to refine his knowledge and skills in the area of Sleep Medicine under able guidance of Dr. Jim Walker and Dr. Robert Farney at LDS Hospital, Salt Lake City, Utah. Continuing with the legacy of his mentors, he is engaged in imparting knowledge of Sleep Medicine to physicians from various streams through lectures, workshops, and training programs in his present institute.

S. R. Pandi-Perumal, MSc, is the President and Chief Executive Officer of Somnogen Canada Inc, a Canadian Corporation. He is a well-recognized sleep researcher, both nationally and internationally, and has authored many publications. His general area of research interest includes sleep and biological rhythms. He is a well-known editor in the field of sleep medicine and has edited over 20 volumes dealing with various sleep-related topics. He received an honorable mention in the New York Times in 2004. The India International Friendship Society awarded him the prestigious Bharat Gaurav award on January 12, 2013. The Bharat Gaurav Award is usually recognition of a person who has made achievements in a particular field, which in turn will put a positive impact on the society at large.

Ahmed S. BaHammam, MD, FRCP (Lon), FRCP (Edin), ABIM, EDIC, FACP, FCCP, is a tenured Professor of Medicine at King Saud University (KSU). Recognized as a leading expert in the field of sleep medicine, both nationally and internationally, Prof. BaHammam established the first academic sleep disorders center in Saudi Arabia and the first Sleep Medicine Fellowship program and subsequently chaired the committee that established the Saudi regulation for accreditation of sleep medicine specialists and sleep technologists. As a founding member of the Saudi Thoracic Society and the Saudi Sleep Medicine community, Prof. BaHammam has organized over 20 workshops on polysomnography. His advanced polysomnography courses have

been conducted in several countries in the Middle East. For his contribution to sleep medicine, he was awarded the Lifetime Achievement Award (2016) by King Saud University. He has published more than 200 scientific articles. He is a member of the editorial board of several international medical journals.

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LIST OF ABBREVIATIONS

10–20	ten–twenty (electrode placement system)	CPAP	continuous positive airway pressure
5-HT	serotonin	CSA	central sleep apnea
AASM	American Academy of Sleep Medicine	CSB	Cheyne-Stokes breathing
AC	alternate current	CVD	cardiovascular disease
AV	atrio-ventricular	Ca ⁺⁺	calcium ion
ABG	arterial blood gas analysis	Cl ⁻	chloride ion
ABIM	American Board of Internal Medicine	CO ₂	carbon dioxide
		CMR	common mode rejection
ALMA	alternate leg muscle activity	CMRR	common mode rejection ratio
ASV	adaptive servo-ventilation	DC	direct current
COPD	chronic obstructive pulmonary disease	DMH	dorsomedial hypothalamus
		ECG	electrocardiogram (or EKG)
		EDS	excessive daytime sleepiness

EEG	electroencephalogram	IRLSSG	International Restless Legs
EFM	excessive fragmentary myoclonus		Syndrome Study Group
EMG	electromyogram	K ⁺	potassium ion
EOG	electrooculogram	KLS	Kleine-Levine syndrome
EPSP	excitatory postsynaptic potential	LC	locus coeruleus
ETCO ₂	end-tidal CO ₂	LDT	laterodorsal tegmental nuclei
GABA	γ-aminobutyric acid	LFF	low-frequency filter (high pass filter)
GERD	gastroesophageal reflux disease	MSLT	multiple sleep latency test
GI	gastrointestinal (tract)	MWT	maintenance of wakefulness test
Glu	glutamate	N3	deep sleep
H	histamine	Na ⁺	sodium ion
HF	heart failure	NE	norepinephrine
HFF	high-frequency filter	NREM	non-rapid-eye-movement sleep
HFT	hypnagogic foot tremor	O ₂	oxygen (saturation)
HTB	high threshold bursting	OCC	out-of-center
HST	home sleep testing	OHS	obesity hypoventilation syndrome
Hz	hertz; a measure of frequency (cycles per second)	OSA	obstructive sleep apnea
		OSAS	obstructive sleep apnea syndrome
IPSP	inhibitory postsynaptic potential	pH	potential of hydrogen

PaCO ₂	partial pressure of CO ₂ in arterial blood	RIP	respiratory inductance plethysmography
PaO ₂	partial pressure of O ₂ in arterial blood	RLS	restless legs syndrome
PAP	positive airway pressure	SA	sino-atrial
PDR	posterior dominant rhythm	SCN	suprachiasmatic nucleus
PFT	pulmonary function tests	SDB	sleep disordered breathing
PLMS	periodic leg movements during sleep	SNRI	serotonin-norepinephrine reuptake inhibitors
PPT	pedunculopontine tegmental nuclei	SOREM	sleep onset rapid eye movement
PSG	polysomnography	SOREMPS	sleep onset REM periods
RAS	reticular activating system	SRS	Sleep Research Society
RBC	red blood cells	TC	thalamocortical (neurons)
RBD	REM sleep behavior disorder	TcCO ₂	transcutaneous CO ₂
REM	rapid-eye-movement sleep	VLPO	ventrolateral preoptic nucleus
RERA	respiratory effort related arousal		
RHT	retinohypothalamic tract

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FOREWORD

Sleep is increasingly recognized, along with a healthy diet and physical activity, as one of the three pillars of sustainable health. Conversely, chronic lack of sleep or disturbed sleep is well known to produce detrimental consequences for both physical and mental health. For instance, epidemiological studies have shown strong associations between sleep loss and sleep disorders, on one hand, and increased risks for cardiovascular and psychiatric disorders, premature cognitive impairments, and even mortality, on the other hand. It may be no surprise then that sleep disorders have become a major public health issue in most modern societies.

Polysomnography is the gold standard for measuring normal sleep and for diagnosing many sleep disorders. It provides the most comprehensive and reliable assessment of multiple physiological parameters during sleep. Many of the discoveries in basic sleep and circadian research and in clinical sleep medicine are the direct results of technological advances, particularly polysomnography. Just to note a few examples, the discovery of rapid-eye movement (rem) sleep, the diagnosis of sleep disorders such as narcolepsy, sleep-related breathing disorders, and REM behavior disorder, as well as the observation of sleep state misperception in some forms of insomnia, could not have been made without polysomnography. Of course, polysomnography is only one tool among several assessment modalities of sleep. Depending on whether the context of assessment is clinical or research, adding a clinical interview,

along with subjective sleep diaries, behavioral devices such as actigraphy, and a variety of patient-questionnaires are likely to yield useful and complementary information and provide the complete assessment of sleep and sleep-related complaints.

The Clinical Atlas of Polysomnography is truly a comprehensive collection of invaluable information and graphical illustrations about everything that is needed to perform the polysomnographic assessment. From basic concepts about normal sleep and sleep disorders, technical information about calibration, artifacts, and various montages, to practical recommendations for managing a sleep laboratory, this atlas represents a superb reference guide. The atlas is filled with useful illustrations of actual records depicting standards for monitoring, artifacts recognition, and key findings associated with different sleep pathologies. A compendium of review questions at the end of each chapter is extremely handy for testing new learning. Although intended primarily for sleep technologists, this atlas will serve as a useful reference for any sleep clinician, researcher, or trainee wanting to learn more about the technical and clinical aspects of evaluating sleep and sleep disorders.

The authors of this atlas, Drs. Ravi Gupta, S.R. Pandi-Perumal, and Ahmed BaHamman, are internationally known leading experts in sleep medicine and sleep research. They are to be commended for compiling this essential tool for a better understanding normal sleep and diagnosing many sleep disorders. This atlas is likely to remain a key reference in the field for years to come.

Charles M. Morin, PhD, FRSC, DABSM

President, World Sleep Society

FOREWORD

It is a great pleasure and honor for me to write the foreword to the book *Clinical Atlas of Polysomnography* by Dr. Ravi Gupta, Dr. S. R. Pandi-Perumal, and Dr. Ahmed S. BaHammam. It is not so because I am doing the same as the President of the Indian Society for Sleep Research and Asian Sleep Research Society. The reason is something different. We, the leaders in Indian Society for Sleep Research, are engaged in Sleep Medicine education across the country and across the spectrum for last ten years by organizing courses for physicians and technicians and had envisioned the development of a book on PSG for readers not only in India but also in Asia. We thought of a book that will be easy to understand and comprehensive and that one can begin a career in sleep medicine by simply reading it. Now we do not have to hunt for such a book. This long-cherished desire of the core group has been accomplished. I thank all the authors for their tremendous effort and commitment to bring this unique book for the growth of Sleep Medicine.

Sleep disorders are now recognized as a major public health issue. Investigating sleep is the most challenging medical investigation as it requires background knowledge of physiology and sleep medicine and expertise in sleep technology. *The Clinical Atlas on Polysomnography* has everything that you want to learn or teach on sleep technology. The physiological principles of respiration, gas exchange, the genesis of electrical potentials with color illustrations make it easy to understand for technicians.

The beginners who are starting a career in Sleep Medicine will be immensely benefitted by this book. It is not merely another book on polysomnography. It is something different. It begins with a description of normal sleep, covers everything about polysomnography, and ends with career development, sleep laboratory management, and financial viability of a sleep laboratory. You will find learning objectives at the beginning of each chapter and some review questions to test your knowledge at the end. The essence of a sleep technology book is quality of representative graphs capturing various physiological and pathological events during sleep. This book offers the best. The authors have put extra efforts to put color graphs for easy understanding.

Recent developments in sleep data acquisition systems and analysis software, including automated computing techniques, make the life of sleep technicians ever challenging. This book describes all the major PSG machines available in the market with their software features.

No doubt the book is a stepping stone for starting a career in Sleep Medicine, and the authors provide the blueprint for future revisions and refinement with readers' feedback.

— **Hrudananda Mallick, MD, PhD, FAMS**

Professor, Physiology

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All India Institute of Medical Sciences, New Delhi

President, Indian Society for Sleep Research

President, Asian Sleep Research Society

PREFACE

The branch of Sleep Medicine came into existence approximately 70 years ago when many physicians who had a keen interest in this area developed themselves as somnologists. Initially, Sleep Medicine was focused towards research; however, as happens in science, with evolution of knowledge, pathological conditions related to sleep (i.e., sleep-disorders) were also recognized. With this advancement of knowledge, the practice and scope of Sleep Medicine extended from bench-side to clinics.

Polysomnography has always been a useful tool for understanding physiological and pathological aspects of sleep. In the past 30 years, sleep laboratories have become places not only for research but also for providing clinical care. The person in command in any sleep laboratory is often a sleep technologist who records and scores the data. He is expected to understand not only the machine and the software that he handles but also to possess at least basic knowledge regarding electrophysiological, technological, clinical, and therapeutic aspects of sleep science.

Recording of data is of paramount importance and, thus, training and certification programs were developed for sleep technologists. Well-structured training programs for sleep technologists also helped to establish a minimum standard of care for patients, as trained sleep technologists must cross the established benchmark of expected knowledge and skills in this area. However, in many parts of

the globe, structured training programs for sleep technologists are not available. In those geographical areas, despite the need felt by sleep physicians, sleep laboratories are difficult to be established and run in the absence of trained sleep technologists. This present book is an attempt to fill that void and to provide information that a sleep technologist must possess.

It was important to maintain consistency and comparability of data within and across sleep laboratories. To address this issue, rules for scoring the polysomnographic data were laid down by eminent scientists. The American Academy of Sleep Medicine has been a forerunner in the development of sleep technology courses and scoring rules and, most recently, on April 1, 2017, it produced the *AASM Manual for the Scoring of Sleep and Associated Events*, version 2.4. These guidelines and rules are at present considered as standard globally, and this book follows the framework of same. However, this book is intended to complement, not to substitute, for the AASM scoring manual, as many areas that are covered in the manual are not covered here.

This book provides basic information regarding normal sleep, sleep disorders, and electrophysiology aspects of sleep that are outside of the scope of the AASM scoring manual. The book will guide you through the fundamental aspects of, for example, types of overnight sleep studies, establishing a sleep laboratory, preparing the patient for a sleep evaluation study, placement of electrodes and other signal recording devices, and scientific aspects of recording of data. This book also includes chapters on depicting real-time illustrations of sleep data as captured in the sleep laboratory, and the scoring of recording data. Information regarding common montages, artifacts, and troubleshooting in the sleep

laboratory will facilitate your journey as a trainee sleep technologist. Graphical one-page representations of overnight recorded data (i.e., histograms) can provide a great deal of useful information. An attempt has been made to explain the interpretation of histograms. It is prudent to summarize the data and observations in a report that is not only comprehensive and informative but also is easy to understand, even by physicians whose primary specialty is not Sleep Medicine. A chapter has been dedicated to explain this in detail. Lastly, we have provided ready-made forms, questionnaires, and documents that can either be used as they are or with some modifications.

We hope that our humble attempt will be welcomed and that readers will find this book useful!

— **RG**

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CREDITS AND ACKNOWLEDGMENTS

This volume owes its final shape and form to the assistance and hard work of many talented people. We would like to express our profound gratitude to the many people who have helped and also to some who have contributed without realizing just how helpful they have been.

First of all, the authors would like to express their reverence towards all those scientists, physicians, and sleep technologists whose dedication and contribution have evolved the area of Sleep Medicine and who are still improving our understanding. This book is an attempt to collectively reflect their work.

Our sincere appreciation goes to Prof. Charles Morin and Prof. Hrudananda Mallick who are well known figures in field of sleep medicine. They graciously agreed to write forewords for this book. We know them as great scientists, successful leaders, acclaimed teachers, revered mentors and last but not the least, as humble persons. Their testimonials mean a lot to us. We also would like to thank Prof. Jan Ulfberg, an eminent scientist, a great physician and mentor for many persons in Sleep Medicine for going through the book prior to the print and providing his insights. We are humbled to receive encouraging comments from him. We want to say him a big, “Thank you!”.

We gratefully acknowledge our corporate partners, namely Philips Respironics Inc., Cadwell Inc., and Somnomedics LLC, who kindly accepted our request to provide requested illustrations for this volume.

The authors would also like to acknowledge several of our friends and colleagues—Dr. Abhishek Goyal (Associate Professor, Department of Pulmonology, All India Institute of Medical Sciences, Bhopal, India), Dr. Rajanish Sharma (Sleep Physician, Rudraksh Clinic, Jaipur, India), Dr. Supriy Jain (Consultant Cardiologist, Jaipur, India), and Dr. Sourav Das (Sleep Physician, Somnos Sleep Clinic, Kolkata, India)—for providing some illustrations for the book. The authors would also like to acknowledge the technical help provided by the following colleagues: Divinagracia E. Gacuan, RPSGT; Smitha George, RPSGT; and Karen Lorraine Acosta, RPSGT, from the University Sleep Disorders Center at King Saud University, Riyadh, Saudi Arabia. Mr. MM Mathavan from the Himalayan Institute of Medical Sciences, Dehradun, has contributed a chapter “Financial Viability for a Sleep Unit” and we are thankful to him for providing insight on this important issue.

The authors would also like to acknowledge the close co-operation we have received from each other. We think we made a good team, even if we say so ourselves!

No volume can be completed without the untiring efforts of many publishing professionals. Producing a volume such as this is a team effort and we acknowledge with gratitude the work of the editorial department of Apple Academic Press. We are especially indebted to Mr. Ashish Kumar, the President of Apple Academic Press, who was an enthusiastic and instrumental supporter from start to finish. Our

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Without a whole host of dedicated individuals, this volume would never have come to completion. We recognize these people individually and collectively for their contribution. To all these people goes our sincere gratitude. Their willingness to contribute their time and expertise made this work possible, and it is to them that the greatest thanks are due. They made our work possible and pleasurable.

For this, and for so much else, we are ever grateful.

—Ravi Gupta, India

S.R. Pandi-Perumal, Canada

Ahmed S. BaHammam, Saudi Arabia

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NORMAL SLEEP

LEARNING OBJECTIVES

After reading this chapter, the reader should be able to:

1. Define sleep and changes in sleep across age.
2. Discuss neurobiological mechanisms of sleep including the two-process model.
3. Discuss different stages of sleep along with physiological changes.
4. Discuss the neurobiology of EEG waves seen across different sleep stages.

Sleep may be defined as a physiological state of unconsciousness that is reversible, cognitive and perceptual disengagement from and to the environment are seen during this temporary unconsciousness, and from which the arousal is

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possible in response to any internal or external stimuli. This definition has several important aspects that will help you understand the physiology of sleep. First, it is a state of unconsciousness that is reversible and this reversibility differentiates it from coma. Second, the person is not aware of the environment during sleep, so he does not perceive (although he may sense it) most stimuli during sleep. Perception is different from sensation – when a sensory stimulus is consciously recognized it is considered as perceived. This suggests that a sleeping person cannot take any conscious decision – rather he reacts on instinct. This explains why patients suffering from sleep-walking when aroused forcibly often commit violent acts. The third part of the definition says that a person may be aroused with any internal or external stimuli. Internal stimuli that may arouse a person include pain,

anxiety or dyspnea. External stimuli are often auditory or tactile in nature. However, these stimuli must be sufficiently intense to arouse the person, and their intensity also varies across the sleep stages.

1.1 SLEEP ACROSS AGE

Sleep has many important parameters, for example, the total duration of sleep, maintenance of sleep, and at what time of the day we fall asleep. Electrophysiologically, sleep may be divided into two main stages: non-rapid-eye-movement (NREM) sleep and rapid-eye-movement (REM) sleep. NREM sleep can be further divided into three stages: N1 (light sleep), N2, and N3 (deep sleep).

A remarkable variation is seen in all these parameters across age. For example, total sleep time of an infant is around 18–20 hours, which reduces as the child grows and comes to adult timing during mid-adolescence (6–8 hours), after which it remains more or less stable. However, it starts declining in the fourth decade of a person's life. During old age, it reduces to 5–6 hours/day. Regarding continuity, infants have fragmented sleep and they tend to wake up multiple times. It becomes consolidated into a single sleep as the age grows. Children often go to bed early at night, however, during adolescence, they develop a phase delay. Phase delay refers to delayed bedtime and wake time. On the other hand, the phase is considered to be advanced in old age. Aging also influences the electrophysiology of sleep. Children have a high proportion of N3 (deep sleep), which reduces as the person grows old.

1.2 NEUROBIOLOGY OF SLEEP

Sleep is dependent upon two processes: homeostatic and circadian. These processes together decide when we will fall asleep and also the other characteristics of sleep, such as depth, duration, maintenance, and proportion of sleep stages.

The homeostatic (also known as “S”) process makes us feel sleepy depending upon the duration of wakefulness. The longer the period of wakefulness, the higher the sleep pressure; in other words, higher are the chances to fall asleep. That is the reason why a person who is awake for a long time falls asleep even during the day. Moreover, this process regulates the proportion of deep sleep (N3 sleep) - the longer the period of wakefulness, the higher the proportion of deep sleep. The homeostatic process is dependent upon two major areas of the brain that are

located close to the hypothalamus. The first is the sleep-promoting area – the ventrolateral pre-optic nucleus (VLPO), which sends inhibitory signals through the GABAergic neurons to the wake-promoting area of the brain. Wakefulness is dependent upon the monoaminergic nuclei of the brain that are the part of the reticular activating system (RAS). Monoaminergic nuclei include serotonergic neurons (located in dorsal and medial raphe nuclei), noradrenergic neurons (locus coeruleus), histaminergic neurons (tuberomammillary nucleus) and cholinergic neurons (located in pedunculopontine (PPT), laterodorsal tegmental (LDT) nuclei, and basal forebrain nuclei). In addition, there are glutaminergic neurons that are diffusely distributed throughout the RAS. When the VLPO sends GABAergic signals to these neurons, sleep ensues. The activity of both wake-promoting and sleep-promoting

areas is modulated through another group of neurons, the hypocretin neurons that are present in the lateral and posterior hypothalamus. Under normal conditions, the hypocretin neurons modulate the activity of the other two areas of the brain in such a manner that only one state of consciousness, that is, wakefulness or sleep prevails ([Figure 1.1](#)). Damage to the hypocretin neurons leads to a condition known as narcolepsy. In this condition, a person is not able to maintain either states and experiences bouts of sleepiness during wakefulness.

The circadian process (process “C”) is dependent upon environmental light. Certain other factors can also regulate this process, for example, food, emotions, social activity, and exercise. These factors are called “zeitgebers.” Among these, light is the strongest factor which can entrain the circadian rhythm. Environmental light falls on the

retina and through the retinohypothalamic tract (RHT) (glutamatergic in nature), it sends signals to the suprachiasmatic nucleus (SCN). The SCN is one of the nuclei of hypothalamus and acts as the 'master clock' circadian clock. During the dark, this sends signals to the pineal gland to secrete melatonin. Melatonin is a hormone that is released into the blood and circulates to the various organs of the body. The SCN also sends signals to the VLPO through the dorsomedial hypothalamus (DMH) and thus can activate it. In the presence of environmental light, melatonin secretion stops. This is why during the dark, we feel sleepy (Figure 1.2).

To fall asleep, it is important that both the homeostatic and circadian processes are in the same phase. If they are not synchronized, then we may feel difficulty in falling asleep or staying awake. Such a condition leads to the

Figure 1.1 Sleep and wake promoting areas in brain: State of wakefulness and sleep are regulated by two areas that exhibit control over each other. Monoaminergic system helps to increase the alertness and forms the part of reticular activating system. These neurons reach cortex and in addition to wakefulness, also responsible for maintaining alertness. GABA neurons from the ventrolateral preoptic area (VLPO) inhibit the monoamine neurons to induce sleep. Hypocretin acts to modulate the activity of both the areas. Laterodorsal tegmental nucleus which is important for wakefulness as well as REM sleep is not shown here.

Figure 1.2 Suprachiasmatic nucleus and its connections: Suprachiasmatic nucleus receives signals from retina and passes them to ventrolateral preoptic area (VLPO) through dorsomedial hypothalamus. Dorsomedial hypothalamus has connections with other areas as well that regulate circadian rhythm of other biological functions in addition to sleep.

generation of circadian rhythm sleep disorders (Figure 1.3).

1.3 SLEEP ARCHITECTURE

Grossly, sleep may be divided into two major stages: rapid eye movement sleep (REM) and non-rapid eye movement sleep (NREM), based upon the eye movements, muscle tone, and waveforms in EEG. NREM sleep can further be divided into three stages: N1 sleep (characterized by theta waves in EEG; slow eye movement, and diminution of muscle tone, Figure 1.4), N2 sleep (theta waves, sleep spindles, and K complexes in EEG; absent eye movements and low muscle tone, Figure 1.5) and N3 sleep (more than 20% of epoch has delta waves, Figure 1.6). REM sleep is characterized

Figure 1.3 Relationship of process C and S in a normal individual: Normally process C and process S overlap with each other so as to increase the propensity to fall asleep at night and propensity to stay awake during the day. Any disruption in this overlapping disrupts the quantity as well as quality of sleep and appears in the form of circadian rhythm sleep disorders.

Figure 1.4 30 seconds epoch showing N1 sleep: This epoch shows mix EEG activity (alpha and theta) along with vertex waves (in circle).

Figure 1.5 30 seconds epoch showing N2 sleep: In this epoch K complex can be seen in the square box and sleep-spindle in circle. Background EEG activity is in theta range.

Figure 1.6 30 seconds epoch showing N3 sleep: This epoch show delta activity. Delta waves are also known as slow waves with frequency of 0.5–2 Hz and amplitude of more than 75 mV.

Figure 1.7 30 seconds epoch showing REM sleep: REM sleep is characterized by low voltage mixed frequency activity, rapid eye movements and atonia.

by low-voltage, mixed-frequency activity in EEG, rapid eye movement, and muscle atonia (Figure 1.7).

These stages follow a characteristic pattern in normal persons where NREM and REM sleep keep alternating at an interval of 90–120 min. Sleep starts with NREM sleep, and after approximately 90 min, the first episode of REM sleep appears. This lasts for a few minutes and after this NREM sleep re-starts. This cycle continues throughout the night and during a 7–8 h sleep, an average healthy person has 4–5 cycles of NREM and REM. In addition, as we have already discussed, deep sleep (N3) is regulated by the process “S,” so when a person falls asleep after hours of wakefulness, N3 sleep is higher in proportion. Thus, the first half of the night is characterized by a high proportion of N3 sleep. As more time is spent asleep,

sleep-pressure lowers, and in the second half of night minimal, if any, N3 sleep is seen. REM sleep is regulated by the process “C” and it is predominantly seen during the second half of the night. Thus, each episode of REM sleep shows progressive lengthening across the night (Figure 1.8).

This has important implications as certain disorders are limited to one sleep stage and they are seen during that part of night. For example, sleep-walking that occurs during N3 sleep is seen more commonly before midnight while REM sleep behavior disorder is more commonly reported close to the morning.

Figure 1.8 Hypnogram: Hypnogram depicts the sleep stages in relation with time. NREM sleep is maximum in the first half of the night, while REM dominates the second half. As the night progresses, duration of N3 periods reduces and that of REM periods increases. NREM-REM has a cycle of around 90–120 min.

1.4 PHYSIOLOGICAL CHANGES FROM WAKEFULNESS TO SLEEP

As the state of consciousness shifts from wakefulness to sleep, and then to different stages of sleep, a number of physiological changes take place inside the body. Many of them are evident during the polysomnography. These changes involve alteration in the brain’s electrical activity, muscle tone, respiration, alterations in the cardiac activity, thermoregulation, spontaneous movements, and in the ability to respond to external stimuli. These changes are summarized in [Table 1.1](#).

1.5 NEUROPHYSIOLOGY OF EEG RHYTHMS FROM WAKEFULNESS TO SLEEP

EEG depicts the difference in the summative electrical potentials of the neuronal cells present

Table 1.1 Physiological Changes During Normal Sleep

	Wakefulness		NREM sleep			REM sleep
	Active	Quiet	N1	N2	N3	
Electrical activity of brain	Beta (15–30 Hz) or Gamma rhythm (30–120 Hz) with occasional theta rhythm (4–7 Hz)	Alpha rhythm (8–14 Hz)	Theta rhythm (4–7 Hz)	Theta rhythm (4–7 Hz) with delta	Delta rhythm (<4 Hz)	Low voltage mixed frequency activity similar to wakefulness
Eye movements	Rapid	Rapid	Slow	Absent	Absent	Bursts of rapid eye movements
Muscle tone	Increased	Increased	Reduced	Reduced	Reduced	Minimal/Atonia
Respiration	Irregular rate and variable amplitude depending upon activity	Regular with uniform amplitude	Regular with slowing of rate compared to wakefulness and uniform amplitude	Regular with slowing of rate compared to wakefulness and uniform amplitude	Regular with slowing of rate compared to wakefulness and uniform amplitude	Erratic rate and amplitude
Cardiac activity	Variable within a range	Variable within a range	Regular beats with slowing of rate	Regular beats with slowing of rate	Regular beats with slowing of rate	Irregular heart beats
Thermoregulation	Present	Present	Present	Present	Present	Absent
Spontaneous movements	High	Reduced	Occasional	Occasional	Occasional	Absent
Ability to response to external verbal stimulus	Intact	Intact	Reduced	Reduced	Reduced	Minimal

in the cortex of the brain that lies beneath the electrodes. The cortex is made up of various types of neurons that include pyramidal cells and interneurons, besides glial cells. Pyramidal cells are excitatory in nature and they remain in contact with other cortical neurons through the fibers that they send to other cortical areas (known as association fibers). They also send fibers to the subcortical nuclei and spinal cord (known as projection fibers). These connections are usually reciprocal and thus, other cortical, subcortical nuclei and information coming from the peripheral nervous system (through spinal cord) regulate their activity in a complex manner. In addition, cortical interneurons that are primarily inhibitory in nature also regulate their activity.

During active wakefulness, EEG activity in the gamma or beta band is often visible.

Fast-spiking activity of the cortical pyramidal neurons through their interaction with the parvalbumin interneurons generates a gamma rhythm in the EEG. It is thought to represent the synthesis of information as gamma rhythms appear during the sensory stimulation. These pyramidal neurons are glutaminergic and their activity is regulated by the parvalbumin interneurons, which are GABAergic in nature. These interneurons have fast-spiking activity and they rhythmically inhibit and disinhibit pyramidal neurons. Parvalbumin interneurons also get a collateral from the pyramidal cells, thus, excitation of the pyramidal neurons excites the parvalbumin interneurons, which in turn, inhibit the pyramidal neurons.

Beta waves also originate in the cortex and they may either represent a slow gamma activity or it may be possible that the parvalbumin

interneurons fire at their natural frequency but some of the pyramidal cells may have a longer refractory period.

Unlike gamma and beta frequency waves, other waveforms of EEG are regulated by the thalamocortical system. Thalamus has relay neurons which receive inputs from the peripheral sensory system and also from the different monoaminergic neurons from the brainstem. These neurons show tonic firing of action potentials. In other words, they show depolarization at regular intervals. On the other hand, when these relay cells are in the state of hyperpolarization, they show bursts of action potential followed by a period of quiescence ([Figure 1.9](#)). Burst firing of the thalamocortical relay neurons is important for the generation of various waveforms seen during NREM sleep.

Thalamic relay neurons receive afferents from the periphery as well as the ascending reticular

Figure 1.9 Tonic firing vs. burst firing in thalamic relay neurons: Different electrophysiological waves are produced by different electrical activity of thalamic relay neurons. (Adapted from Qiang Zhou, Dwayne W. Godwin, Donald M. O'Malley, Paul R. Adams. Visualization of Calcium Influx Through Channels That Shape the Burst and Tonic Firing Modes of Thalamic Relay Cells. *Journal of Neurophysiology* Published 1 May 1997 Vol. 77 no. 5, 2816-282.)

activating system. They send their efferent to the thalamic reticular neurons and to the pyramidal cells in the cortex. Cortical pyramidal cells, in turn, send efferents to the relay neurons and the thalamic reticular neurons. It must be noted that thalamic relay neurons and pyramidal cells send excitatory signals, thus, they excite each other and the reticular neurons. Reticular neurons, on the other hand, are inhibitory in nature, and they receive a copy of signals from both the thalamocortical relay neurons and the corticothalamic pyramidal neurons. Reticular neurons, in turn, project to the thalamic relay neurons ([Figure 1.10](#)).

Alpha rhythms are seen during quiet wakefulness, especially in the occipital region. Generation of alpha activity is dependent upon the thalamocortical system, in addition to the cholinergic neurons from the brainstem. GABAergic

Figure 1.10 Thalamocortical system of neurons: Thalamocortical relay neurons supply to the pyramidal neurons in cortex. Cortical pyramidal neurons send their projection back to relay neurons. Both the neurons also send a copy of their signals to reticular GABAergic neurons, which in turn regulates the activity of relay neurons.

neurons located in the lateral geniculate body periodically silence the high threshold bursting thalamocortical neurons of the occipital area and result in the generation of the alpha rhythm. High threshold bursting (HTB) thalamocortical neurons get depolarized because of cholinergic inputs from the brainstem that acts on the muscarinic receptors present on these neurons. In addition, HTB neurons interact with each other through gap junctions (which is the fastest way of communication between neurons) and, thus, they fire synchronously. Since the activation of muscarinic receptors regulates depolarization of neurons, withdrawal of acetylcholine inputs during the initiation of sleep is depicted as slowing of the EEG to theta rhythms.

Theta rhythms are seen during wakefulness, during N1, N2, and REM sleep. It has been suggested that theta rhythms may represent a slow

alpha and, thus, could be regulated by the brainstem cholinergic inputs.

Sleep spindles are 10–14 Hz frequency sinusoidal waves lasting for at least 0.5 seconds ([Figure 1.5](#)). These are seen during N2 sleep and are generated by burst firing of the thalamocortical relay neurons and reticular neurons. These sleep spindles are transmitted to the cortex through relay neurons. Connections between various pyramidal cells in the cortex spread them to the widespread cortical areas. Sleep spindles result in hyperpolarization of relay neurons and thus prevent the peripheral sensations from reaching to the cortex. Thus, they help in maintaining sleep.

Delta waves seen during N3 sleep (slow-wave sleep) have their origin both in the thalamus as well as the cortex. Connections between the

thalamus and cortex help in synchronization of the two sources of delta waves while connections between various cortical cells help to spread them over widespread cortical areas.

REM sleep is characterized by low voltage mixed frequency activity and sawtooth waves in EEG. REM sleep is modulated by laterodorsal tegmental/ pedunculopontine tegmental (LDT/PPT) cholinergic nuclei situated in the brainstem. These nuclei, depolarize thalamic neurons leading to cortical activation that is important for generation of dreams. These cells also activate GABAergic cells in ventomedial medulla that secrete GABA and glycine on the anterior horn cells in spinal cord leading to profound atonia.

Changes in brain's electrical activity that occur during sleep are depicted in [Figure 1.11](#).

1.6 ATONIA DURING REM SLEEP

Profound muscle atonia develops during REM sleep, leading to multiple ramifications that are clinically important. For example, by producing atonia in upper airway muscles, in particular, genioglossus, it narrows the caliber of the upper airway and increases risks for hypopnea and apnea; when it appears during wakefulness, it manifests as cataplexy, which is a sign of narcolepsy; lastly, absence of atonia during REM sleep leads to the REM sleep behavior disorder.

It is produced by the glycine-mediated (glycinergic) inhibition of the anterior horn cells in the spinal cord and the hypoglossal nerve by the REM-on cells of the sub-dorsolateral tegmental nucleus.

1.7 CONCLUDING REMARKS

Sleep and wakefulness are regulated by two interconnected areas of the brain, which exert a fine

tuning on each other to maintain one of the two states. Sleep is regulated by the circadian as well as the homeostatic processes. Throughout the sleep, neuronal activity keeps changing, which is

responsible for the generation of various physiological characteristics that help to determine the different sleep stages.

Figure 1.11 EEG, EOG, and chin EMG during various stages of sleep and wakefulness.

FURTHER READING

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REVIEW QUESTIONS

1. Infant sleep is different from adult sleep as:
 - A. first stage to appear is REM sleep
 - B. first stage to appear is NREM sleep
 - C. first stage to appear is N2 sleep
 - D. does not have frequent arousals?
2. As the age progresses, following change is seen in sleep:
 - A. sleep duration increases
 - B. sleep is dominated by REM sleep
 - C. sleep shows frequent arousals
 - D. sleep appears shifted to delayed phase
3. Sleep pressure is regulated by:
 - A. circadian process
 - B. homeostatic process
 - C. electrophysiological process
 - D. environmental timing
4. Master circadian clock is situated in:
 - A. ventro-lateral preoptic nucleus
 - B. dorsomedial nucleus
 - C. interlaminar nucleus
 - D. suprachiasmatic nucleus
5. Low voltage mixed activity is seen during:
 - A. REM sleep
 - B. quiet wakefulness
 - C. active wakefulness
 - D. N3 sleep
6. Slowing of EEG during sleep initiation is seen because of:
 - A. withdrawal of dopaminergic input
 - B. withdrawal of glutaminergic input
 - C. withdrawal of cholinergic input
 - D. withdrawal of GABAergic input
7. Sleep spindles are generated by:
 - A. burst firing of brainstem neurons
 - B. burst firing of suprachiasmatic neurons
 - C. burst firing of thalamocortical neurons
 - D. burst firing of cerebellar neurons
8. Thermoregulation is impaired during:

- A. N1 sleep
 - B. N2 sleep
 - C. N3 sleep
 - D. REM sleep
9. Profound atonia is seen during:
- A. quiet Wakefulness
 - B. REM sleep
 - C. NREM sleep
 - D. active wakefulness
10. Patient has irregular breathing during:
- A. REM sleep
 - B. N2 sleep
 - C. quiet wakefulness
 - D. deep sleep

ANSWER KEY

1. A 2. C 3. B 4. D 5. A 6. B
7. C 8. D 9. B 10. A