Case Studies in Sleep Neurology

Common and Uncommon Presentations

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Edited by

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To my fellow torchbearers, who shone the light in multiple directions.

To our faithful readers, who trusted the wisdom of our teachings.

To my family, who patiently accepted the absences.

Antonio Culebras

Contents

The following cases described herein have been published previously

Case 24 Adapted from the following publication, with permission from the publisher: Schenck CH. Uncontrolled intimacy: sexual sleep disorders [Case report]. *Sleep Review* 2007; **8**:24–28.

Foreword

Sleep medicine, for most clinicians, is a new clinical discipline in medicine and one which has appeared almost overnight. To those who thought that all that needed to be known was taught in medical school or in other postgraduate clinical programs, the reality is that very little formal education in sleep medicine has occurred in clinical programs and the clinician is now faced with having to understand the basic science, the underlying physiology and pathophysiology of sleep, and apply that understanding to help diagnose and treat the more than 80 clinical sleep disorders that have currently been described[1]. This book, *Case Studies in Sleep Neurology*, goes a long way in helping the clinician develop the clinical skills to understand, diagnose and treat many of those 80 sleep disorders, but not all, and after reading this book the clinician will be left with an enthusiastic desire to expand his or her knowledge by seeking out and learning about the many additional sleep disorders that could not possibly be covered in this comprehensive volume.

Although all of us sleep on a daily basis and appreciate the importance of full alertness in performing our occupational and social activities, many clinicians, other than those trained in sleep medicine, have little awareness of the importance of sleep and wake issues in the clinical practice of patients with medical, psychiatric and even surgical disorders. Sleep is a function of the brain, yet even in neurology there is still little appreciation of its importance in routine neurological practice. This book helps to highlight some of the neurological aspects of sleep medicine that will aid, not only the sleep specialist, but also the neurologist in managing patients that may have multiple co-morbidities.

Whether one diagnoses one of the most common sleep disorders, such as obstructive sleep apnea syndrome, or one of the more esoteric sleep disorders, such as catathrenia, which is described in this book, the clinician will come to realize that neurological function is an important component of all sleep disorders. Although standard texts on sleep medicine usually provide detailed descriptions of the sleep disorders, in clinical practice patients are more complex, often having multiple medical or psychiatric illnesses, and their clinical course may be complicated by numerous psychoactive medications. The management and course of such patients can only be addressed by books that detail the diagnostic and clinical progress such as described here in *Case Studies in Sleep Neurology*.

Sleep medicine has always been a part of clinical neurology, even before Gélineau described narcolepsy, which some clinicians initially thought could be a psychiatric disorder. Yet to the neurologist, the absence of reflexes during cataplectic attacks confirmed a neurophysiological component to one of the most common disorders of excessive sleepiness. The electroencephalogram, a powerful tool to evaluate neuronal activity, was applied to help understand the underlying physiological basis of sleep and wakefulness, and although partly supplanted by newer diagnostic tests, it is still the basis for determining the cyclical features of the sleep–wake process and is widely utilized in the diagnosis of sleep disorders.

Newer, more advanced electroencephalographic techniques utilizing wider electrode arrays, video, and spectral analysis are helping to clarify both the diagnosis and the central nervous system locations of the effects of sleep and sleep deprivation on the underlying brain. Coupled with analysis of executive function by means of performance tests, studies have shown that the prefrontal cortex (PFC) is a prime area of impairment in sleep loss and excessive sleepiness. Such studies are being applied to many sleep disorders, including the evaluation of both the effects of excessive sleepiness, and the neurotoxic intravascular components of sleep disorders such as obstructive sleep apnea syndrome.

A PubMed search of published articles on neurology and sleep for 2009 revealed nearly 1000 publications suggesting that 2010 will be the decade of advances in the understanding of the brain's role in sleep, wakefulness and sleep loss, as advanced neurological investigative tests involving neurochemistry, neurogenetics and neuroimaging are applied clinically.

The neurochemical control of sleep involves multiple neurotransmitter systems, but most investigations have focused on hypocretin, histamine, dopamine, serotonin and acetylcholine. The recent recognition that the neuropeptide hypocretin is absent in patients with narcolepsy and cataplexy has led to a better understanding of the neurochemical basis of sleep disorders and led to consideration of utilizing neurochemical analysis in establishing sleep diagnoses.[2] In addition, more recently, decreased histaminergic neurotransmission has been shown in narcolepsy and idiopathic hypersomnia, regardless of hypocretin status; the significance of this finding is still unclear.[3] These findings hold promise for new treatments for the sleep disorders that might include hypocretin agonists or histamine H3 antagonists; neurochemical agents that are currently under investigation.

The neurogenetic control of the sleep–wake cycle is an exciting area of future exploration. Numerous genes have been described in animals that influence the sleep–wake cycle and some of these have clinical significance. Some patients with advanced sleep phase syndrome, and more recently some with delayed sleep phase syndrome, have been shown to have an alteration of the period, PER, gene,

believed to be a major contributor to the clinical phenotype. Candidate PER3 genes have been discovered that are associated with individual differences in the vulnerability to sleep loss.[4] Future studies that involve candidate genes and neuroimaging may help find biomarkers for neurobehavioral vulnerability to sleep loss and help identify the source of variance in human neurobehavioral responses to sleep deprivation.

Newer, advanced neuroimaging techniques allow for the quantification of a variety of aspects of brain function including brain structure, metabolism, blood flow and receptor binding. These studies have helped understand the brain areas involved in sleep disturbance. Sleep deprivation is associated with global declines in absolute cerebral metabolism as assessed by [^{18}F]FDG positron emission tomography (PET), and regionally these declines are most notable in the PFC and thalamus.[5] These regions have also been shown on functional MRI to be affected by sleep deprivation.[6] Regional cerebral blood flow studies utilizing SPECT scans have shown increased PFC activity that was reversed by chronic administration of modafinil in narcoleptic patients, suggesting that "sleepiness" could result from alterations in the thalamocortical arousal networks that are affected by modafinil therapy.[7]

All of these newer advanced neurological techniques will become more available to the clinician as the research and clinical data grow, and their appropriate role will need to be understood and applied by the sleep medicine clinician.

For most of the abnormal behaviors during sleep such as REM-sleep behavior disorder, sleepwalking, nocturnal frontal lobe epilepsy, rhythmic behavior disorder, and others, video-polysomnography as described in this book is essential to characterize the clinical features of the disorders. Neurochemical analysis of hypocretin has a place in the management of narcolepsy; neurogenetics will play a larger role as our knowledge expands. Many of the clinical cases described in this book, including sleep disorders associated with multiple sclerosis, subdural hematoma, nocturnal frontal lobe epilepsy, and thalamic lesions have utilized newer neuroimaging techniques to aid in the diagnosis.

The clinician can start the process of understanding the role of advanced neurological investigative means and the appropriate clinical management of sleep disorder patients by reading the case histories contained in *Case Studies in Sleep Neurology*.

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Abbreviations

ADHD	attention deficit hyperactivity disorder
ADNFLE	autosomal dominant nocturnal frontal lobe epilepsy
AHI	apnea–hypopnea index
AI	apnea index
BECTS	benign epilepsy with centrotemporal spikes
BID	twice a day
BMI	body mass index
bpm	beats per minute
BRA	benzodiazepine receptor agonist
CAP	cyclic alternating pattern
CBT	cognitive behavioral therapy
CMT	Charcot–Marie–Tooth disease
CPAP	continuous positive airway pressure
CSA	central sleep apnea
CSF	cerebrospinal fluid
CSR	Cheyne–Stokes respiration
CSWS	continuous spike and wave in sleep
CT	computed tomography
ECG	electrocardiogram
EDS	excessive daytime sleepiness
EEG	electroencephalogram
EMG	electromyogram
EOG	electro-oculogram
ET_{CO2}	end-tidal CO_2
FDA	US Food and Drug Administration

GABA	gamma-aminobutyric acid
HIV	human immunodeficiency virus
MMT	methadone maintenance treatment
MRI	magnetic resonance imaging
MSA	multiple system atrophy
MSLT	multiple sleep latency test
NES	nocturnal eating syndrome
NFLE	nocturnal frontal lobe epilepsy
NPD	nocturnal paroxysmal dystonia
NREM	non-rapid eye movement
OSA	obstructive sleep apnea
OSAHS	obstructive sleep apnea–hypopnea syndrome
OSAS	obstructive sleep apnea syndrome
PAMS	periodic arm movements of sleep
PAP	positive airway pressure
PLegMS	periodic leg movements of sleep
PLM	periodic limb movement
PLMA	periodic limb movement while awake
PLMD	periodic limb movement disorder
PLMS	periodic limb movements of sleep
PO	per os (by mouth)
PRN	when necessary
PSG	polysomnography
PSM	propriospinal myoclonus
$PtcCO_2$	transcutaneous CO_2
PTSD	post-traumatic stress disorder
QAM	once a day in the morning
QHS	at every bedtime
QPM	once a day in the evening
RBD	REM-sleep behavior disorder

RDI	respiratory disturbance index
REM	rapid eye movement
RLS	restless legs syndrome
RMD	rhythmic movement disorder
SB	sleep-related bruxism
SNRI	selective norepinephrine reuptake inhibitor
SPECT	single-photon-emission computed tomography
SRED	sleep-related eating disorder
SSRI	selective serotonin reuptake inhibitor
TID	three times a day
TST	total sleep time
WASO	wake after sleep onset

Introduction

After a long day roaming the hot plains of Castille, Don Quixote and his faithful squire Sancho Panza decided to call the day off and rest under a lone tree. They shared a meager supper of stale bread, musty cheese from La Mancha and rancid red wine. A few grapes found at the bottom of their satchel topped the repast. Despite the frugality of the meal, Sancho felt the customary post-prandial slumber coming and without further ado fell asleep. It displeased Don Quixote, perpetual insomniac, that Sancho had only but one sleep that lasted him from night till morning. "Look how serene the night is, and how lonely is this place, which invites us to vary one slumber with a little watching. Get up, in Heavens name!" exclaimed Don Quixote. Alarmed, Sancho responded, "I only know that while I sleep I have neither fear, nor hope, nor trouble, nor glory. Good luck to him who invented sleep, the cloak that covers all of man's thoughts, the food that takes away all hunger, the water that quenches all thirst, the fire that warms the cold, the cold that cools the heat, the general coin, in short, with which all things are bought, the balance and weight that levels the shepherd with the king and the fool with the wise man. There is only one bad thing about sleep, as I have heard say, and it is that it looks like death, for between one sleeping and one dead there's mighty little difference."

Chapter LXVIII. Miguel de Cervantes Saavedra. Don Quixote of La Mancha. Translated by Walter Starkie. Published by the New American Library, Inc. New York and Toronto. The New English Library Limited, London, 1957 and 1964.

Sleep is the only free voluptuosity given to humans by Nature. Sleep is as necessary as food or drink. When sleep fails, many other biological functions suffer. Sleep is a function of the brain and the neurology of sleep its corollary. And yet, so numerous are the ramifications and so extensive the reach of sleep and its disorders, that sleep medicine remains a multidisciplinary body at the center of which lies sleep apnea, a pervasive disease that has emerged as a public health problem, as have sleep deprivation, excessive daytime sleepiness and fatigue. In the end, however, the neurology of sleep will prevail as the core discipline underlying sleep functions and dysfunctions, the study of which in the hotbed of the brain will lead to a better understanding of their nature.

With great excitement and enthusiasm, we present this book featuring case studies in sleep neurology. The book presents a series of clinical situations

representative of problems that challenge the clinical-solving abilities of practitioners in the neurology of sleep, also known as neurosomnology. The book focuses attention on the major categories of sleep medicine including insomnia, hypersomnias, sleep-breathing disorders, parasomnias and circadian dysrhythmias with emphasis on the neurology of sleep. Both usual and unusual cases are presented with the aim of creating a teaching tool that stimulates the thinking process in sleep neurology along established lines of practice. Each case is introduced with an allusive title, followed by a clinical history, an examination and special studies. This sets the stage for the question asking the diagnosis, treatment or management of the case. The follow-up section states the clinical diagnosis and describes the proper clinical actions to be taken based on the results of tests, with a discussion of the differential diagnosis where appropriate. Each presentation ends with general remarks based on current knowledge and standards of practice. A section entitled "Pearls and gold" summarizes the teaching, take-home points. The bibliography introduces the reader to one or two historical references, where available, followed by a recommended review article, and in all cases to five to ten specific citations. Illustrations have been added where appropriate.

The result is a book containing 40 case histories that provoke and educate clinicians at all stages in their careers. The book is intended to be a didactic tool that dares clinical skills, stimulates memory and provides orientation for additional reading. The target audience is sleep medicine specialists and neurologists. Physicians in training in the discipline of sleep and physicians interested in the knowledge of clinical sleep medicine, with particular curiosity for neurological situations, will find the book singularly readable and useful. The authors are skilled clinicians and seasoned writers with academic titles and vast experience in sleep medicine. As constituents of an international elite in sleep neurology, many are part of that first generation of sleep specialists that has enjoyed the privilege and been granted the unique opportunity of describing new disorders and novel clinical conditions of sleep, contained herein.

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