Sanjeev V. Kothare
Anna Ivanenko
Editors

Parasomnias

Clinical Characteristics and Treatment

Springer

Parasomnias

Sanjeev V. Kothare • Anna Ivanenko
Editors

Parasomnias

Clinical Characteristics and Treatment

Springer

Editors
Sanjeev V. Kothare
Associate Medical Director (Neurology)
Center for Pediatric Sleep Disorders
Epileptologist, Division of Epilepsy &
Clinical Neurophysiology
Boston Children's Hospital
Associate Professor, Department of
Neurology
Harvard Medical School
Fegan 9, 300 Longwood Avenue
Boston, MA 02115

Anna Ivanenko
Feinberg School of Medicine,
Alexian Brothers Medical Center
Northwestern University
Elk Grove Village, Illinois
USA

ISBN 978-1-4614-7626-9
ISBN 978-1-4614-7627-6 (eBook)
DOI 10.1007/978-1-4614-7627-6
Springer New York Heidelberg Dordrecht London

Library of Congress Control Number: 2013943008

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

Within the past two decades, enormous progress has been made in the field of sleep neuroscience and sleep medicine. Due to a widespread use of sleep diagnostic technologies, numerous sleep-related behaviors have been described and classified as sleep disorders. Epidemiological studies revealed a high prevalence of parasomnias in all stages of human life with a high rate of comorbidities among other medical, neurological, and psychiatric conditions.

This volume was inspired by the growing interest in various aspects of sleep medicine and the need for a practical guide to parasomnias which would address the clinical needs of patients ranging from early childhood to old age.

The goal of this textbook is to integrate the most updated research and clinical data pertaining to parasomnias. It provides a comprehensive review of neuropathophysiology, diagnosis and treatment for parasomnias, and other unusual physiological events arising during sleep. Special attention is devoted to differential diagnosis and therapeutic interventions currently available for parasomnias and their medico-legal liability.

This book is intended for a wide variety of clinicians and researchers who are interested in sleep medicine and the neurobiology of sleep. Sleep disorders cross multiple medical disciplines and this volume will be useful for primary care practitioners as well as for neurologists, psychiatrists, pulmonologists, psychologists, and many others who care for patients with sleep disturbances.

Each chapter of the book is written by experts in their field and provides up-to-date review of the topic. We would like to acknowledge all the contributors for their enthusiasm, outstanding efforts, and dedication to the field of sleep medicine that made this project possible. We offer special gratitude to the editorial department of Springer Press for their outstanding team effort in producing this textbook. We are especially thankful to Ms. Portia Levasseur, a Developmental Editor, and to Mr. Gregory Sutorius, a Senior Editor for Springer, for being instrumental in preparing this textbook and for navigating every step of its production.

We would like to thank our families whose support and encouragement were invaluable throughout the preparation process of this book. Finally, we extend our deep appreciation to our patients who continue to teach us and inspire our professional growth and development in the evolving field of sleep medicine.

Sanjeev V. Kothare and Anna Ivanenko

Contents

Contributors

Myriam Abdennadher 90 St. Marys Street, Unit 3–6, Boston, MA 02215, USA
e-mail: drmed_abd@yahoo.fr

Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, Boston, USA

Ruchi Arora Jenny Lind Children's Department, Norfolk and Norwich University Hospital, Colney Lane, Norwich NR4 7UY, UK
e-mail: ruchi.arora@nnuh.nhs.uk

Ravindra Arya Department of Neurology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, MLC 2015, Cincinnati, OH 45229, USA

Ronald E. Becker Harvard Medical School, Center for Pediatric Sleep Disorders, Boston Children's Hospital, FEGAN 10, 300 Longwood Avenue, 02115 Boston, MA, USA
e-mail: ronald.becker@childrens.harvard.edu

Solange Margery Bertoglia Department of Psychiatry and Human Behavior, Thomas Jefferson University, 833 Chestnut Street, Suite 210, Philadelphia, PA 19107, USA
e-mail: solange.margery@jefferson.edu

Connie M. Bongiorno Department of Library Services, Munson Medical Center, 1105 Sixth Street, Traverse City, MI 49684, USA
e-mail: cbongiorno@mhc.net

Smit S. Chauhan Department of Pediatric Sleep Medicine, Boston Children's Hospital, 300 Longwood Avenue, Fegan 9, Boston, MA 02115, USA
e-mail: drsmitchauhan@gmail.com

Youngran Chung Department of Pediatric Pulmonary Medicine, Northwestern University Feinberg School of Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA
e-mail: youngran.y@gmail.com

846 N. Euclid Ave., Oak Park, IL 60302, USA

Michel A. Cramer Bornemann Department of Neurology, Hennepin County Medical Center, 701 Park Avenue South (G8), Minneapolis, MN 55415, USA
e-mail: michel9626@yahoo.com

Karl Doghramji Thomas Jefferson University, 211 South Ninth Street, Suite 500, Philadelphia, PA 19107, USA
e-mail: karl.doghramji@jefferson.edu

Robert C. Dumont Raby Institute for Integrative Medicine at Northwestern, LLC, Chicago, IL, USA
e-mail: rdumont11@gmail.com

846 N. Euclid Ave., Oak Park, IL 60302, USA

Thomas Freedom Sleep Medicine, North Shore University Health System, Skokie, IL, USA
e-mail: TFreedom@northshore.org

Pritzker School of Medicine, University of Chicago, Chicago, IL, USA

Department of Neurology, Glenbrook Hospital, 60026 Glenview, IL, USA

Ramadevi Gourineni 3420 Adams Road, 60523 Oakbrook, IL, USA
e-mail: rgourineni@nmff.org

Madeleine M. Grigg-Damberger Department of Neurology, University of New Mexico, MSC10 5620, One University of NM,Albuquerque, NM87131-0001, USA
e-mail: MGriggD@salud.unm.edu

Michael J. Howell Department of Neurology, University of Minnesota Medical Center, 717 Delaware St., SE, Rm. 5106, Minneapolis, Minnesota 55414-2959, USA
e-mail: howel020@umn.edu

Aatif M. Husain Department of Medicine (Neurology), Duke University Medical Center, Durham, NC 27710, USA
e-mail: erick.viorritto@duke.edu

Anna Ivanenko Ann & Robert H. Lurie Children's Hospital of Chicago, 225 East Chicago Avenue, Chicago, Illinois 60611-2605, USA
e-mail: aivanenko@sbcglobal.net

Sejal V. Jain Department of Neurology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, MLC 2015, Cincinnati, OH 45229, USA
e-mail: Sejal.Jain@cchmc.org

Joseph Kaleyias Division of Pediatric Neurology, Department of Pediatrics, University Hospital of Patras, Rio, 26504 Patras, Greece
e-mail: kaleyias@hotmail.com

Sujay Kansagra Pediatric Neurology Sleep Medicine Program, Duke University Medical Center, DUMC 3936, Durham, NC 27705, USA
e-mail: sujay.kansagra@duke.edu

Umakanth Khatwa Sleep Laboratory, Division of Respiratory Diseases, Boston Children's Hospital, 333 Longwood Ave, LO 486, Boston, MA 02115, USA
e-mail: umakanth.khatwa@childrens.harvard.edu

Suresh Kotagal Division of Child Neurology, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905, USA
e-mail: kotagal.suresh@mayo.edu

Sanjeev V. Kothare Center for Pediatric Sleep Disorders, Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, USA
e-mail: sanjeevkothare@hotmail.com

Robert A. Kowatch Department of Psychiatry Ohio State Medical Center/Nationwide Children's Hospital, 700 Children's Drive, J West 4th Floor, Room G4-4921, Columbus, OH 43023, USA
e-mail: robert.kowatch@nationwidechildrens.org

Barry Krakow Department of Psychiatry Ohio State Medical Center/Nationwide Children's Hospital, 700 Children's Drive, J West 4th Floor, Room G4-4921, Columbus, OH 43023, USA
e-mail: robert.kowatch@nationwidechildrens.org

Yael Latzer Faculty of Social Welfare and Health Sciences, University of Haifa, Haifa, Israel
e-mail: latzer@zahav.net.il

Kiran Maski Department of Neurology, Boston Children's Hospital, Harvard Medical School, 333 Longwood Avenue, 4th Floor, Boston, MA 02115, USA
e-mail: kiran.maski@childrens.harvard.edu

Poojitha Matta Emory University, Atlanta, GA, USA
e-mail: poojitha.matta@emory.edu

8189 Londonberry Road, Nashville, TN 37221, USA
e-mail: poojithamatta@gmail.com

Sricharan Moturi Adolescent Psychiatry, Rolling Hills Hospital, 2014 Quail Hollow Circle, Franklin, TN 37067, USA
e-mail: charanmd@gmail.com

Cynthia D. Nichols Sleep Disorders Center, Munson Medical Center, 1105 Sixth Street, Traverse City, MI 49684, USA
e-mail: cnichols@mhc.net

Milena Pavlova Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
e-mail: mpavlova1@partners.org

Frank M. Ralls Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Internal Medicine, University of New Mexico, 1101 Medical Arts Ave., ND, Bldg. #2, Albuquerque, NM 87102, USA
e-mail: fralls@salud.unm.edu

Sriram Ramgopal Department of Neurology, Boston Children's Hospital, Boston, MA, USA
e-mail: Sriram.Ramgopal@childrens.harvard.edu

8 Garfield Lane East, Andover, MA 01810, USA

Ujjwal P. Ramtekkar Department of Child and Adolescent Psychiatry, Boston Children's Hospital, Harvard Medical School, 300 Longwood Avenue, Fegan 8, Boston, MA 02115, USA
e-mail: Ujjwal.Ramtekkar@childrens.harvard.edu

Harish Rao Sleep Medicine, Boston Children's Hospital, Harvard Medical School, Boston, USA
e-mail: Harish.rao@childrens.harvard.edu

Sachin Relia Division of Child and Adolescent Psychiatry, Medical College of Wisconsin, Milwaukee, WI 53326, USA
e-mail: sachinrelia@gmail.com

6492 Bantry Bay St., Dublin, CA 94568, USA

Orna Tzischinsky Department of Psychology, Emek Yezreel Academic College, Emek Yezreel, 19200 Israel
e-mail: orna@yvc.ac.il

Bradley V. Vaughn Department of Neurology, CB 7025, University of North Carolina, Chapel Hill, NC 27599-7025, USA
e-mail: vaughnb@neurology.unc.edu

Pierguiseppe Vinai Studi Cognitivi Research Group, GNOSIS Non-profit Research Group, v Langhe 64, Magliano Alpi, 12060 Italy
e-mail: piervinai@tin.it

Erick N. Viorritto 299B Hanes House, 330 Trent Drive, Box 102350, Duke University Medical Center, Durham, NC 27710, USA
e-mail: aatif.husain@duke.edu

Keith R. Warren Department of Sleep Medicine, Chicago Sleep Group, Winfield, IL, USA
e-mail: keith.warren@sublung.com

Clarence Watson Department of Psychiatry, Delaware Psychiatric Center, New Castle, DE, USA
e-mail: cwatson@watsonforensics.com

Two Pala Plaza, Ste. 300, Bala Cynwyd, PA 19004, USA

Shelly K. Weiss Division of Neurology, Department of Pediatrics, Hospital for Sick Children, Rm. 6526, Gerrard Wing, 555 University Avenue, Toronto, ON M5G 1X8 Canada
e-mail: shelly.weiss@sickkids.ca

University of Toronto, Toronto, ON M5S 1A1 Canada

Lisa Wolfe Department of Medicine, Northwestern Memorial Hospital, 675 North St. Claire St., Suite 18-250, 60611 Chicago, IL, USA
e-mail: lwolfe@northwestern.edu

Antonio Zadra Department of Psychology, Université de Montréal, C.P. 6128, succ. Centre-ville, Montréal, Quebec, Canada
e-mail: antonio.zadra@umontreal.ca

Center for Advanced Research in Sleep Medicine, Hˆopital du Sacré-Coeur de Montréal, Montréal, Quebec, Canada

Marcin Zarowski Polysomnography and Sleep Research Unit, Department of Developmental Neurology, Poznan University of Medical Sciences, Poznan, Poland
e-mail: marcin.zarowski@gmail.com, zarowski@ump.edu.pl

Department of Neurology, Boston Children's Hospital, Boston, MA, USA

Abbreviations

AD	Alzheimer's disease
ADHD	Attention deficit hyperactivity disorder
ADNFLE	Autosomal dominant nocturnal frontal lobe epilepsy
AED	Antiepileptic drug
ARDS	acute respiratory distress syndrome
ASDs	Autism spectrum disorders
CAP	Cyclic alternating pattern
CAP	Cyclic alternating patterns
CNVH	Complex nocturnal visual hallucinations
CPGs	Central pattern generators
DLB	Dementia with Lewy bodies
EEG	Electroencephalogram
EMG	Electromyography
ENW	Episodic nocturnal wanderings
FLEP	scale Frontal lobe epilepsy and parasomnias scale
GERD	gastroesophageal reflux disease
HH	Hypnagogic hallucinations
HLA	Human leukocyte antigen
ICSD	International classification of sleep disorders
iRBD	idioapathic REM behavior disorder
MSLT	Multiple sleep latency test
NFLE	Nocturnal frontal lobe epilepsy
NPD	Nocturnal paroxysmal dystonia
NREM	Nonrapid eye movement
NTLE	Nocturnal temporal lobe epilepsy
ODD	Oppositional defiant disorder
OSA	Obstructive sleep apnea
PAs	Paroxysmal arousals
PD	Parkinson disease
PH	Peduncular hallucinosis
PLMS	Periodic limb movements of sleep
PLMS/D	Periodic limb movement syndrome/disorder

PSG	Polysomnogram
PSG	Polysomnography
RBD	Rapid eye movement behavior disorder
REM	Rapid eye movement
RLS	Restless legs syndrome
RMD	rhythmic movement disorder
SDB	Sleep disordered breathing
SPECT	Single-proton emission computed tomography
SRE	Sleep-related epilepsy
SRED	sleep-related eating disorder
SSRI	Selective serotonin reuptake inhibitors
SWA	Slow wave activity
UARS	Upper airway resistance syndrome
VPSG	Video-polysomnography

Part I
Overview

Chapter 1
Introduction

Sanjeev V. Kothare and Anna Ivanenko

Sleep has been the one of the most fascinating mysteries in the history of the mankind. Descriptions of sleep-related behaviors date back to the ancient civilizations and can be found in the ancient Egyptian, Greek, Roman, Chinese, and Indian manuscripts. For a long time, behaviors such as sleepwalking and sleep terrors were perceived as dangerous conditions associated with mental disorders. Dreaming, sleep dissociative states, and sleep paralysis were regarded by Aristotele and Plato as demonic and associated with the development of psychopathology [1]. Sleepwalking was thought to be related to hysteria, and for a long time was considered to be a dissociative disorder [2]. Modern research has demonstrated an increased prevalence of parasomnnias among patients with psychiatric disorders. However, parasomnias are now being interpreted as physiological events and not as an expression of psychopathology.

There are two main classification systems that include parasomnias: International Classification of Sleep Disorders (ICSD-2) [3] and Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) [4]. ICSD-2 divides parasomnnias into three main categories: disorders of arousal, parasomnias associated with REM sleep, and other parasomnias. DSM-IV currently includes only four types of parasomnias: nightmare disorder, sleep terrors, sleepwalking, and parasomnnias not otherwise specified. An upcoming DSM-V, although not yet published, is expected to include a wider spectrum of parasomnias including REM behavior sleep disorder.

The term "parasomnia" was first introduced by the French physician Henri Roger in 1932 in the reference to sleep-related behaviors, such as sleep terrors [5]. The word "parasomnia" originates from the Greek words "para" and "somnus" meaning "around sleep". There were early clinical descriptions of various parasomnias made

S. V. Kothare (✉)
Center for Pediatric Sleep Disorders, Department of Neurology,
Boston Children's Hospital, Harvard Medical School,
Boston, MA 02115, USA
e-mail: sanjeevkothare@hotmail.com

A. Ivanenko
Ann & Robert H. Lurie Children's Hospital of Chicago,
225 East Chicago Avenue, Chicago, Illinois 60611-2605, USA
e-mail: aivanenko@sbcglobal.net

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_1,

in 1932 by Kouretas and Scouras as well as Roger, and in 1939 by Nathaniel Kleitman [5–7]. Electroencephalographic (EEG) monitoring of sleep and discovery of REM sleep with subsequent classification of sleep into NREM and REM sleep created a new era in the neurophysiological research of parasomnias.

Sleep related behaviors such as sleep-walking, night terrors, confusional arousals, and head-banging were shown to occur in NREM sleep, especially in slow wave sleep (SWS). Extensive research was conducted in the 1960s to distinguish abnormal nocturnal behaviors such as sleepwalking from epileptic seizures. In his research, Broughton (1968) demonstrated that these behaviors are of nonepileptic origin and should not be mistaken for nocturnal epilepsy [8]. In cases of sleep-related epilepsy, frontal lobe focus is the most common, with mesiotemporal region being less frequently involved. Although both parasomnias and nocturnal epileptic seizures are similar in their semiology, it is critical to distinguish them because treatment for epileptic seizures is quite different from treatment for parasomnias.

More recently, the relationship between sleep-disordered breathing and parasomnias was identified based on several large epidemiological studies. They demonstrated higher rates of obstructive sleep apnea in patients with sleepwalking, nocturnal bruxism, sleep terrors, and confusional arousals [9–12]. Treatment of sleep disordered breathing has been shown to alleviate parasomnias.

There has been significant progress made in the understanding of the genetic influences on parasomnias. Twin studies have indicated higher rate of concordance for sleepwalking in monozygotic twin versus dizygotic twins emphasizing genetic factors in the etiology of parasomnias [13]. Familial cases of sleepwalking, narcolepsy, and REM sleep behavior disorder have also shown to be specific for DQB1 alleles of human leukocyte antigen (HLA) haplo-type [14–16].

Zucconi et al. have proposed cyclic alternating pattern (CAP) as a measure of sleep instability that was later found to be elevated in patients with parasomnias [17]. CAP is an intrinsic oscillation of arousals throughout NREM sleep that typically occurs every 20–40 s. It provides physiological background for normal sleep phenomena such as K complexes and to pathological events such as sleepwalking or confusional arousals. CAP has been proposed as a measure of NREM sleep instability and as a biomarker of treatment response. For example, CAP rate decreases significantly in response to continuous positive airway pressure (CPAP) therapy in patients with obstructive sleep apnea and associated sleepwalking. Quantitative EEG analysis of sleep conducted in patients with chronic parasomnias showed a decrease in delta power during the first and second NREM sleep cycle [18, 19]. This suggests that NREM instability is characteristic of patients with parasomnias.

Polysomnographic research of sleep related behaviors resulted in differentiation of NREM and REM related parasomnias. In 1987, a new category of parasomnia named “REM sleep behavior disorder” was introduced in the medical literature [20]. REM sleep behavior disorder represents a dissociation of physiological features of REM sleep with disappearance of normal atonia of REM sleep while other characteristics of REM sleep are still present. Clinical state dissociation has been proposed as the neurophysiological basis for REM behavior sleep disorder and for the disorders of arousal [21]. This model implies a mixture of wakefulness and NREM sleep or REM sleep with varying degrees of behaviors and autonomic arousal present at the

same time. It supports the concept that sleep is not a "whole-brain" phenomenon, but, rather, sleep and wakefulness can co-occur in different brain regions simultaneously [21]. Intracerebral EEG recordings performed during NREM parasomnia have provided support for the concept of "local" sleep in the etiology of parasomnias [22]. Neuroimaging studies using positron emission tomography (PET), functional magnetic resolution imaging (fMRI), and single-photon emission computed tomography (SPECT) have brought additional insight to pathophysiology of parasomnias. They demonstrated the associated activation or deactivation in certain regions of the brain during episodes of parasomnia [23].

The growing understanding of parasomnias has resulted in an increased rate of recognition and treatment of these conditions that are frequently chronic and debilitating. Although parasomnias occur predominantly at night, they may have a significant impact on the patient's social/emotional functioning as well as academic and vocational performance. Children and adolescents are especially vulnerable to parasomnias that can be severe and persistent at a young age causing significant sleep fragmentation and sleep loss.

Violent behaviors associated with some forms of parasomnia have significant medicolegal ramifications. A new field of sleep medicine, forensic sleep medicine, has emerged in response to a growing need to deal with the medicolegal aspects of parasomnias that may present with the significant risk of self-harm or potential risks of injury to others.

Sleep-related eating disorder (SRED) is characterized by food ingestion after an arousal from nighttime sleep. It has been recognized at a growing rate among patients of all ages. Night eating syndrome (NES) is associated with abnormal circardian rhythm of meal-time while patients have a complete awareness of their behavior and a normal time of sleep onset. SRED and NES are often associated with other sleep disorders and were shown to be frequently associated with restless leg syndrome (RLS) [24]. An overlap between the symptomatology and the polysomnographic characteristics of SRED and NES were demonstrated in a recent study providing new insights to the pathophysiology of nocturnal eating behaviors [25].

Although there has been significant progress made in the understanding of pathophysiology as well as differential diagnosis and assessments of parasomnias, the therapeutic options have remained limited. However, there has been more evidence-based research done on the behavioral interventions and educational strategies for parasomnias. These studies show the effectiveness of behavioral therapy in reducing the frequency of sleep-related behaviors and in lowering risks of injury associated with parasomnias. Known pharmacological therapies include benzodiazepines and antidepressants. Nonpharmacological interventions consist of hypnosis and scheduled awakenings. There have been a growing number of studies exploring the effectiveness of alternative therapies for parasomnias.

The goal of this volume is to provide a comprehensive review of pathophysiological, epidemiological, developmental, clinical, and medico-legal aspects of parasomnias across the lifespan. This book aims to be academically rigorous and clinically useful to practicing clinicians who treat patients with sleep disorders. Special attention is given to pediatric presentations of parasomnias and types of treatments available for children and adolescents suffering from parasomnias.

The book is designed into eight sections. The first section covers epidemiology, pathophysiology, classification, and diagnostic approach to parasomnias. The second section focuses on arousal disorders covering clinical characteristics and neurophysiological features of sleepwalking, confusional arousals, and sleep terrors in adults and among children and adolescents. The third section of the book provides an overview of sleep–wake transition disorders with comprehensive discussion of sleep starts and sleep-talking. The fourth section deals with parasomnias associated with REM sleep. It covers neurobiological and psychological functions of dreams and describes clinical characteristics of nightmare disorder and REM-behavior sleep disorder in both pediatric and adult population of patients. Separate chapters are dedicated to sleep-related hallucinations and recurrent isolated sleep paralysis with a detailed overview of prevalence, differential diagnosis, and available treatments for these conditions.

Section five of the book covers parasomnias classified as Others in the ICSD-2 and includes paroxysmal nocturnal dystonia, sleep-related dissociative disorder, sleep bruxism, sleep enuresis, sleep-related eating disorder, and overlap parasomnias. The authors of these chapters have provided an extensive review of these medical conditions with the guidelines on how they should be differentiated based on their clinical presentation and neurophysiological findings. Special attention is devoted to frontal lobe epilepsy and other forms of nocturnal epilepsy that may present similarly to parasomnias. Additionally, several chapters in section six cover a variety of medical, neurological, and psychiatric disorders presenting with parasomnias and provide clinical algorithm to differential diagnosis of other sleep disorders and parasomnias. Treatment interventions are covered in section seven of the book and include non-pharmacological, pharmacological, and alternative medicine interventions currently known to be effective for parasomnias. Finally, section eight of this volume deals with the very important medicolegal aspects related to parasomnias. It introduces the readers to the issues of safety, patient advocacy, expert testimonies, education, and prevention regarding complicated clinical cases of sleep-related behaviors.

All chapters have illustrative cases and practical points at the end of each chapter, which we believe will enhance the reading and learning experience of the clinician.

We are honored to edit this volume and would like to thank an outstanding panel of authors for their contributions to the book. We hope that this book will contribute to our growing knowledge on sleep disorders and spur additional interest in sleep medicine among clinicians of different specialties that are dealing with patients who suffer from sleep problems.

References

1. Roccatagliata G. A history of ancient psychiatry. Westport, Connecticut: Greenwood Press; 1986. pp. 107, 108, 216.
2. Ellenberger H. The discovery of the unconscious: the history and evolution of dynamic psychiatry. New York: Basic Books; 1970.
3. American Academy of Sleep Medicine. International classification of sleep disorders: diagnostic and coding manual. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.

4. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 2000.
5. Roger H. Les Troules du Sommeil. Paris: Masson et Cei; 1932. pp. 275–83.
6. Kouretas D, Scouras P. Sur un trouble particulier du sommeil: le cauchemar. Encephale. 1932,7:622–7.
7. Kleitman N. Sleep and wakefulness. Chicago: University of Chicago Press; 1939. pp. 280–9.
8. Broughton RJ. Sleep disorders: disorders of arousal? Enuresis, somnambulism, and nightmares occur in confusional states of arousal, not in "dreaming sleep". Science. 1968;159:1070–8.
9. Ohayon M, Guilleminault C, Priest R. How frequent are night terrors, sleep walking and confusional arousals in the general population: their relationship to other sleep and mental disorders. J Clin Psychiatry. 1999;60:268–76.
10. Ohayon MM, Li KK, Guilleminault C. Risk factors for sleep bruxism in the general population. Chest. 2001;119:53–61.
11. Espa F, Dauvilliers Y, Ondze CB, Billiard M, Besset A. Arousal reactions in sleepwalking and night terrors in adults: the role of respiratory events. Sleep. 2002;25:871–5.
12. Goodwin JL, Kaeming KL, Fregosi RF, Rosen GM, Morgan WJ, Smith T, et al. Parasomnias and sleep disordered breathing in Caucasian and Hispanic children—the Tucson children's assessment of sleep apnea study. BMC Med. 2004;2:14.
13. Bawkin H. Sleep-walking in twins. Lancet. 1970;2(7670):446–7.
14. Schenck CH, Garcia-Rill E, Segall M, Noreen H, Mahowald MW. HLA class II genes associated with REM sleep behavior disorder. Ann Neurol. 1996;39(2):261–3.
15. Rogers AE, Meehan J, Guilleminault C, Grumet FC, Mignot E. HLA DR15(DR2) and DQB1*0602 typing studies in 188 narcoleptic patients with ctaplexy. Neurology. 1997;48(6):1550–6.
16. Lecendreux M, Bassetti C, Dauvilliers Y, Mayer G, Neidhart E, Tafti M. HLA and genetic susceptibility to sleepwalking. Mol Psychiatry. 2003;8(1):114–7.
17. Zucconi M, Oldani A, Ferini-Strambi L, Smirne S. Arousal fluctuation in non-rapid-eye-movement parasomnia: the role of the cyclic alternating pattern as a measure of sleep instability. J Clin Neurophysiol. 1995;12:147–54.
18. Gaudreau H, Joncas S, Zadra A, Montplaisir J. Dynamics of slow-wave activity during the NREM sleep in sleepwalkers and control subjects. Sleep. 2000;23:755–60.
19. Guilleminault C, Poyares D, Abat F, Palombini L. Sleep and wakefulness in somnambulism, a spectral analysis study. J Psychosomat Res. 2001;51:411–6.
20. Schenck CH, Bundlie SR, Patterson AL, Mahowald MW. Rapid eye movement sleep behavior disorder: a treatable parasomnia affecting older adults. JAMA. 1987;257:1786–9.
21. Mahowald MW, Bornemann MA, Schenck CH. State dissociation, human behavior, and consciousness. Curr Top Med Chem. 2011;11:2391–402.
22. Terzaghi M, Sartori I, Tassi L, Didato G, Rustioni V, LoRusso G, et al. Evidence of dissociated arousal states during NREM parasomnia from as intracerebral neurophysiological study. Sleep. 2009;32(3):409–12.
23. Bassetti C, Vella S, Donati F, Wielepp P, Weder B. SPECT during sleepwalking. Lancet. 2000;356(9228):484–5.
24. Howell MJ, Schenck CH. Nocturnal eating and sleep related eating disorders are common in patients with restless legs syndrome. Sleep. 2010;11(6):583–5.
25. Vinai P, Ferri R, Ferini-Strambi L, Cardetti S, Anelli M, Vallauri P, et al. Defining the borders between Sleep-Related Eating Disorder and Night Eating Syndrome. Sleep Med. 2012;13(6):686–90.

Chapter 2
Pathophysiology of Parasomnias

Suresh Kotagal

Introduction

Parasomnias may occur at the transition from wakefulness to non-rapid eye movement (NREM) sleep, e.g., hypnic starts, during NREM sleep, e.g., teeth grinding, head banging, sleep walking, confusional arousals, and sleep terrors, or during rapid eye movement or REM sleep, e.g., nightmares and REM sleep behavior disorder [1, 2]. The occurrence of parasomnias in preschool age children is almost ubiquitous. In a series of approximately 1000 children followed prospectively between the ages of 2 and 6 years, Petit et al. found that 88 % of children in their cohort had manifested at least one parasomnia during the study period [3]. The highest incidence of parasomnias is in preschool age children, with a gradual reduction into later childhood. Adults also experience parasomnias, though to a lesser degree than children. The observations of Mahowald and Schenck underscore the point that one of the key features of parasomnias is the dissociation of behaviors characteristic of one state (wakefulness/REM sleep or NREM sleep) and their superimposition on to another state [1].

No satisfactory theory explains the clustering of NREM parasomnias into early childhood. A valid theory in this regard must explain the relative paucity of NREM parasomnias during the first 12 months of life, their frequent occurrence in preschool age children, and the gradual dissipation during the second decade.

Phylogenic Aspects

The Tendency for Dissociation of Elements Sleep and Wakefulness States Is Ubiquitous

Instead of *sequentially* manifesting wakefulness and sleep, some marine mammals manifest these states *simultaneously*, such as during the process of unihemispheric

S. Kotagal (✉)
Division of Child Neurology, Mayo Clinic, 200 First Street,
SW, Rochester, MN 55905, USA
e-mail: kotagal.suresh@mayo.edu

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_2,

sleep. This temporal co-occurrence of wakefulness and sleep in marine mammals subserves thermoregulation and the maintenance of vigilance during continuous living in the aquatic environment. Unihemispheric sleep has been documented in bottle nosed dolphins, seals, beluga whales, and killer whales [4, 5]. In the beluga whale and the dolphin, the hemisphere contralateral to the eye that is kept open and out of the water remains awake, while the opposite hemisphere remains asleep [5]. Terrestrial mammals transition to bihemispheric sleep, with presence of high voltage activity on the electroencephalogram (EEG) during NREM sleep [6]. A tendency to retain some electrophysiological properties of wakefulness even during sleep persists in precocial species mammals such as the elephant and the giraffe, which routinely manifest sleep state dissociation in the form of sleeping while standing [7, 8]—a feat that requires the maintenance of balance and tonic lower extremity extensor muscle contraction while still asleep.

Ontogenic Aspects

Sleep State Dissociation Is Highly Prevalent in Human Newborns and Infants

The maturation of human neonatal REM and NREM bihemispheric sleep emerges in utero from a background of undifferentiated, spontaneous fetal activity, [9, 10], which has also been termed "pre-sleep" by Hamburger [9]. With progressive maturation of the prematurely born infant, the independent oscillations of neuronal activity, autonomic function, and overt behavior become cohesively organized into distinct sleep states termed active and quiet sleep (synonymous with REM and NREM sleep respectively) [11]. An overlap between sleep states (sleep–wake dissociation) is fairly common in full-term babies, however, and about 5 % of newborn sleep is characterized as "indeterminate" during which there is intermingling of elements of both active and quiet sleep [12]. With progressive cortical maturation, indeterminate sleep resolves over the ensuing weeks.

An important feature of human newborn sleep is the presence of stereotyped, nonepileptic patterns of behavior such as nonnutritive sucking or bicycling which represent the intrusion of patterns of wakefulness onto sleep (sleep–wake dissociation) [13, 14]. These behaviors remain fragmentary and subtle, however, simply because the synaptically immature cortical neuronal network, cerebellar system, and incomplete myelination of the pyramidal tracts limit outward expression of sustained motor activity. Indeed the period from birth to 12 months may be a "silent period" from the standpoint of paucity of expression of the results of sleep state dissociation in the form of NREM parasomnias.

Central Pattern Generators As Mediators of Stereotyped NREM Sleep Behaviors

Sleep state dissociation may lead to stereotypic motor activity during NREM sleep in the form such as sleep walking [1]. The generation of stereotyped movements at the spinal cord level levels is due to activation of networks of interneurons and motor neurons that are also referred to as central pattern generators (CPGs) [15–17]. The spinal CPGs must however be activated by rostral, evolutionarily conserved command centers that are located in mesopontine and diencephalic regions [16]. Stimulation of these regions gives rise to walking, trotting, or galloping in cats, depending upon stimulation strengths [16]. Rhythmic suckling in newborn animals can be generated by activation of rhombomeres containing the VII and XII cranial nerve nuclei [18]. The CPG for fictive mastication, which may be relevant to bruxism (teeth grinding), is located in the pons and medulla, with projections to the motor nucleus of the cranial nerve V, and cranial nerves VII and XII [19]. Based upon the entire genome analysis, it has now been established that expression of the CPG for another stereotypic motor sleep pattern, i.e., periodic limb movements in sleep, which is most likely localized to the spinal cord, is mediated by an intronic variant on the *BTBD9* (*broad complex, tramtrack, and bric-a-brac*) gene complex that is located on chromosome 6p21.2 [20]. It has been established that stereotyped patterns of movement such as walking can be generated in segments of the mammalian sacral spinal cord even after it has been deafferented—these spinal generators might be relevant to the phenomenon of sleep walking [21]. *Based upon the type of CPG that has been activated, one may therefore observe clinical sleep phenomena such as periodic limb movements, sleep walking, rhythmic movement disorder, head banging, or bruxism.*

The input received by CPGs is both glutaminergic and serotonergic [16, 21, 22]. The application of NMDA receptor antagonists to regions of the spinal cord leads to suppression of the activity of spinal CPGs [23]. Descending serotonergic projections from the raphe nucleus to the spinal cord also play a role in inhibiting spontaneous and synchronous rhythmic activities of the spinal level [24, 25]. Genetic factors [20] and sleep disorders such as sleep disordered breathing may also activate spinal or brainstem CPGs.

Does Synaptic Pruning Trigger Childhood NREM Parasomnias?

Why NREM parasomnias abruptly start becoming manifested by 2–3 years of age is unclear. It has been established however that around 8 months in the human visual cortex and by 24 months in the frontal cortex, there is commencement of a process of synaptic pruning which removes redundant excitatory and inhibitory synapses. Approximately 40 % of synapses in the cerebral cortex are eliminated through this process, which is complete by age of 11 years [26–28]. This synaptic pruning process occurs in the cerebrum, cerebellum, as well as in the brainstem. The elimination of

unwanted synapses is an important facet of plasticity of the developing nervous system. At least in the cerebellum, activation of the NMDA type of glutamate receptors is involved in synapse elimination [25]. Concurrently, a process of programmed cell death is also initiated in the cerebrum. Both programmed cell death and synaptic pruning are physiologic and adaptive processes that limit competition for trophic factors and eliminate aberrantly developed connections [25].

Starting around 2 years of age, therefore, a genetic predisposition to sleep state dissociation and activation in sleep of subcortical CPGs, especially when combined with activation of these CPGs (e.g., from sleep apnea, gastroesophageal reflux, or periodic limb movement activity), may trigger patterns of abnormal motor behavior that are characterized as confusional arousals, sleep terrors, or sleep walking. Downregulation of descending cortical to subcortical inhibitory projections that have GABAergic properties or a relative deficiency of serotonergic inhibition at the level of the spinal cord may play a key role in disinhibiting brainstem or spinal cord CPGs, the consequence of which is NREM parasomnias.

This sequence of events, though very plausible, may be difficult to confirm. It is well recognized however that synaptic reorganization during early childhood plays a role in triggering another episodic phenomenon—epilepsy [29]. The hypothesis suggested in this chapter is further supported by the prompt resolution of NREM parasomnias upon treatment with GABA agonists such as clonazepam. Over the first decade and a half, concurrent with progressive maturation of these GABAergic inhibitory projection systems, parasomnias gradually subside. In adults with neurodegenerative processes of the brainstem, there may however be reactivation of brainstem CPGs during sleep and their clinical expression as parasomnias.

The *BTBD9* gene complex that has been established on the basis of whole genome analysis as being involved in the pathogenesis of periodic limb movement disorder is evolutionarily conserved from the *Drosophila.* It is involved in repression of transcription, cytoskeleton regulation, gating of ion channels and ubiquitin dependent protein degradation [30]. It is possible that hitherto undiscovered genes that are involved in the expression of other stereotypic patterns of human behavior in sleep characteristic of NREM parasomnias are also of the same lineage. The search for the genetic basis of NREM parasomnias might need to focus on evolutionarily conserved, homeobox genes that mediate the activity of central pattern generators. From marine mammals to humans, the dictum that ontogeny recapitulates phylogeny may once again hold true!

REM Parasomnias

The pathophysiology of nightmares or “bad dreams” and REM sleep behavior disorder is less clear than that of the NREM parasomnias. Anxiety has been implicated as a risk factor for nightmares. Pagel has characterized dreaming as a complex cognitive state that is affected by a variety of social, medical, or psychological variables [31]. He also indicates that evidence of dream content and its effect on

wakefulness is hard to obtain in children [31]. This has likely impeded our understanding of childhood nightmares. Nightmare focused cognitive behavioral therapy (with exposure and image rehersal therapy) have better outcome indirect therapies such as relaxation [32].

With regard to REM sleep behavior disorder (RBD) in childhood, what we do know is that in contrast to adults, there is no association with synucleinopathies such as dementia with Lewy body disease or Parkinson disease. RBD may however appear in the early stages of childhood narcolepsy–cataplexy, or with structural brainstem disease, such as neoplasms and Chiari malformations. RBD has also been reported in children with neurodevelopmental disabilities such as autism and Smith Magenis syndrome [33]. Drugs like risperidone and selective serotonin reuptake inhibitors might also predispose to RBD. The repertoire of motor behavior in childhood RBD seems less violent and complex as compared to that of adults (author's opinion). Typically, yelling, thrashing about in sleep, and in some rare occasions, violence directed at a co-sleeping sibling are encountered. Some patients may not show clinical RBD symptoms, but may possess only the polysomnographic correlate, i.e., REM sleep without atonia. It is therefore important to routinely pay close attention to the chin and leg electromyogram during the scoring of children's polysomnograms for evidence of increased muscle tone. The pathophysiology of childhood RBD, though not confirmed, is likely similar to that of adults, with dysfunction of the "REM-off" neurons that are located in the dorsolateral pontine tegmentum. This could lead to uninhibited transmission of descending motor impulses through the brainstem to the spinal cord and activation of motor behaviors.

Practical Points

- The sleep–wake history is key to making a specific parasomnia diagnosis. It can be supplemented by video clips of the events recorded by the parents in the home environment.
- In the case of recurrent and problematic arousal parasomnias, it is helpful to determine if an increased tendency for arousals has developed as a consequence of obstructive or central sleep apnea, gastroesophageal reflux, or periodic limb movement disorder. Treating these underlying triggers may lead to resolution of the arousal parasomnia.
- Since nocturnal seizures can mimic parasomnias, a 16-channel EEG montage should be utilized during polysomnography whenever possible.

Conclusion

The pathophysiology of parasomnias is multifactorial, related to an interplay of genetic and environmental factors. Both phylogenic and ontogenic aspects need also to be considered in arriving at a comprehensive understanding of these sleep-related phenomena.

References

1. Mahowald MW, Schenck CH. Dissociated states of wakefulness and sleep. Neurology. 1992;42(7 Suppl 6):44–51.
2. Mahowald MW, Schenck CH. Insights from studying human sleep disorders. Nature. 2005;437:1279–85.
3. Petit D, Touchette E, Tremblay RE, Boivin M, Montplaisir J. Dyssomnias and parasomnias in early childhood. Pediatrics. 2007;119:e1016–25
4. Sekiguchi Y, Koshima S. Resting behaviors of captive bottlenose dolphins (Tursiops truncatus). Physiol Behav. 2003;79:643–53.
5. Lyamin OI, Mukhametov LM, Siegel JM. Relationship between sleep and eye state in cetaceans and pinnipeds. Archives Italiennes de Biologie. 2004;142:557–68.
6. Siegel JL. Clues to the function of mammalian sleep. Nature. 2005;237:1264–71.
7. Tobler I. Is sleep fundamentally different between mammalian species? Behav Brain Res. 1995;69:35–41.
8. Tobler I. Behavioral sleep in the Asian elephant in captivity. Sleep. 1992;15:1–12.
9. Hamburger V. Fetal behavior. In: Hafez ES, editor. The mammalian fetus: comparitive biology and methodology. Springfield: Charles C. Thomas; 1975. pp. 69–81.
10. Frank MG, Heller C. The ontogeny of mammalian sleep: a reappraisal of alternative hypotheses. J Sleep Res. 2003;12:25–34.
11. Parmelee AH, Wenner WH, Akiyama Y, Schultz M, Stern E. Sleep states in premature infants. Dev Med Child Neurol. 1967;9:70–77.
12. Ellingson RJ. EEGs of premature and full-term newborns. In: Klass DW, Daly DD, editors. Current practice of clinical electroencephalography. New York: Raven Press; 1979. pp. 149–177.
13. Saraga M, Resic B, Krnic D, Jelavic T, Krnić D, Sinovcić I, et al. A stereotypic “elbowing” movement, a possible new primitive reflex in newborns. Pediatr Neurol. 2007;36:84–87.
14. Hafstrom M, Kjellmer I. Non-nutritive sucking in sick pre-term infants. Early Hum Dev. 2001;63:37–52.
15. Grillner S. Neurobiological bases of rhythmic motor acts in vertebrates. Science. 1985;228:143–49.
16. Grillner S, Wallen P, Saitoh K, Kozlov K, Robertson B. Neural bases of goal directed locomotion in vertebrates—an overview. Brain Res Rev. 2008;57:2–12.
17. Rossignol S, Dubuc R, Gossard JP. Dynamic sensorimotor interactions in locomotion. Physiol Rev;2006;86:89–154.
18. Nakamura Y, Katakura N, Nakajima M, Liu J. Rhythm generation for food-ingestive movements. Prog Brain Res. 2004;143:97–103.
19. Lund JP, Kolta A. Brainstem circuits that control mastication: do they have anything to say during speech? J Commun Disord. 2006;39:381–90.
20. Stefansson H, Rye DB, Hicks A, Petursson H, Ingason A, Thorgeirsson TE, et al. A genetic risk factor for periodic limb movements in sleep. N Engl J Med 2007;357:639–47.
21. Mor Y, Lev-Tov A. Analysis of rhythmic patterns produced by spinal neural networks. J Neurophysiol. 2007;98:2807–17.
22. Gezelius H, Wallen-Mackenzie A, Enjin A, Lagerstrom M, Kullander K. Role of glutamate in locomotor rhythm generating neuronal circuitry. J Physiol Paris. 2006;100:297–303.
23. Cramer NP, Li Y, Keller A. The whisking rhythm generator: a novel mammalian network for the generation of movement. J Neurophysiol. 2007;97:2148–58.
24. Cowley KC, Zaporozhets E, Maclean JN, Schmidt BJ. Is NMDA receptor activation essential for the production of locomotor-like activity in the neonatal spinal cord? J Neurophysiol. 2005;94:3805–14.
25. Branchereau P, Chapron J, Meyrand P. Descending -hydroxytryptamine raphe inputs repress the expression of serotonergic neurons and slow the maturation of inhibitory systems in mouse embryonic spinal cords. J Neurosci. 2002;22:2598–606.

26. Volpe JJ. Neuronal proliferation, migration, organization and myelination. In: Volpe JJ, editor. Neonatal neurology. Philadelphia: WB Saunders; 1995. pp. 73–4.
27. Cruz DA, Eggan SM, Lewis DA. Postnatal development of pre and post synaptic GABA markers at chandelier cell connections with pyramidal neurons in monkey prefrontal cortex. J Comp Neurol. 2003;465:385–400.
28. Huttenlocher PR, de Courten C. The development of synapses in the striate cortex of man. Human Neurobiol. 1987;6:1–9.
29. Swann JW, Pierson MG, Smith KL, Lee CL. Developmental neuroplasticity: roles in early life seizures and chronic epilepsy. Advance Neurol. 1999;79:203–16.
30. Stogios PJ, Downs GS, Jauhal JJ, Nandra SK, Prive GG. Sequence and structural analysis of BTB domain proteins. Genome Biol. 2005;6(10):R82.
31. Pagel JF. What physicians need to know about dreams and dreaming. Curr Opinion Pulm Med. 2012;18(6):574–9.
32. Lancee J, Spoormaker VI, Krakow B, van den B. A systematic review of cognitive behavioral therapy for nightmares: toward a well established treatment. J Clin Sleep Med. 2008;4(5):475–80.
33. Lloyd R, Tippman-Piekert M, Slocumb N, Kotagal S. Characteristics of REM sleep behavior in childhood. J Clin Sleep Med. 2012;8:127–31.

Chapter 3
Classification of Parasomnias

Erick N. Viorritto and Aatif M. Husain

Introduction

Parasomnias are described in the International Classification of Sleep Disorders, 2nd edition (ICSD-2) as "undesirable physical events or experiences" that occur during sleep itself or during transition into or arousal out of sleep [1]. The phenomena contained within this category of disorders may include movements, autonomic disturbances, emotional experiences, abnormal perceptions, behaviors, or combinations of these component features. It is not surprising then that parasomnias include an array of disorders with varied presentations.

Given the broad nature of the definition, there is significant overlap between parasomnias and other sleep disorders. The initial ICSD included many clinical entities as parasomnias that have subsequently been reclassified in ICSD-2. For example, sleep related bruxism and sleep related leg cramps have been moved into a different category, the sleep related movement disorders [1, 2]. In this chapter, an outline of the various parasomnias will be presented according to the categorization used by the ICSD-2. Details of the various parasomnias discussed here, including their management, will be presented in subsequent chapters.

Categories of Parasomnia

The current classification scheme separates parasomnias based upon the sleep stage in which they predominantly occur [1] (Table 3.1). Under this system, the disorders are divided into (1) non-rapid eye movement (NREM) parasomnias, such as disorders

A. M. Husain (✉)
299B Hanes House, 330 Trent Drive, Box 102350,
Duke University Medical Center, Durham, NC 27710, USA
e-mail: aatif.husain@duke.edu

E. N. Viorritto
Department of Medicine (Neurology), Duke University Medical Center,
Durham, NC 27710, USA
e-mail: erick.viorritto@duke.edu

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_3,

Table 3.1 Categories of parasomnias according to the International Classification of Sleep Disorders, 2nd edition. (Source: Data from [1])

Categories of parasomnias	
Non-REM parasomnias	Confusional arousals Sleepwalking Sleep terrors
Parasomnias associated with REM sleep	REM sleep behavior disorder Recurrent isolated sleep paralysis Nightmare disorder
Other parasomnias	Sleep related dissociative disorder Sleep related groaning (Catathrenia) Exploding head syndrome Sleep related hallucinations Sleep related eating disorder Sleep enuresis Parasomnia: unspecified Parasomnia due to drug or substance Parasomnia due to medical condition

of arousal, (2) disorders associated with rapid eye movement (REM) sleep, and (3) other parasomnias, a category that includes parasomnias that occur independent of sleep stage. Another useful distinction is that of separating primary parasomnias from parasomnias secondary to drugs or substances, and parasomnias secondary to general medical conditions.

NREM Parasomnias

NREM parasomnias include disorders of arousal as well as disorders of sleep–wake transition. The disorders of arousal are the most common parasomnias [3] and include confusional arousals, sleep terrors, and sleepwalking. These parasomnias are more common in childhood and usually resolve as the child gets older. A feature of parasomnias within this category is their exacerbation by things that deepen sleep such as CNS depressants and rebound from sleep deprivation, as well as by features that increase the number of arousals one experiences [4]. Other sleep disorders, such as periodic leg movements and sleep apnea, can serve to increase disorders of arousal in this way [4]. Because NREM sleep is more common in the first third of the night, the behaviors associated with NREM parasomnias tend to emerge during this time period [5]. Thus, the time of occurrence can provide a clinical clue when evaluating a patient with unusual nighttime behavior.

Confusional Arousals These brief episodes, generally lasting less than 10 minutes, present as confusion, disorientation, inappropriate responses to external stimuli, and impaired perception [6]. While the individual may exhibit some automatisms, the

fearfulness characteristic of sleep terrors is absent, as is the complex motor activity that is seen in sleepwalking. The episodes are followed by a period of retrograde amnesia to the event.

Sleepwalking Sleepwalking, or somnambulism, shares the impaired responsiveness and disorientation seen in other NREM parasomnias. Its hallmark is complex motor activity, in which the individual gets up from bed and begins to walk about. Other complex behaviors such as cooking and driving may be seen, however the individual exhibits a degree of clumsiness and lack of attention to their surroundings which can result in severe injury from falling over furniture or down stairs, or cutting oneself on broken windows or mirrors. Episodes last around 15 minutes but longer events lasting hours have been reported [6]. Episodes of sleep walking violence, including homicides, have also been reported [7]. Sleep sex (also referred to as sexsomnia) has also been increasingly reported as a subset of sleepwalking with particular forensic implications [8]. As in confusional arousals, complete amnesia to the event is typical upon waking [6].

Sleep Terrors Sleep terrors are abrupt events in which the individual sits up, appearing frightened, and often screams. There is evidence of sympathetic arousal with dilated pupils and tachycardia, and the individual is usually inconsolable [6]. Despite appearing awake, the individual is unresponsive to external stimuli, just as with confusional arousals and sleepwalking. After a period of seconds to 2–3 minutes, he or she will usually return to sleep and have amnesia to the event on waking [6].

REM Parasomnias

This category contains three disorders that are associated with REM sleep. Two of the disorders (REM sleep behavior disorder (RSBD) and recurrent isolated sleep paralysis) represent dyscoordination of the atonia that is a hallmark of normal REM sleep. The third parasomnia associated with REM sleep is nightmare disorder [1]. Because REM sleep is more common in the latter part of the night, these disorders typically occur in the second half of the sleep time.

REM Sleep Behavior Disorder

RSBD is characterized loss of the normal skeletal muscle atonia during REM sleep, with subsequent dream-enactment behavior. Upon waking, individuals can usually recall the dream but do not remember acting it out. Unlike most other parasomnias, RSBD is more common as individuals get older and has a strong male predominance. It is often associated with other neurological conditions, most classically Parkinson disease, but can also be seen independently [9]. An association of RSBD with psychiatric disorders, particularly posttraumatic stress disorder, has been noted as well [10].

Recurrent Isolated Sleep Paralysis

Where RSBD is the inappropriate loss of REM-related skeletal muscle atonia, recurrent isolated sleep paralysis represents the presence of skeletal muscle atonia inappropriately in the setting of wakefulness. The episodes occur most frequently at the beginning of the sleep period, with another peak near the end of the sleep period. While gross movements are impossible, the individual is often able to open his or her eyes and remains aware of the surroundings. These episodes resolve spontaneously after a few minutes, and in some individuals may be aborted by tactile stimulation [6]. These episodes are classically seen in association with narcolepsy, but can also be seen in normal individuals, especially in conjunction with changes in sleep schedule or other sleep disruptions.

Nightmare Disorder

Frequent awakening from sleep with recall of frightening dreams is the hallmark of nightmare disorder. There is full-alertness on awakening without confusion or disorientation, in contrast to sleep terrors where the individual will appear anxious and fearful but also have impaired responsiveness. The individual with nightmare disorder has clear recall of his or her dream. Nightmares are usually accompanied by delayed return to sleep after the episode, and they often occur in the second half of the night. Both these characteristics help differentiate nightmare disorder from sleep terrors [1].

Other Parasomnias

The third category of parasomnias recognized in ICSD-2 consists of a diverse group of phenomena that do not have a restriction to either REM or NREM sleep.

Sleep Related Dissociative Disorder

Dissociation, the immature psychological defense mechanism of isolating traumatic or distressing experiences, manifests in five categories according to the Diagnostic Statistical Manual of Mental Disorders, Fourth edition (DSM-IV). These are dissociative amnesia, dissociative identity disorder, dissociative fugue, depersonalization disorder, and dissociative disorder not otherwise specified [11]. Of these, dissociative identity disorder, dissociative fugue, and dissociative disorder NOS have been associated with sleep-related episodes [12]. These episodes occur during wakefulness, in the period immediately prior to sleep onset or after awakening. The spectrum of behaviors that can be exhibited during a dissociative episode can include agitation,

fugue states in which the patient will leave the home and travel without being able to recall the details of their past, or show the emergence of distinct personalities that control their behavior. Many patients with sleep-related dissociative episodes will also exhibit daytime episodes, and have a history of traumatic events such as abuse.

Sleep Related Groaning (Catathrenia)

In sleep related groaning, the individuals exhibit prolonged expiratory groaning during sleep. Most individuals with this parasomnia exhibit these episodes on a nightly basis, and do not show any movements or respiratory distress, and patients do not report dreaming in association with the episodes. For many individuals, the catathrenia arises both during REM and NREM sleep [13, 14].

Exploding Head Syndrome

Exploding head syndrome (EHS) is a typically benign condition in which the individual experiences a loud noise, occasionally accompanied by a flash of light, or a sudden jerk during drowsiness or sleep onset. While usually painless, it may be accompanied by a brief stab of pain [1]. The episodes are benign and generally resolve on its own, and are may be a sensory variant of the hypnic jerk.

Sleep Related Hallucinations

Hallucinations occurring in relation to sleep are termed hypnagogic if they occur during sleep onset, and hypnopompic if they occur on waking from sleep. These hallucinations are most commonly visual; however, other sensory modalities can also occur. For example, a common kinetic hallucination is of falling down an abyss [15]. While hallucinations can be seen in a large proportion of individuals with narcolepsy [16], they are also quite common in the general population, occurring in up to 39 % of individuals [15].

Another form of sleep related hallucinations are complex nocturnal visual hallucinations that generally occur when an individual awakens during the night. They are visual in nature, and individuals report distorted images of people or animals; the individual often has impaired insight into the nature of the hallucination [17]. Complex visual hallucinations may be idiopathic or associated with other diseases of the central nervous system, in which case the hallucinations may not be limited to the nighttime [17]. Associated disorders include alpha-synucleinopathies (dementia with Lewy bodies, Parkinson disease) as well as in the setting of severe vision loss, such as Charles Bonnet Syndrome.

Sleep Related Eating Disorder

Sleep related eating disorder consists of recurrent episodes of uncontrollable eating and drinking during the night [1]. Individuals may have full awareness during the episode, or they may occur in the setting of a confusional awakening after which the patient goes back to sleep with impaired recollection the next morning [18]. Individuals usually report an uncontrollable drive to eat rather than hunger as the force behind their behavior and preferentially seek out high calorie items. Adverse effects can come from the ingestion of toxic or non-food items, injuries from getting up to seek food at night or from performing dangerous activities while cooking food [18]. Other consequences can include daytime fatigue from frequent awakenings, weight gain, and morning anorexia. This parasomnia often has a chronic course.

Sleep Enuresis

Sleep enuresis is defined in the ICSD-2 as recurrent involuntary voiding of urine during sleep at least twice per week for a minimum of three consecutive months. The individual must be at least 5 years of age [1]. A distinction is made between incontinence, which is an uncontrolled leakage of urine, and enuresis, which is intermittent incontinence restricted to sleep. Classification of this disorder can also be primary, in which the individual has never had a period of dry sleep, versus secondary, in which a child has developed a period of at least 6 months in which they have slept through the night without enuresis but later develop nocturnal enuresis.

Parasomnia Due to Drug or Substance

The ICSD-2 lays out principles for the diagnosis of parasomnia due to drug or substance [1]. There must be a close association between exposure and onset of the parasomnia. The parasomnia can either be a new parasomnia for the individual or a worsening of or re-emergence of a previously diagnosed parasomnia. The parasomnias most commonly associated with substances are the disorders of arousal, sleep-related eating disorder, and RSBD. Implicated medications include neuroleptics, antidepressants, benzodiazepines, non-benzodiazepine hypnotics, and alcohol. It should be noted, however, that for most medications, careful study of their relationship to sleep architecture and parasomnias has not been undertaken.

Parasomnia Due to Medical Condition

Parasomnias within this category emerge as a manifestation of an underlying neurological or medical condition [1]. These can be further separated into two distinct categories—disorders of sleep that occur in association with other conditions (such as RSBD seen in Parkinson disease) versus symptoms arising from a separate organ system that manifest preferentially during sleep (such as nocturnal frontal lobe seizures, or nighttime gastroesophageal reflux).

Conclusion

The parasomnias encompass a heterogeneous group of undesirable events occurring during or around sleep, including unusual behaviors, emotional experiences, and abnormal perceptions. The current classification scheme seeks to first differentiate these disorders by the predominant stage of sleep in which they arise, however, there is clearly a significant set of parasomnias that can arise from either sleep state and defy classification into either the NREM or REM parasomnia category. As further work is done clarifying the pathophysiology of the various parasomnias, further changes in the parasomnia classification are to be expected.

Practical Points

- Parasomnias are "undesirable physical events or experiences" that occur during sleep itself or during transition into or arousal out of sleep.
- The ICSD-2 classifies parasomnias based upon whether they predominantly occur during REM sleep, during NREM sleep, or independent of sleep stage.
- NREM parasomnias consist of disorders of arousal and disorders of sleep–wake transition and generally occur in the first half of the night.
- NREM parasomnias include confusional arousals, sleepwalking (including sleep sex), and sleep terrors.
- REM parasomnias generally occur in the latter third of the night. These include REM sleep behavior disorder, recurrent isolated sleep paralysis, and nightmare disorder.
- Other parasomnias not restricted to a particular sleep stage include sleep related dissociative disorder, sleep related groaning (catathrenia), exploding head syndrome, sleep related hallucinations, sleep related eating disorder, and sleep enuresis.
- Also included in this category are parasomnias due to drugs or substances, and parasomnias due to medical conditions.

References

1. American Academy of Sleep Medicine. International Classification of Sleep Disorders, 2nd edition: Diagnostic and Coding Manual. Westchester, IL: American Academy of Sleep Medicine; 2006.
2. American Academy of Sleep Medicine. International Classification of Sleep Disorders, Revised: Diagnostic and Coding Manual. Rochester, MN: American Academy of Sleep Medicine; 2004.
3. Farid M, Kushida CA. Non-rapid eye movement parasomnias. Curr Treatment Options Neurol. 2004;6:331–7.
4. Pressman MR. Factors that predisponse, prime and precipitate NREM parasomnias in adults: clinical and forensic implications. Sleep Med Rev. 2007;11:5–30.
5. Boursalian LJ, Schenck CH, Mahowald MW, Lagrange AH. Differentiating parasomnias from nocturnal seizures. J Clin Sleep Med. 2012;15:108–12.
6. Derry CP, Duncan JS, Berkovic SF. Paroxysmal motor disorders of sleep: the clinical spectrum and differentiation from epilepsy. Epilepsia. 2006;47:1775–91.
7. Broughton R, Billings R, Cartwright R, Doucette D, Edmeads J, Edwardh M, et al. Homicidal somnambulism: a case report. Sleep. 1994;17:253–64.
8. Rosenfeld DS, Elhajjar AJ. Sleepsex: a variant of sleepwalking. ArchSexual Behav. 1998;27:269–78.
9. Iranzo A, Santamaria J, Rye DB, Valldeoriola F, Marti MJ, Munoz E, et al. Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD. Neurology. 2005;65:247–52.
10. Husain A, Miller P, Carwile S. REM sleep behavior disorder: potential relationship to post-traumatic stress disorder. J Clin Neurophys. 2001;18:148–57.
11. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (4th edition, text revision). Washington, DC: American Psychiatric Association; 2000.
12. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Scott R, Mahowald MW. Dissociative disorders presenting as somnambulism: polygraphic, video and clinical documentation (8 cases). Dissociation. 1989;2:194–204.
13. Vetrugno R, Lugaresi E, Plazzi G, et al. Catathrenia (nocturnal groaning): an abnormal respiratory pattern during sleep. Eur J Neurol. 2007;14:1236–43.
14. Vetrugno R, Provini F, Plazzi G, Vignatelli L, Lugaresi E, Montagna P. Catathrenia (nocturnal groaning): a new type of parasomnia. Neurology. 2001;56:681–3.
15. Ohayon MM. Prevalence of hallucinations and their pathological associations in the general population. Psychiatry Res. 2000;97:153–64.
16. Silber MH, Krahn LE, Slocumb N. Clinical and polysomnographic findings in narcolepsy with and without cataplexy: a population-based study [abstract]. Sleep. 2003;26:A282–A3.
17. Silber MH, Hansen MR, Girish M. Complex visual hallucinations: clinical and neurobiological insights. Brain Res. 1998;6:363–6.
18. Winkelman JW. Clinical and polysomnographic features of sleep-related eating disorder. J Clin Psychiatry. 1998;59:14–9.

Chapter 4
Diagnosing Parasomnias

Madeleine M. Grigg-Damberger and Frank M. Ralls

Introduction

Parasomnias are undesirable or unusual motor, behavioral, and/or experiential events that occur predominantly during (or in the transitions from and to) sleep [1]. If violent or dangerous, parasomnias can injure the patient (or those who attempt to intervene), and when frequent, they can disrupt the sleep/wake schedules and daytime functioning of the patient, bed partner, and/or family. Many parasomnias are impaired sleep state synchronization or "state dissociation" disorders [2, 3]. Transitions between wakefulness, non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep usually occur smoothly and completely, but when more gradual or oscillating rapidly, the physiological markers of one sleep state can linger or intrude into another [2].

A prototypical state dissociation disorder is narcolepsy with cataplexy in which (1) cataplexy is the sudden onset of REM sleep atonia while awake in response to an emotion-laden event; (2) sleep paralysis is an early or lingering appearance of REM sleep atonia, and (3) hypnic hallucination fragments of REM sleep dreams persist into wakefulness. Other state dissociations include sleepwalking (SW), sleep terrors (STs), REM sleep behavior disorder (RBD), sleep paralysis, and sleep inertia. Incomplete declarations of sleep/wake state of one sleep/wake state into another may also explain out-of-body experiences [4], lucid dreaming [5, 6], visual hallucinations in patients with Parkinson's disease (PD) [7], and alien abduction [8].

M. M. Grigg-Damberger (✉)
Department of Neurology, University of New Mexico,
MSC10 5620, One University of NM,
Albuquerque, NM 87131-0001, USA
e-mail: MGriggD@salud.unm.edu

F. M. Ralls
Division of Pulmonary, Critical Care, and Sleep Medicine,
Department of Internal Medicine, University of New Mexico,
1101 Medical Arts Ave., ND, Bldg. #2, Albuquerque, NM 87102, USA
e-mail: ralls@salud.unm.edu

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_4,

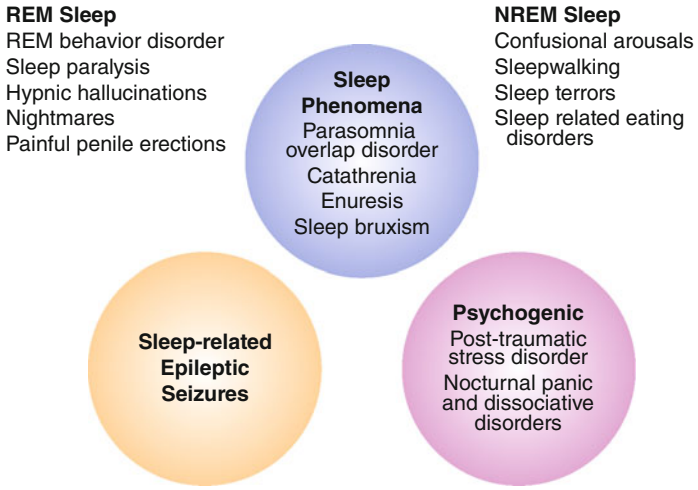


Fig. 4.1 Wide range of parasomnias that sleep specialists encounter

Diagnosing Parasomnias

When asked to diagnose paroxysmal events or abnormal movements during sleep, begin by asking whether these only occur around or during sleep [9]. If these also occur when awake, consider whether the patient has a movement disorder when awake. Contrary to older teachings, most diurnal movement disorders (including tremor, dystonia, chorea, hemiballismus, and myoclonus) persist or intermittently recur in sleep (albeit more intermittent and reduced in frequency and duration than when awake).

Then obtain a detailed description of the events regarding (1) stereotyped or variable; (2) consciousness is preserved before, during, and/or after them; (3) number and time(s) of occurrence related to sleep onset; (4) precipitating factors; (5) recall of the events; (6) potential to cause injury; (7) daytime consequences of them including cognitive slowing or daytime sleepiness; and (8) sleep/wake habits of the individual searching for irregular sleep/wake schedules and partial sleep deprivation.

Next obtain thorough medical, sleep, social, and family histories, specifically asking whether they have a prior personal and/or family history of parasomnias or sleep/wake problems. A physical examination should follow, searching for a movement disorder when awake, dementia, confusion, depression, anxiety, upper airway or body habitus at risk for obstructive sleep apnea (OSA), and underlying cardiac, pulmonary, neurodegenerative, or peripheral nerve disorders.

Based on the clinical descriptions provided by observers (often unreliable because they are aroused after the onset of an event), determine whether the nighttime movements are simple or complex. Box 4.1 summarizes the differential diagnosis of paroxysmal nocturnal events (PNEs) referred to sleep specialists for diagnosis. Figure 4.1 shows the wide range of parasomnias that sleep specialists encounter. Figure 4.2 provides a flow chart for assessing parasomnias on the basis of their time of occurrence and most salient clinical feature.

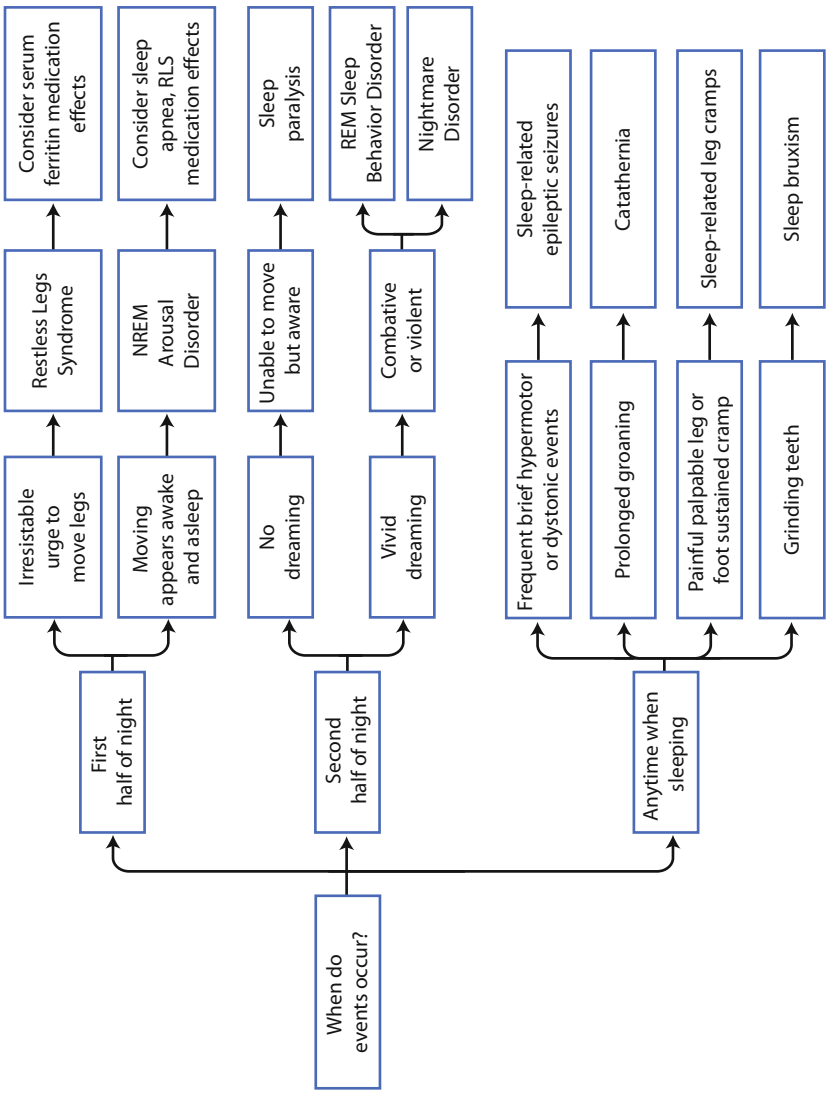


Fig. 4.2 Flow chart for evaluating parasomnias according to the time of occurrence and salient clinical features

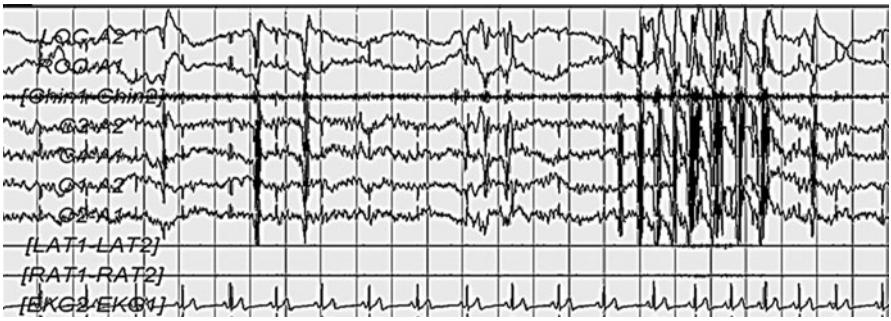


Fig. 4.3 Sleep bruxism

Age-Related Prevalence and Risk Factors for Parasomnias Contribute to Our Diagnostic Expectations

Parasomnias are most common in children and decrease in prevalence with increasing age [10]. Approximately 85 % of children between the ages of 30 months and 6 years talk in their sleep, 46 % have sleep bruxism (SB), 40 % have STs, 25 % have nocturnal enuresis, 15 % sleepwalk, and 9 % exhibit head banging or body rocking. Forty percent of 6- to 16-year-old children have at least one episode of an NREM arousal parasomnia (disorders of arousal (DoA)) (most between ages 11 and 12 years) [10]. However, only 2–3 % of children have more than one DoA per month. The majority of children who sleepwalk stop SW by age 13 years, but it persists in 24 % of frequent sleepwalkers. If one parent has a history of sleepwalking, the risk of a child developing sleepwalking behaviors is 40–45 %; if both parents are affected, then the risk of a child developing this behavior increases to 60–65 %. Somniloquy (sleeptalking) occurs in 50–80 % of children, but in half the cases, sleeptalking occurs only a few times a year. Ten percent of children with sleeptalking, talk nightly. The risk for sleeptalking increases with stress, sleep deprivation, alcohol, and fever, and in those with other primary sleep disorders (DoA, sleep-disordered breathing (SDB), and/or RBD).

SB is another parasomnia that is much more prevalent in children and tends to persist in a larger percent of adults than other parasomnias. SB occurs in one-third of children, 8 % of young and middle-aged adults, and 3 % of the elderly. Figure 4.3 shows an example of SB. Major risk factors for SB in adults include emotional stress, tobacco or caffeine use, heavy alcohol use, type A personality, and other sleep disorders such as sleep apnea or periodic leg movements in sleep (PLMS). SB is probably an extreme audible expression of rhythmic masticatory muscle activity (RMMA). RMMA occurs in most normal subjects when sleeping, and grinding of teeth during sleep probably represents a central pattern generator emerging during sleep.

Adults are far less likely to sleepwalk. A recently published large prospective cross-sectional study of 19,136 adults in the general US population found 3.6 % reported “nocturnal wandering” (NW within the previous year, but only 1 % had ≥ 2

episodes per month [11]. NW in adults tended to be a chronic condition: 81 % reported having episodes of NW for more than 5 years. A family history of NW was reported by 31 % of participants who reported NW. Other risk factors for frequent NW (≥ 2 per month) were OSA (odds ratio [OR] 3.9, circadian rhythm disorder (OR 3.4), insomnia disorder (OR 2.1), alcohol abuse/dependence (OR 3.5), major depressive disorder (OR 3.5), and obsessive compulsive disorder (OR 3.9) using over-the-counter sleeping pills (OR 2.5) or selective serotonin reuptake inhibitors (OR 3.0).

Chronic RBD is a complex parasomnia characterized by abnormal and often violent motor behaviors and complex vocalizations in which patients appear to enact their dreams while in REM sleep [12]. Chronic RBD usually presents after age 50 years, although any age group can be affected [13]. Chronic RBD is much more common in men [14–17]. RBD is also common in individuals with narcolepsy-cataplexy [18–20]. RBD can be misdiagnosed as sleep-related epilepsy, agitated SW, nocturnal panic attacks, nocturnal hallucinations, agitated delirium in intensive care units, sundowning, and/or intentional spouse abuse.

RBD can be idiopathic or secondary. Secondary RBD can be related to neurodegenerative disorders, other neurological disorders, sleep disorders, or medications, including withdrawal states [21]. Chronic symptomatic RBD in older adults is most often associated with an α-synucleinopathy, which manifests as either dementia with Lewy bodies (DLB), PD, or multiple system atrophy (MSA) [16, 22–31]. RBD is often the *first* clinical sign of an α-synucleinopathy, preceding other early nonmotor signs (olfactory dysfunction and depression) of parkinsonism and/or dementia by years or decades [17, 16, 32–34]. Prospective studies found that 38–65 % of patients with idiopathic RBD (iRBD) followed longitudinally subsequently developed a α-synucleinopathy most often 7–13 years after the onset of RBD [16, 34–36]. The 5-year risk for developing a neurodegenerative disease in patients with iRBD was 18 %, increasing to 41 % and 52 % at 10 and 12 years, respectively [36].

The challenging clinical problem is to identify which older adult with iRBD will develop a neurodegenerative disease (in case preventative treatments were available). Early biomarkers found in many patients with iRBD before signs of parkinsonism and/dementia develop that may increase the likelihood that they will later develop a neurodegenerative disease include impaired olfaction [37]; greater echogenicity of the substantia nigra [37]; impaired decision making [38]; markedly reduced sympathetic cardiac ^{123}I-MIBG (metaiodobenzylguanidine) uptake [39]; significant gray matter volume reduction on brain MRI in the anterior lobes of cerebellum, tegmental pons, and left parahippocampal gyrus [40]; and decreased regional cerebral blood flow in the precuneus, limbic lobe, and cerebellar hemispheres [41].

Some patients with dream-enactment behaviors and unpleasant dreams are found to only have severe OSA ("pseudo-RBD"); the abnormal behaviors observed in both REM and NREM sleep were not associated with REM sleep without atonia (RSWA), and continuous positive airway pressure (CPAP) therapy eliminated the abnormal behaviors, unpleasant dreams, daytime sleepiness, and snoring [42]. RBD has also been observed in 10–15 % of patients with narcolepsy with cataplexy [18, 43, 44] and RSWA without clinical RBD in others [43]. RBD in patients with narcolepsy needs to

be distinguished from SW and periodic limb movements during sleep (PLMS) and abnormal dreaming, all more common in these patients. Medications prescribed to treat their cataplexy can induce or aggravate RBD [44–46]. One study found epilepsy coexisting with RBD in 13 % of 80 older adults with epilepsy [47]. Suffice it to say, separating these out can be challenging. RBD and RSWA when seen in children, adolescents, or younger adults warrants consideration of narcolepsy with cataplexy, Tourette's syndrome, medication effect, or an autoimmune or limbic encephalitis [48, 49].

Parasomnias Common in Normal Individuals

Four particularly common parasomnias occur in normal individuals and most often require only reassurance of their usually benign nature. These are sleep starts, hypnic hallucinations, sleep paralysis, and rhythmic movement disorder (RMD). Sleep starts (also known as hypnic jerks) occur in the wake to sleep transition with one or two abrupt myoclonic flexion jerks often accompanied by a feeling of falling, a sensory flash, and/or dream-like imagery. Sleep starts occur occasionally in 70 % of the adult population and are associated with insufficient sleep.

Hypnic hallucinations are vivid perceptual experiences, which most often occur at sleep onset (95 % of the time), but also occur rarely upon awakening. Most people report a sensation of hearing voices or feeling someone else is nearby. Approximately 70 % of people have experienced these symptoms and are more frequent and severe in those with irregular sleep/wake schedules or narcolepsy with cataplexy. Excessive caffeine or other stimulant use, intense work or exercise, and emotional stress can increase the intensity of hypnic hallucinations.

Sleep paralysis is a transient inability to move despite being fully awake during a transition between sleep and wakefulness. It represents a brief persistence of the skeletal muscle motor suppression of REM sleep lingering into wakefulness. It occurs most often and with greatest frequency in individuals who have narcolepsy with cataplexy, particularly in the transition from REM sleep to wakefulness. Fewer than 10 % of adults, but as many as 40 % of teens and college students, have had at least one episode of sleep paralysis, most often triggered by sleep deprivation. Isolated sleep paralysis without other features of narcolepsy also runs in families [50].

RMD are episodes of rhythmic head banging, body rocking, or leg rolling (often accompanied by humming or chanting), which usually occur just before sleep onset, but may persist into NREM 1 or 2 sleep, and rarely recur in REM sleep [51–53]. Nearly 66 % of 9-month-old infants (both neurodevelopmental normal and abnormal) exhibit RMD, but the prevalence falls to 8 % at age 4 years. RMD that persists in later childhood is more likely to occur in children with neurodevelopmental, psychiatric, and/or autism spectrum disorders. Sleep specialists every few years encounter an adult with RMD, most have had it since childhood, but rare cases report it beginning following head injury or encephalitis. A case series of 24 adults with RMD found that RMD first began in childhood in all cases, and a family history was rare [51]. In some, OSA triggered arousals with a recurrence of their movements. Figure 4.4 shows a polysomnography (PSG) of a 40-year-old man with RMD.

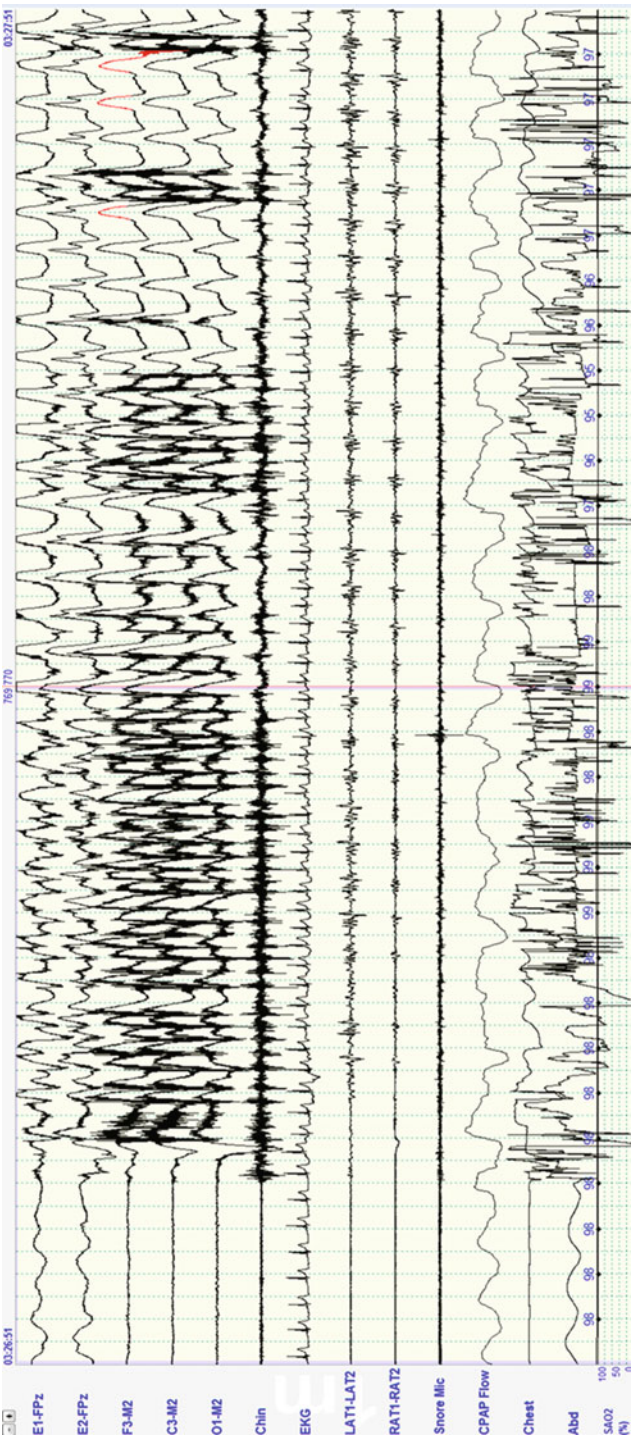


Fig. 4.4 Rhythmic movement disorder

Another common RMD is hypnagogic foot tremor (HFT), which is a rhythmic foot movement found in 5 % of healthy adults. It may involve one or both feet. Figure 4.5 shows a PSG of a 52-year-old subject with symptoms of HFT since early adulthood. HFT is a benign finding that rarely disturbs the patient but may disturb the patient's partner.

Indications for Video-Polysomnography When Evaluating Parasomnias

Clinical practice parameters published by the American Academy of Sleep Medicine (AASM) recommend video-polysomnography (video-PSG) to evaluate PNEs that are (1) unusual or atypical because of age of onset, time of night, duration, or particular accompanying motor behaviors (e.g., stereotyped, repetitive, dystonic, or focal); (2) frequent ($\geq$ 2–3 nights per week); and (3) potentially injurious, and/or disruptive to the patient or family. Video-PSG is warranted to differentiate atypical nocturnal behaviors from nocturnal seizures, to help identify when OSA or other sleep disorders are causing or contributing to frequent parasomnias, enuresis, or to control epileptic seizures [1, 54].

A PSG is unnecessary if the nocturnal behavior events in a *young* child are typical, noninjurious, infrequent, and not disruptive to the child or family [1, 54]. Common, uncomplicated, noninjurious parasomnias (such as SW, STs, sleeptalking, nightmares, bruxism, and enuresis) can usually be diagnosed by a clinical history [1, 54]. Typical NREM 3 arousal disorder features in a young child, which usually do not need a PSG for diagnosis, are summarized in Box 4.2.

One caveat, though: STs or SW events that are unusually frequent (occurring more than 2–3 times per week) warrant PSG to identify another sleep disorder precipitating them (most often OSA, occasionally periodic limb movement disorder). OSA was found on overnight PSG in 58 % of 84 prepubertal children who had STs and/or SW, restless legs syndrome (RLS) with PLMS in two [55]. Tonsillectomy in 43 eliminated both the OSA and parasomnias. Two had RLS, and its treatment with pramipexole eliminated their confusional arousals, restless legs, and PLMS.

Video-PSG is usually warranted in adults with suspected DoA, which begin or recur in adulthood, occur more than 2–3 times per week, are potentially injurious, could be seizure-related but the initial clinical evaluation and a standard electroencephalogram (EEG) inconclusive, and/or are accompanied by symptoms suggestive of SDB, periodic limb movement disorder, suspected or known epilepsy, and/or excessive daytime sleepiness. Video-PSG in adults with frequent SW/STs often identifies concomitant OSA, occasionally PLMs. On occasion, the PNE proves to be sleep-related epilepsy.

On occasion, video-PSG is requested to evaluate forensic cases where parasomnias and/or other sleep disorders or drugs are a contributing factor [56–59]. Violent behaviors arising from sleep are reported by 2 % of the adult population [60]. Violent or potentially injurious parasomnias include DoA, RBD, sleep-dissociative disorders, and nocturnal seizures with postictal confusion. A single video-PSG is likely to

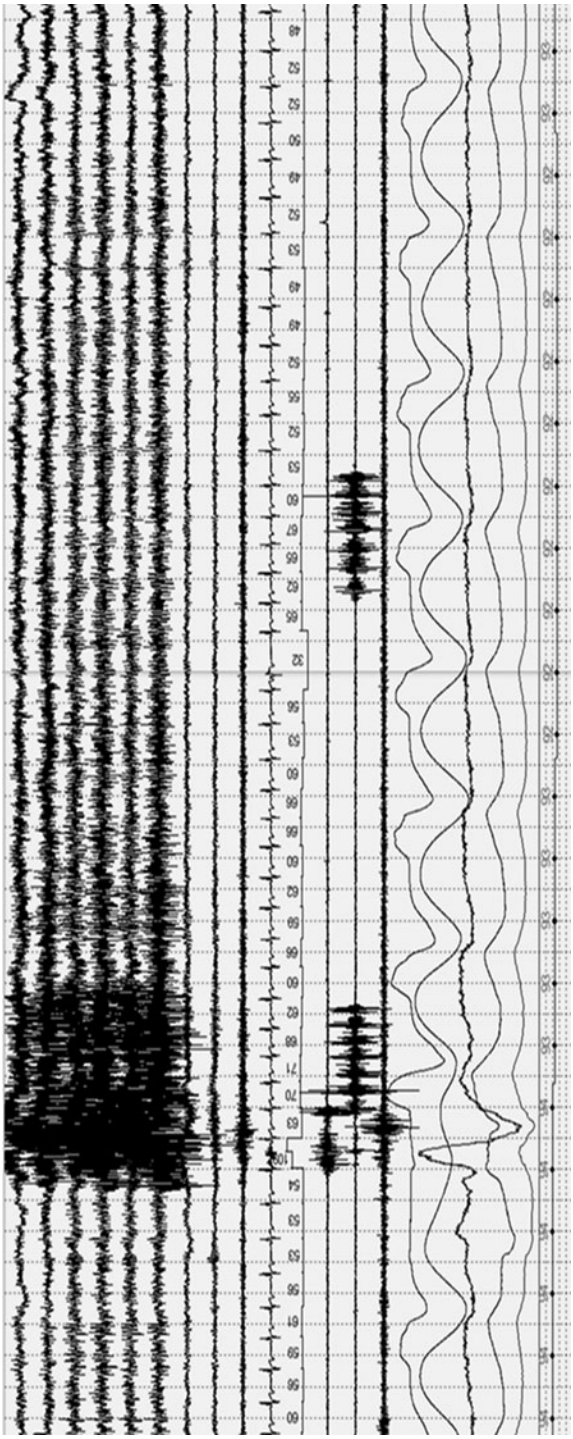


Fig. 4.5 Hypnagogic foot tremor

identify RBD and OSA and less likely to capture a DoA or sleep-dissociative event. However, whether the event(s), which prompted the evaluation, were triggered by the parasomnia or sleep disorders often remains uncertain. Box 4.3 summarizes guidelines proposed to assist in determining the putative role of an underlying sleep disorder in a specific violent act [56].

Diagnostic Algorithm for Evaluating Suspected Sleep-Related Seizures

If you suspect sleep-related seizures and the patient has not had a routine outpatient EEG, request one. However, epileptiform abnormalities are far more likely to be found on routine EEG in children than adults with epilepsy. Epileptiform activity will be found on the first routine EEG in approximately half of the children with clinically diagnosed epilepsy [61–63] but in only 3 % of the studied US veterans (mean age 55 years, range 21–97 years) [64].

Many studies have been published over a half century debating whether partial () or total sleep deprivation increases the likelihood that interictal epileptiform discharges (IEDs) will be found in a routine EEG. Some argue that sleep deprivation does not offer greater activation than sleep alone, whereas others assert total sleep deprivation activates IEDs. We agree with investigators who argue that sleep deprivation only increases the likelihood that NREM sleep will be recorded. Confirming this view, a prospective study of 820 EEGs recorded in children showed the following: (1) NREM sleep was observed in 57 % of sleep-deprived, 44 % of partially sleep-deprived, and 21 % of non-sleep-deprived pediatric EEGs; (2) a sixfold increased yield of recording NREM 2 sleep with sleep deprivation and 2.8-fold increase with partial sleep deprivation; (3) the OR that IEDs would be found was *not* increased by the presence of sleep or the use of total or partial sleep deprivation; and (4) the *only* significant effect of sleep deprivation was to increase the odds that sleep would occur [65]. Sleep is likely to occur with only partial sleep deprivation [66]. A better mix of sleep yield and cost containment is to request a child older than 2 years to stay awake 2 h later than usual the night before the EEG, performing sleep-deprived EEGs in the morning, and request children younger than 2 years to have no naps on the day of the EEG.

If sleep is not easily obtained in a routine outpatient EEG in a child, consider oral melatonin as a sedative (since conscious sedation with choral hydrate is rarely done now). A recent study found that melatonin induced sleep in 80 % of 70 children within a mean of 25 min [67]. We are far less concerned about sleep deprivation in adolescent or adult. A sufficient number of studies in adults provide evidence that total sleep deprivation remains an easy and cost-effective strategy to increase the likelihood of recording IEDs [68–70].

If the routine outpatient EEG obtaining sleep is nondiagnostic and the child's paroxysmal events are daily (even if only in sleep), consider a 4- or 8-h daytime recording in the EEG laboratory (with partial sleep deprivation or sleep deprivation the night before). Recording of 4–8 h in 230 children captured and confirmed the

nature of the paroxysmal events in 80 % of children whose events occurred on a daily basis [71].

If a patient's spells occur only at night and are frequent (2–3 times per week, better yet 1–3 times per night), consider ordering a video-PSG with expanded EEG before prolonged inpatient video-EEG monitoring, especially if concomitant OSA or RBD is suspected. NFLE is one of the few partial epilepsies that sleep specialists may confirm by a single night of video-PSG because patients with NFLE tend to have multiple seizures. Patients with NFLE from the same case series mentioned earlier averaged 3 ± 3 (range 1–20) seizures per night of video-PSG and a mean of 20 ± 11 seizures per month (61 %, > 15 seizures per month) [72].

If the first (or second) routine video-EEG with sleep is normal and your clinical suspicion for a sleep-related epilepsy remains, request continuous inpatient video-EEG monitoring (long-term monitoring (LTM)) for 2–5 days when (1) the nocturnal behaviors do not occur nightly or every other night; (2) a primary sleep disorder (e.g., OSA or childhood RLS) is unlikely; (3) a history exists of postictal agitation or wandering, and/or (4) cooperation of the patient is questionable. The likelihood of recording the typical epileptic or nonepileptic paroxysmal events in LTM ranges from 45–96 % if the patient is having ≥ 1 event per week [71, 73, 74].

Technical Considerations and Challenges of Video-Polysomnography to Diagnose Parasomnias

The AASM practice parameters recommend the following for video-PSGs done to diagnose parasomnias: (1) "additional EEG derivations in an expanded bilateral montage" to diagnose paroxysmal arousals or other sleep disruptions thought to be seizure-related when the initial clinical evaluation and results of a standard EEG are inconclusive; (2) recording surface EMG activity from the left and right anterior tibialis and extensor digitorum muscles; (3) obtaining good audiovisual recording; (4) having a sleep technologist present throughout the study to observe and document events; and (5) sleep specialists who are not experienced or trained in recognizing and interpreting both PSG and EEG abnormalities should seek appropriate consultation or should refer patients to a center where this expertise is available [1].

It is probably best to record at least 18 channels of EEG during video-PSG despite the only two published studies evaluating how many channels of EEG are needed to identify seizures in a video-PSG found that recording 18 channels of EEG during video-PSG did not improve the ability to recognize frontal lobe seizures [75, 76]. The ability to recognize frontal lobe seizures by EEG alone was not helped by more EEG channels, slower screen times, or midline electrodes. Temporal lobe seizures during sleep were most likely to be identified if EEG channels were placed over the temporal regions.

We sometimes encounter unanticipated IEDs on a PSG. Determining whether epileptiform activity is unilateral, bilateral, asymmetric, or shifting left to right is far easier if we remap the standard PSG EEG montage referencing the ipsilateral

electrode to the contralateral mastoid (e.g., F4-M1, F3-M2, C4-M1, C3-M2, O2-M1, O1-M2 shown in Fig. 4.6a) to the ipsilateral mastoid (i.e., F4-M2, F3-M1, C4-M2, C3-M1, O2-M2, O1-M1 in Fig. 4.6b). Routinely recording the alternative EEG derivations (Fz-Cz, Cz-Oz) can be useful for detecting electrographic seizure activity over the CZ in nocturnal frontal lobe epilepsies because artifact is often least there. Scoring sleep studies in patients with epilepsy can be difficult especially when IEDs are frequent, even more difficult when their sleep spindles are of low amplitude or dysmorphic, and/or when inappropriate alpha intrusions are present [77].

Patients with RBD characteristically exhibit excessive tonic activity in their chin electromyogram (EMG) and/or excessive phasic activity in their chin and/or limb EMG. In routine PSG, we only record EMG from the chin and anterior tibialis leg muscles. We add surface EMG electrodes to the wrist extensors when recording patients with suspected RBD [1, 78–80]. The excessive motor activity and RSWA typical of RBD will usually be found in a single night of PSG. A retrospective analysis of video-PSG recorded in 55 adults with RBD who have at least two consecutive video-PSGs found that RBD could be diagnosed in 95 % of patients by recording and carefully analyzing the amounts of REM-related EMG activity, RSWA, and motor events observed on video-PSG [81]. No significant difference in the amounts of phasic and tonic EMG activity during REM sleep between nights 1 and 2 were found, but dream-enactment behaviors were most susceptible to night-to-night variability.

The habitual nocturnal event may not be captured by one night of in-laboratory video-PSG, particularly if the events are DoA [80, 82, 83]. Investigators from Montreal were able to trigger 1–3 SW/ST events in all 10 adults with SW/STs by having them remain awake for 25 h and repeatedly ringing a loud buzzer (most often 40–90 db) during NREM 3 sleep. *However,* clinical confirmation of RSWA and/or RBD may be missed by a single night of video-PSG.

Video-Polysomnographic Features of the Parasomnias Most Often Encountered in the Sleep Laboratory

The parasomnias most likely to be recorded in a sleep laboratory include DoA, RBD, and sleep-related hypermotor seizures (usually nocturnal frontal lobe epilepsy).

NREM Arousal Disorders

DoA most often occur 90–180 min after sleep onset in the transition from NREM 3 (occasionally NREM 2) sleep to wakefulness or REM sleep [84, 85]. They typically last for a few minutes, are nonstereotyped, and can be provoked by sensory stimuli (OSA, a loud noise, or bright light half-awakening the patient). During these events, the patient appears confused, disoriented, and is slow to respond. Their eyes are open (as opposed to closed during RBD or NFLE); visual inspection functions but objects are often misidentified (e.g., trying to use the bedside water glass as a telephone

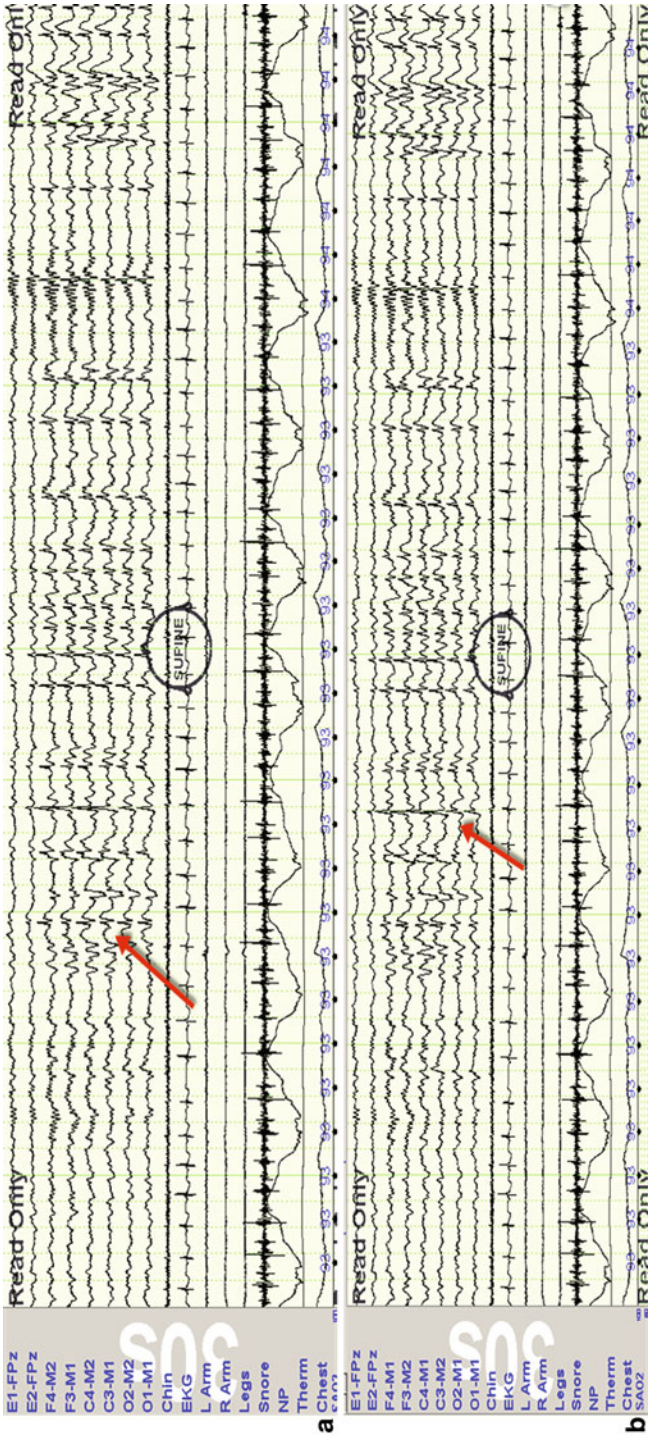


Fig. 4.6 **a**, **b** Unexpected rolandic spikes in NREM 2 sleep in a 7-year-old child

receiver, the closet as a bathroom). They have little or no responsiveness to their external environment and exhibit automatic behaviors. They are difficult to arouse from an event, and if aroused, they recall only fragmentary dream-like images (often of being trapped or attacked). The onset of DoA event is best identified by the appearance of tachycardia from NREM 3 sleep: the acceleration of the heart rate is typically greatest for an ST or agitated sleepwalking, moderate for confusional arousal, and least for passive SW.

During a confusional arousal, the patient often suddenly sits up in bed, may then fumble with bedclothes, thrash, flail or kick, moan, whimper, and/or utter often unintelligible words. Passive SW often begins as a confusional arousal, but the patient leaves the bed, walking toward a sound, light, or a particular room. While SW, the person may eat, urinate in a closet or next to the toilet, or walk outside. Sleep-related eating and sexual behaviors (often atypical from the individual's usual behavior when awake) have also been reported [57, 86].

STs and agitated SW often begin with a blood-curdling scream or cry, the patient exhibiting severe agitation, greater fear, more vocalization, and marked sympathetic arousal with mydriasis, tachycardia, tachypnea, and sweating. They flee their bed screaming or crying, run through the house, down the stairs, or out the front door. They may recoil and have increased agitation when touched or held; innocent attempts by bystanders to touch or direct them may then lead to injury (to themselves or others). Agitated sleepwalkers are more often adolescents or adults. Even violent DoA usually last a few to rarely as long as 30 min, often followed by a calm return to bed or sleep somewhere else in the house or outside. Episodes end with a return to sleep and retrograde amnesia for the events (although some adults can recall fragments of some events). Violent DoA in adults can cause injury to a patient or bedpartner, and self-injury during a DoA may be misdiagnosed as suicide [87].

EEG during a DoA event in 38 adult sleepwalkers (mean age 29 years, 55 % men) was characterized by either regular rhythmic hypersynchronous delta or theta activity, or high amplitude delta intermixed with alpha or beta activity [85]. Figure 4.7 shows a confusional arousal recorded from NREM 3 sleep in a 7-year-old boy. Studies comparing sleep microarchitecture and EEG power in adults with SW or STs with controls report that patients with SW/STs have (1) increased number of brief arousals from NREM 3 sleep especially during the first NREM cycle of a night; (2) reduced delta power of the slow wave activity especially during first NREM cycle; (3) slower decay of EEG delta power of NREM 3 sleep across recurring cycles of NREM sleep; and (4) alterations in cyclic alternating pattern during NREM sleep consistent with increased NREM 3 sleep instability. More work is needed to see if individuals with DoA can be identified by abnormalities in their sleep microarchitecture.

REM Behavior Disorder

RBD episodes usually appear in the first 90 min after sleep onset, typically last 1–5 min, and recur 3–5 times at 90–120 min intervals across an entire night of sleep during recurring periods of REM sleep. As opposed to DoA, patients with RBD

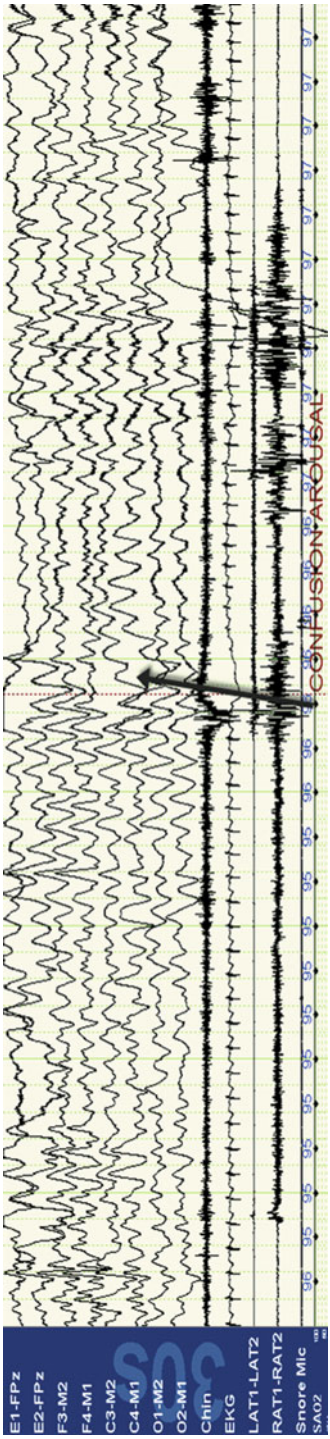


Fig. 4.7 Confusional arousal from NREM 3 sleep in a 7-year-old boy

are easily aroused from an event. Once aroused, they are able to recount dreams (if not too demented) that correspond to the observed behaviors [88, 89]. Their eyes are typically closed during events. Their heart rates most often do *not* increase during RBD events. A recent study found that heart rate responses were reduced in patients with RBD associated with parkinsonism and iRBD compared with controls [90]. Impaired heart rate responses probably represent an early loss of autonomic function.

RBD behaviors are often more plentiful and severe at the end of the night when REM sleep is most plentiful [91]. Paroxysmal motor RBD behaviors were more likely to occur in phasic portions of REM sleep (when rapid eye movements and saw tooth waves are seen) rather than in tonic REM sleep [92]. A case-control study of five PD patients with RBD found that limb jerking was the most common behavioral expression of RBD [78]. Motor behaviors during RBD dream-enactment events are much more frequent than vocalizations [91].

RBD motor behaviors can be simple (talking, shouting, excessive jerking of limbs or body) or complex (arm flailing, slapping, kicking, sitting up, leaping from bed, running, crawling, gesturing, swearing) [93]. A case-control video-PSG study found that 75 % of RBD motor events lasted < 2 s, 83 % were simple, 14 % complex, 11 % associated with vocalizations, and 4 % violent in the patient with RBD. RBD averaged 54 ± 23 limb movements per 10 min of REM sleep compared with 4 ± 2 per hour in healthy age- and gender-matched controls. Because RBD behaviors are typically brief, we recommend carefully reviewing the video when RSWA is most intense.

Motor behaviors during REM sleep in the control subjects were usually simple (91 %). Motor movements during RBD tend to be repetitive, quick, jerky, not self-centered, and rarely involve the environment in an appropriate manner. A specific posture of the hand (limp wrist with flexed digits) during grasping movements was seen in video-PSG of 48 % of 65 RBD patients [94]. The motor behaviors of RBD behaviors were similar whether the patient had PD, narcolepsy, or iRBD [94]. Patients with RBD can also enact nonviolent dreams: singing, dancing, saluting, marching, clapping, or snapping their fingers [95]. Speech in RBD events can vary from mumbling to logical sentences. De Cock et al. found that 38 % of 53 PD patients moved much better and had louder, more intelligible speech during their RBD episodes than when awake [96].

RBD is also regarded as a dream disorder: patients report that the content of their dreams become increasingly violent and disturbed. Their dreams often involve frighteningly unfamiliar people or animals, confrontation, attacking or chasing themes, and the behaviors often depict the sleeper defending himself. The personality, temperament, and behavior of RBD patients when awake are typically incongruent with the nocturnal aggressive behaviors. Of note, D'Agostino et al. demonstrated that the dreams of RBD patients were no more violent than those of the general population, and the "mild" waking temperament is an early subtle sign of the apathy that is commonly described in the context of neurodegenerative disorders [97].

Video-PSG confirmation of RSWA is required to diagnose RBD [1]. RBD is diagnosed by (1) excessive amounts of phasic and/or tonic submentalis and/or excessive

phasic limb EMG activity during REM sleep on video-PSG; (2) the presence of abnormal REM sleep clinical dream enactment behaviors during video-PSG and/or a clinical history of sleep-related injurious, potentially injurious, or disruptive behaviors; and (3) exclusion of substance abuse, other medical, neurological, psychiatric or sleep disorder, or medication(s) that may better explain the sleep disturbance [98–101].

Criteria for scoring RSWA was published by the AASM in 2007 and were based on limited literature available then [98]. A 30-s epoch of REM sleep is regarded as containing excessive *tonic* activity when the amplitude of the chin EMG is of higher amplitude than its lowest amplitude during NREM sleep for 50 % or more of the epoch. Excessive *phasic* EMG activity in REM sleep is scored by subdividing the 30-s PSG epoch into ten consecutive 3-s mini-epochs, identifying and tallying the number of 3-s mini-epochs that contain phasic EMG activity lasting 0.1–5.0 s, which is at least four times as high as the baseline EMG activity. If five or more 3-s mini-epochs of a 30-s epoch of REM sleep contain excessive phasic EMG activity, the REM sleep epoch is regarded as containing excessive phasic EMG activity. If a video-PSG contains excessive EMG activity during REM sleep but the patient has no clinical history suggestive of dream-enactment behaviors and none seen on the PSG, we say the PSG shows RSWA. However, RBD behaviors may not be captured by a single night of PSG.

Unfortunately, the AASM rules for scoring RSWA in a PSG do *not* specify which (and how many) skeletal muscles should be recorded during a video-PSG to confirm RBD or RSWA. Recent studies show that excessive phasic EMG activity and RSWA during REM sleep is more frequent in distal than proximal limb muscles and more frequent in upper limbs than lower limbs. RSWA cannot be scored on the basis of chin EMG alone, but requires recording and scoring of excessive phasic EMG activity in the upper and lower distal limb muscles. One study recorded *13* different muscles in 17 RBD patients (nine with PD) to determine which combination of muscles provides the highest rates of phasic EMG activity during REM sleep in patients with RBD. They found that the greatest amounts of excessive phasic EMG activity were observed in the mentalis, flexor digitorum superficialis, and extensor digitorum brevis muscles [102]. This combination of muscles detected 82 % of all mini-epochs containing phasic EMG activity, whereas only 55 % of excessive phasic activity would be scored if only the chin EMG was recorded. Another recorded EMG activity from *five* muscle groups (mentalis, left/right anterior tibialis, and left/right brachioradialis) found that the greatest amounts of excessive phasic EMG activity were recorded from the mentalis and brachioradialis muscles [103].

The AASM rules for scoring RSWA and RBD in a PSG do not indicate what percentage of 30-s epochs of REM sleep need to contain RSWA to diagnose it [78, 104–108]. A retrospective analysis of video-PSG data in 80 patients with iRBD and 80 age- and gender-matched controls found that a *tonic* chin EMG density (percentage of 2-s mini-epochs of REM sleep) $\geq$ 30 %, phasic chin EMG density $\geq$ 15 %, and $\geq$ 24 leg movements per hour of REM sleep would correctly identify RBD in 82 % of their 80 patients but misidentified it in one control [109]. Another study suggested that $\geq$ 10 % of REM sleep spent with elevated EMG tone or phasic burst activity

would confirm a diagnosis of clinical RBD (based on the receiver–operator curves) providing a sensitivity of 89 % but a specificity of only 57 % [110]. The percentage of PSG epochs of REM sleep containing RSWA may increase with duration of the underlying disorder: one study of 11 patients with iRBD found that the chin tonic EMG activity during REM sleep increased from 30 to 54 % when a second PSG was recorded a mean of 5 years later [111]. Figure 4.8 shows an example of RSWA recorded in a 79-year-old man.

Sleep-Related Hypermotor Seizures

Clinical features that warrant concern for sleep-related epileptic seizures are as follows: (1) events occur any time in the night, just after falling asleep, or shortly before awakening in the morning; (2) multiple events a night; and (3) occasional occurrence of these events when awake or during a brief nap. Sleep-related hypermotor seizures are often initially misdiagnosed as DoA [112–120]. Two-thirds of nocturnal hypermotor seizures emanate from the frontal lobe, one-third from the temporal lobe [121, 122], and a few from the insular region [123]. Clinical features of nocturnal hypermotor seizures are summarized in Box 4.4 [72, 120, 124–127]. Patients with NFLE often have attacks of varying severity, and minor ones are hard to distinguish from arousals seen in healthy normal controls; these are summarized in Table 4.1 [72, 128]. Normal nonepileptic arousals from sleep are best distinguished by motor behaviors that are slower, fewer, less repetitive, less stereotyped, and not associated with dystonic features [128].

Because NFLE seizures are usually brief in duration, most do not leave their beds. Occasionally, longer NFLE seizure may lead to "wandering." Focal seizures that lead to ictal or postictal "wandering" most often emanate from the temporal lobe, particularly the right temporal, and most often begin during wakefulness [121, 122, 129–131]. Studies suggest sleep (or epilepsy) specialists will most likely identify nocturnal events as NFLE if these have an abrupt explosive onset from NREM 2 sleep and hypermotor or asymmetric dystonic posturing accompany them [132]. Many patients with NFLE may complain that their seizures disrupt their sleep (and often they do). Fifty percent of 33 patients with NFLE complained of nocturnal awakenings compared with 22 % of controls; 36 % of patients complained of EDS (11 % of controls), and those who complained of EDS were more likely to report frequent nocturnal awakenings [133].

Be advised that 80 % of adults with NFLE have no IEDs in their EEGs when awake or asleep, 20–54 % have no scalp-recorded ictal EEG activity during many or most of their seizures, and 25 % have normal interictal and ictal EEGs [72, 120]. The lack of scalp ictal EEG activity in NFLE has been attributed to following reasons: (1) muscle artifact often obscures the tracing; (2) events often last < 20–30 s; (3) little or no postictal slowing; and/or (4) the epileptic focus is "buried" in the mesial frontal or inferior frontopolar regions "hidden" from scalp EEG recordings. Given this, the diagnosis of NFLE in these patients is confirmed by recording multiple seizures, noting their relatively stereotyped nature and clinical semiology.

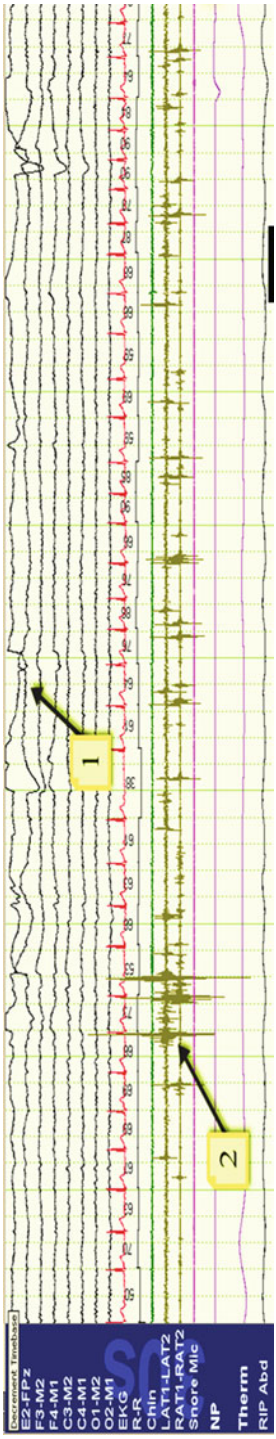


Fig. 4.8 RSWA recorded in a 79-year-old man

Table 4.1 Nocturnal frontal lobe epilepsy characterized by paroxysmal attacks of increasing complexity

Attack type	Duration	Clinical features
Minor attacks	2–4 s	Stereotyped head, axial, or limb movements
Paroxysmal arousals	5–10 s	Abrupt arousal accompanied by trunk and head elevation often with vocalization and a frightened expression
Major attacks (formerly called "nocturnal paroxysmal dystonia")	20–30 s	Begin as an abrupt arousal and rapidly progress to bipedal automatisms, rhythmic twisting movements of trunk, bizarre repetitive hypermotor behaviors, and/or asymmetric dystonic or tonic postures
Episodic nocturnal wanderings	> 1–3 min	Begin as a paroxysmal arousal process followed by leaping from bed, walking, running, screaming, or loud vocalization; often accompanied by fear and bizarre behaviors

Ictal EEG activity may accompany 80 % of NFLE seizures (although it is typically brief and rapidly obscured by muscle artifact). When ictal EEG activity is present in NFLE, it can be unilateral low-voltage paroxysmal fast activity, rhythmic theta activity, or flattening of the EEG over the frontocentral, frontocentral-temporal, frontotemporal or parasagittal regions. A unilateral onset may be followed by early or late spread of the ictal activity to the contralateral hemisphere. When ictal EEG activity in NFLE is bilateral, it is usually maximal over the frontal, frontocentral, or frontotemporal regions, begins as either rhythmic fast or low-voltage fast activity, and sometimes lateralizes to the side of the epileptogenic focus. An example of a nocturnal frontal seizure recorded in our sleep laboratory is shown in Fig. 4.9.

Alternative Methods for Diagnosing Parasomnias

Derry et al. (2006) designed a frontal lobe epilepsy and parasomnias (FLEP) scale to assess the likelihood that a PNE was likely to be NFLE based on the clinical history alone [134]. The FLEP consists of a series of questions based on an initial series of cases and clinical expertise. Responses to the questions asked in the FLEP scale that favored nocturnal seizures were as follows: events last < 2 min, occur ≥ 3–5 times per night, and behaviors during these events are highly stereotyped. Highly variable clinical semiology or onset after age 55 years lessens the likelihood that a PNE is NFLE. A patient with a score of zero or less on the FLEP scale is very unlikely to have epilepsy, and any patient with a score of $> +3$ is very likely to have epilepsy, whereas video-EEG or PSG monitoring is needed for those with an FLEP score of $+1$ to $+3$. For NFLE, the FLEP scale had a sensitivity of 71 %, a specificity of 100 %, a positive predictive value of 100 %, and a negative predictive value of 91 % [134]. Manni et al. (2008) found the FLEP scale usually identifies NFLE but it is less reliable for differentiating SW from epileptic nocturnal wandering and distinguishing RBD from epilepsy [135]. The FLEP scale in 71 subjects (mean age 54 ± 21 years,

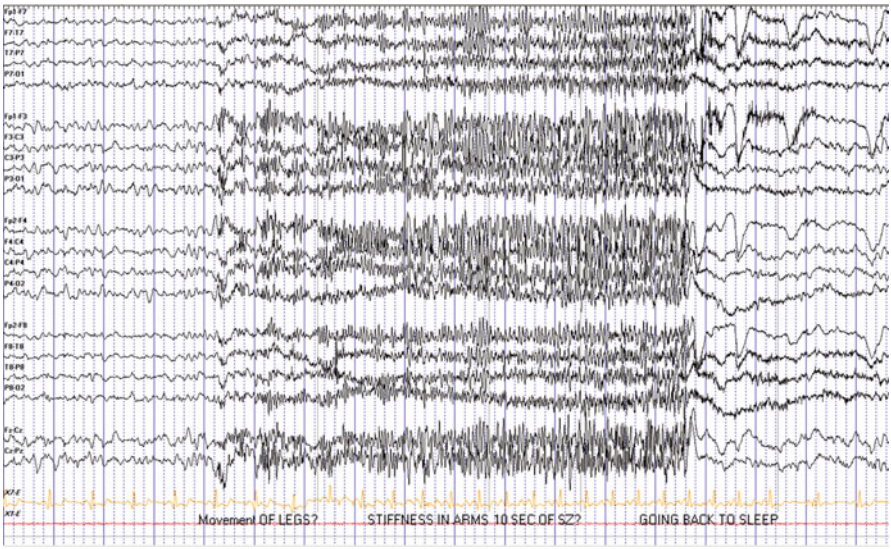


Fig. 4.9 A nocturnal frontal lobe seizure

11 had DoA, 14 NFLE, and 46 iRBD) incorrectly diagnosed four (6 %) of the patients (specifically NFLE patients who had epileptic nocturnal wandering). FLEP scores were in the equivocal range (+ 1 to + 3) in 31 % of the patients requiring video-PSG or video-EEG. Consider asking the family to record home video of the nocturnal events [136–140]. These are simple to request and obtain if events are frequent enough, but most often, the crucial beginning of an event is lost.

The RBD Screening Questionnaire (RBDSQ) is available in English, German, and Japanese and validated in these populations [141–144]. It consists of ten items with 13 yes/no questions (maximum possible score 13). An RBDSQ score of 5 or more showed a sensitivity of 92 % and specificity of 93 % for RBD when subjects were compared with the general population, but a sensitivity of 96 % and specificity of 57 % when it was used in patients with PD.

Future Directions

We need to understand (1) the mechanisms which underlie cortical excitation emerging from sleep in patients with sleep-related epilepsies; (2) the role of sleep in sudden unexpected death in patients with epilepsy; (3) the influence of circadian rhythms and chronotypes on different epilepsy syndromes; (4) whether IEDs and seizures, when sufficiently frequent, impair long-term development and cognitive functioning in neonates and children; (5) whether treating OSA in patients with epilepsy improves seizure control; and (6) why sleep macro- and microarchitecture is altered in patients with epilepsy. More specific guidelines for scoring RSWA in a PSG are sorely needed.

The link between sleep DoA and epilepsy has been elucidated through advancements in monitoring and evaluation techniques utilized during sleep studies. It is evident that treatment strategies can begin from either a neurological or a sleep medicine approach. However, it is also clear that further study into the structural and chemical etiologies of both disorders will be necessary to understand how to best improve overall function and that a multidisciplinary model will best serve patients with these disorders.

Practical Points

1. Parasomnias are most common in children and decrease in prevalence with increasing age; most resolve in the teenage years.
2. Parasomnias that occur > 2–3 times per week warrant a PSG to identify another sleep disorder or seizure disorder that may be a precipitating factor.
3. Most diurnal movement disorders (including tremor, dystonia, chorea, hemiballismus, and myoclonus) persist or intermittently recur in sleep.
4. RBD (dream enactment) should prompt a referral to a sleep specialist or neurologist as it may be related to a sleep disorder and is associated with development of a neurodegenerative disease.

Case Example

A 67-year-old man presented with his wife of 40 years who after waking up, found that he was standing on his feet, holding a television above his head, and about to throw it against the wall. His wife reports that his nighttime movements began 5 years ago. The movements would range from waving an arm in the air to punching and kicking gestures and occurred a few times per month. Recently, the behaviors occur almost nightly. A few times, she was awakened because of aggressive physical contact. This behavior became so disruptive and frightening to the wife that she decided to sleep in another room. She reported that at times she hears yelling or the sounds of someone punching the bed; however, she is too frightened to go into the bedroom to see what her husband is doing. She does not understand how such a kind and gentle man can become so violent at night. It was only after constant urging from their children and the most recent event that she was willing to discuss this issue. The patient reported that he dreams of someone attacking him or his family and finds himself walking up from the dream defending the people he loves. The patient states that he has felt fatigued over the past year, but attributes this to getting older. He also feels depressed at times when it takes him longer to complete tasks compared with that taken a “few years ago.”.

Hematologic studies were normal; however, the physical examination revealed a mild resting tremor in the left hand, decreased expression on the face, and slow but steady ambulation. No paucity of speech or rigidity was present.

Diagnosis: early Parkinson’s disease

This case presents classic findings of RBD, which is specific for dream enactment due to the loss of the normal atonia of REM sleep. Behaviors include movement of a limb, vocal expressions, and violent behavior. Individuals affected are typically men over the age of 50 years, and events are often paradoxical to normal wake personality and behaviors. In this patient, RBD was a precursor to the development of PD. The likelihood of developing a neurodegenerative disease (PD, DLB, and MSA) within 5 years is 42 % in individuals with RBD. This patient was referred to a neurologist for ongoing care. In the interim, the patient was started on pharmacy grade melatonin at 3 mg, 1–2 h prior to his anticipated bedtime. Melatonin at doses of 0.5–12 mg is $>$ 80 % effective in controlling RBD behaviors and promotion of the atonia of REM. In follow-up, the wife reported that the bedtime movements have stopped and she is able to sleep by his side again. This case demonstrates a common barrier to diagnosis of RBD, in that patients may be reluctant to discuss this problem with their provider. It is important to ask patients over the age of 50 years and their families if dream enactment occurs as the treatment has great potential to improve the quality of life for those affected.

Box 4.1: Differential Diagnosis of Paroxysmal Nocturnal Events

- NREM arousal disorder (confusional arousal, sleep walking, sleep terror);
- Sleep-related epilepsy;
- REM sleep behavior disorder (RBD) and pseudo-RBD due to obstructive sleep apnea;
- Nightmare disorder and post-traumatic stress disorder;
- Sleep-related panic attacks;
- Sleep-related dissociative disorder;
- Sleep-related choking, laryngospasm, or gastroesophageal reflux;
- Sleep-related rhythmic movement disorder (often with vocalization);
- Sleep-related expiratory groaning (catathrenia);
- Sudden death when sleeping due to myocardial infarction, Brugada syndrome, untreated OSA, sudden unexpected death in epilepsy, and trauma;
- Sleep bruxism, rhythmic masticatory muscle activity and faciomandibular myoclonus;
- Sleep-related hypnagogic foot tremor.

Box 4.2: "Typical" NREM 3 Arousal Disorder Features in Young Children Who Usually Do Not Need a PSG for Diagnosis

- Occur in first third of the night when NREM 3 predominates;
- Appear confused and disoriented;
- Exhibit automatic motor behaviors and autonomic disturbances, which suggest sympathetic activation;
- Difficult to arouse from episode;

- Positive family history of sleepwalking/sleep terrors;
- Fragmentary hypnic imagery or no recall of event;
- Cannot be consoled;
- May resist intervention;
- Moderate to high likelihood of injury in agitated sleepwalking or sleep terrors;
- Little or no responsiveness to external environment.

Box 4.3: Guidelines to Assist in Determining the Role of a Sleep Disorder in a Specific Violent Act (58)

1. A reasonable basis (by history or video-PSG) to suspect a sleep disorder. Similar episodes with benign or morbid outcome should have occurred previously;
2. Duration of the violent act was brief (minutes);
3. Violent behavior had an abrupt onset, was impulsive, senseless, and without apparent motivation;
4. Victim was someone merely present, and who may have been stimulus for the arousal;
5. Immediately following return of consciousness, the individual exhibits perplexity or horror, without attempt to escape, conceal, or cover-up the action.
6. Evidence of lack of awareness of the individual during the event;
7. Usually some degree of amnesia during the event, which may not be complete;
8. In NREM arousal events, the act may occur on awakening usually 1 h after falling asleep, may occur upon attempts to awaken the patient, and may have been potentiated by alcohol, sedative/hypnotic, or prior sleep deprivation.

Box 4.4: Clinical Features of Nocturnal Hypermotor Seizures

- An abrupt, often explosive, onset awakening from grossly undisturbed NREM 2 sleep;
- Asymmetric dystonic or tonic postures;
- Thrashing, pedaling, and kicking of the lower extremities;
- Tend to be “fairly” stereotyped in appearance for the individual patient;
- Brief (typically lasting 20-30 s, less than 1–2 min);
- Patients are often aware during the seizure, but say they cannot control their movements or vocalizations;
- No postictal confusion or amnesia;
- Twenty percent have no accompanying scalp-recorded ictal EEG activity.

References

1. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J Jr, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep. 2005 Apr 1;28(4):499–521. (PubMed PMID: 16171294)
2. Mahowald MW, Cramer Bornemann MA, Schenck CH. State dissociation, human behavior, and consciousness. Curr Top Med Chem. 2011;11(19):2392–402. (PubMed PMID: 21906025. Epub 2011/09/13. eng.)
3. Mahowald MW, Schenck CH. Insights from studying human sleep disorders. Nature. 2005 Oct 27;437(7063):1279–85. (PubMed PMID: 16251953. Epub 2005/10/28. eng.)
4. Cheyne JA, Girard TA. The body unbound: vestibular-motor hallucinations and out-of-body experiences. Cortex. 2009 Feb;45(2):201–15. (PubMed PMID: 18621363. Epub 2008/07/16. eng.)
5. Voss U, Frenzel C, Koppehele-Gossel J, Hobson A. Lucid dreaming: an age-dependent brain dissociation. J Sleep Res. 2012 Dec;21(6):634–42. (PubMed PMID: 22639960. Epub 2012/05/30. eng.)
6. Voss U, Holzmann R, Tuin I, Hobson JA. Lucid dreaming: a state of consciousness with features of both waking and non-lucid dreaming. Sleep. 2009 Sep;32(9):1191–200. (PubMed PMID: 19750924. Pubmed Central PMCID: 2737577. Epub 2009/09/16. eng.)
7. Manni R, Terzaghi M, Ratti PL, Repetto A, Zangaglia R, Pacchetti C. Hallucinations and REM sleep behaviour disorder in Parkinson's disease: dream imagery intrusions and other hypotheses. Conscious Cogn. 2011 Dec;20(4):1021–6. (PubMed PMID: 21071244. Epub 2010/11/13. eng.)
8. McNally RJ, Clancy SA. Sleep paralysis, sexual abuse, and space alien abduction. Transcult Psychiatry. 2005 Mar;42(1):113–22. (PubMed PMID: 15881271. Epub 2005/05/11. eng.)
9. Walters AS. Clinical identification of the simple sleep-related movement disorders. Chest. 2007 Apr;131(4):1260–6. (PubMed PMID: 17426241)
10. Klackenberg G. Somnambulism in childhood–prevalence, course and behavioral correlations. A prospective longitudinal study (6–16 years). Acta Paediatr Scand. 1982 May;71(3):495–9. (PubMed PMID: 7136663)
11. Ohayon MM, Mahowald MW, Dauvilliers Y, Krystal AD, Leger D. Prevalence and comorbidity of nocturnal wandering in the U.S. adult general population. Neurology. 2012 May 15;78(20):1583–9. (PubMed PMID: 22585435. Epub 2012/05/16. eng.)
12. Trotti LM. REM sleep behaviour disorder in older individuals: epidemiology, pathophysiology and management. Drugs Aging. 2010 Jun 1;27(6):457–70. (PubMed PMID: 20524706. Epub 2010/06/09. eng.)
13. Chiu HFK, Wing YK, Chung DWS, Ho CKW. REM sleep behavior disorder in the elderly. Int J Geriat Psychiatry. 1997;12:888–91.
14. Olson EJ, Boeve BF, Silber MH. Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. Brain. 2000 Feb;123(Pt 2):331–9. (PubMed PMID: 10648440)
15. Schenck CH, Hurwitz TD, Mahowald MW. Symposium: Normal and abnormal REM sleep regulation: REM sleep behaviour disorder: an update on a series of 96 patients and a review of the world literature. J Sleep Res. 1993 Dec;2(4):224–31. (PubMed PMID: 10607098. Epub 1993/12/01. eng.)
16. Iranzo A, Molinuevo JL, Santamaria J, Serradell M, Marti MJ, Valldeoriola F, et al. Rapid-eye movement sleep behaviour disorder as an early marker for a neurodegenerative disorder: a descriptive study. Lancet Neurol. 2006 Jul;5(7):572–7. (PubMed PMID: 16781987. Epub 2006/06/20. eng.)
17. Postuma RB, Gagnon JF, Vendette M, Montplaisir JY. Idiopathic REM sleep behavior disorder in the transition to degenerative disease. Mov Disord. 2009 Nov 15;24(15):2225–32. (PubMed PMID: 19768814. Epub 2009/09/22. eng.)
18. Billiard M. REM sleep behavior disorder and narcolepsy. CNS Neurol Disord Drug Targets. 2009 Aug;8(4):264–70. (PubMed PMID: 19689308. Epub 2009/08/20. eng.)

19. Nevsimalova S, Prihodova I, Kemlink D, Lin L, Mignot E. REM behavior disorder (RBD) can be one of the first symptoms of childhood narcolepsy. Sleep Med. 2007 Nov;8(7–8):784–6. (PubMed PMID: 17569582. Epub 2007/06/16. eng.)
20. Nightingale S, Orgill JC, Ebrahim IO, de Lacy SF, Agrawal S, Williams AJ. The association between narcolepsy and REM behavior disorder (RBD). Sleep Med. 2005 May;6(3):253–8. (PubMed PMID: 15854856. Epub 2005/04/28. eng.)
21. Aurora RN, Zak RS, Auerbach SH, Casey KR, Chowdhuri S, Karippot A, et al. Best practice guide for the treatment of nightmare disorder in adults. J Clin Sleep Med. 2010 Aug 15;6(4):389–401. (PubMed PMID: 20726290. Pubmed Central PMCID: 2919672. Epub 2010/08/24. eng.)
22. Weyer A, Minnerop M, Abele M, Klockgether T. REM sleep behavioral disorder in pure autonomic failure (PAF). Neurology. 2006 Feb 28;66(4):608–9. (PubMed PMID: 16505328. Epub 2006/03/01. eng.)
23. Boeve BF, Silber MH, Ferman TJ, Lucas JA, Parisi JE. Association of REM sleep behavior disorder and neurodegenerative disease may reflect an underlying synucleinopathy. Mov Disord. 2001 Jul;16(4):622–30. (PubMed PMID: 11481685. Epub 2001/08/02. eng.)
24. Boeve BF, Silber MH, Parisi JE, Dickson DW, Ferman TJ, Benarroch EE, et al. Synucleinopathy pathology and REM sleep behavior disorder plus dementia or parkinsonism. Neurology. 2003 Jul 8;61(1):40–5. (PubMed PMID: 12847154)
25. Boeve BF, Silber MH, Ferman TJ. REM sleep behavior disorder in Parkinson's disease and dementia with Lewy bodies. J Geriatr Psychiatry Neurol. 2004 Sep;17(3):146–57. (PubMed PMID: 15312278. Epub 2004/08/18. eng.)
26. Boeve BF, Saper CB. REM sleep behavior disorder: a possible early marker for synucleinopathies. Neurology. 2006 Mar 28;66(6):796–7. (PubMed PMID: 16567693)
27. Boeve BF, Silber MH, Saper CB, Ferman TJ, Dickson DW, Parisi JE, et al. Pathophysiology of REM sleep behaviour disorder and relevance to neurodegenerative disease. Brain. 2007 Nov;130(Pt 11):2770–88. (PubMed PMID: 17412731. Epub 2007/04/07. eng.)
28. Gagnon JF, Postuma RB, Mazza S, Doyon J, Montplaisir J. Rapid-eye-movement sleep behaviour disorder and neurodegenerative diseases. Lancet Neurol. 2006 May;5(5):424–32. (PubMed PMID: 16632313)
29. Stiasny-Kolster K, Doerr Y, Moller JC, Hoffken H, Behr TM, Oertel WH, et al. Combination of 'idiopathic' REM sleep behaviour disorder and olfactory dysfunction as possible indicator for alpha-synucleinopathy demonstrated by dopamine transporter FP-CIT-SPECT. Brain. 2005 Jan;128(Pt 1):126–37. (PubMed PMID: 15548552. Epub 2004/11/19. eng.)
30. Postuma RB, Lang AE, Massicotte-Marquez J, Montplaisir J. Potential early markers of Parkinson disease in idiopathic REM sleep behavior disorder. Neurology. 2006 Mar 28;66(6):845–51. (PubMed PMID: 16567700. Epub 2006/03/29. eng.)
31. Mahowald MW, Schenck CH, Bornemann MA. Pathophysiologic mechanisms in REM sleep behavior disorder. Curr Neurol Neurosci Rep. 2007 Mar;7(2):167–72. (PubMed PMID: 17355839)
32. Claassen DO, Josephs KA, Ahlskog JE, Silber MH, Tippmann-Peikert M, Boeve BF. REM sleep behavior disorder preceding other aspects of synucleinopathies by up to half a century. Neurology. 2010 Aug 10;75(6):494–9. (PubMed PMID: 20668263. Pubmed Central PMCID: 2918473. Epub 2010/07/30. eng.)
33. Boeve BF, Silber MH, Ferman TJ, Kokmen E, Smith GE, Ivnik RJ, et al. REM sleep behavior disorder and degenerative dementia: an association likely reflecting Lewy body disease. Neurology. 1998 Aug;51(2):363–70. (PubMed PMID: 9710004. Epub 1998/08/26. eng.)
34. Schenck CH, Bundlie SR, Mahowald MW. Delayed emergence of a parkinsonian disorder in 38 % of 29 older men initially diagnosed with idiopathic rapid eye movement sleep behaviour disorder. Neurology. 1996 Feb;46(2):388–93. (PubMed PMID: 8614500. Epub 1996/02/01. eng.)
35. Schenck CH, Bundlie SR, Mahowald MW. REM sleep behavior disorder (RBD): delayed emergence of parkinsonism and/or dementia in 65 % of older men initially diagnosed

with idiopathic RBD, and an analysis of the maximum and minium tonic and/or phasic electromyographic abnormalities found during REM sleep. Sleep. 2003;26 (Suppl.):A316.
36. Postuma RB, Gagnon JF, Vendette M, Fantini ML, Massicotte-Marquez J, Montplaisir J. Quantifying the risk of neurodegenerative disease in idiopathic REM sleep behavior disorder. Neurology. 2009 Apr 14;72(15):1296–300. (PubMed PMID: 19109537. Epub 2008/12/26. eng.)
37. Shin HY, Joo EY, Kim ST, Dhong HJ, Cho JW. Comparison study of olfactory function and substantia nigra hyperechogenicity in idiopathic REM sleep behavior disorder, Parkinson's disease and normal control. Neurol Sci. 2012 Jul 28. (PubMed PMID: 22843227)
38. Sasai T, Miyamoto T, Miyamoto M, Iwanami M, Abe T, Matsuura M, et al. Impaired decision-making in idiopathic REM sleep behavior disorder. Sleep Med. 2012 Mar;13(3):301–6. (PubMed PMID: 22285107)
39. Miyamoto T, Miyamoto M, Iwanami M, Hirata K. Follow-up study of cardiac ^{123}I-MIBG scintigraphy in idiopathic REM sleep behavior disorder. Eur J Neurol. 2011 Oct;18(10):1275–8. (PubMed PMID: 21914050)
40. Hanyu H, Inoue Y, Sakurai H, Kanetaka H, Nakamura M, Miyamoto T, et al. Voxel-based magnetic resonance imaging study of structural brain changes in patients with idiopathic REM sleep behavior disorder. Parkinsonism Relat Disord. 2012 Feb;18(2):136–9. (PubMed PMID: 21924943)
41. Hanyu H, Inoue Y, Sakurai H, Kanetaka H, Nakamura M, Miyamoto T, et al. Regional cerebral blood flow changes in patients with idiopathic REM sleep behavior disorder. Eur J Neurol. 2011 May;18(5):784–8. (PubMed PMID: 21143707)
42. Iranzo A, Santamaria J. Severe obstructive sleep apnea/hypopnea mimicking REM sleep behavior disorder. Sleep. 2005 Feb 1;28(2):203–6. (PubMed PMID: 16171244. Epub 2005/09/21. eng.)
43. Dauvilliers Y, Rompre S, Gagnon JF, Vendette M, Petit D, Montplaisir J. REM sleep characteristics in narcolepsy and REM sleep behavior disorder. Sleep. 2007 Jul 1;30(7):844–9. (PubMed PMID: 17682654. Pubmed Central PMCID: 1978363. Epub 2007/08/09. eng.)
44. Schenck CH, Mahowald MW. Motor dyscontrol in narcolepsy: rapid-eye-movement (REM) sleep without atonia and REM sleep behavior disorder. Ann Neurol. 1992 Jul;32(1):3–10. (PubMed PMID: 1642469. Epub 1992/07/01. eng.)
45. Ahmed QA. Effects of common medications used for sleep disorders. Crit Care Clin. 2008 Jul;24(3):493–515, vi. (PubMed PMID: 18538197. Epub 2008/06/10. eng.)
46. Abril B, Carlander B. Touchon J, Dauvilliers Y. Restless legs syndrome in narcolepsy: a side effect of sodium oxybate? Sleep Med. 2007 Mar;8(2):181–3. (PubMed PMID: 17275405. Epub 2007/02/06. eng.)
47. Manni R, Terzaghi M, Zambrelli E. REM sleep behaviour disorder in elderly subjects with epilepsy: frequency and clinical aspects of the comorbidity. Epilepsy Res. 2007 Dec;77(2–3):128–33. (PubMed PMID: 17980556. Epub 2007/11/06. eng.)
48. Lloyd R, Tippmann-Peikert M, Slocumb N, Kotagal S. Characteristics of REM sleep behavior disorder in childhood. J Clin Sleep Med. 2012 Apr 15;8(2):127–31. (PubMed PMID: 22505856. Pubmed Central PMCID: 3311408)
49. Lam SP, Li SX, Mok V, Wing YK. Young-onset REM sleep behavior disorder: beyond the antidepressant effect. Sleep Med. 2012 Feb;13(2):211. (PubMed PMID: 22137105)
50. Roth B, Buuhova S, Berkova L. Familial sleep paralysis. Schweiz Arch Neurol Neurochir Psychiatr. 1968;102(2):321–30. (PubMed PMID: 5734594. Epub 1968/01/01. eng.)
51. Mayer G, Wilde-Frenz J, Kurella B. Sleep related rhythmic movement disorder revisited. J Sleep Res. 2007 Mar;16(1):110–6. (PubMed PMID: 17309770)
52. Stepanova I, Nevsimalova S, Hanusova J. Rhythmic movement disorder in sleep persisting into childhood and adulthood. Sleep. 2005 Jul 1;28(7):851–7. (PubMed PMID: 16124665)
53. Manni R, Terzaghi M. Rhythmic movements during sleep: a physiological and pathological profile. Neurol Sci. 2005 Dec;26 Suppl 3:s181–5. (PubMed PMID: 16331393. Epub 2005/12/07. eng.)

54. Aurora RN, Lamm CI, Zak RS, Kristo DA, Bista SR, Rowley JA, Casey KR. Practice parameters for the non-respiratory indications for polysomnography and multiple sleep latency testing for children. Sleep. 2012;35(11):1467–73.
55. Guilleminault C, Palombini L. Pelayo R, Chervin RD. Sleepwalking and sleep terrors in prepubertal children: what triggers them? Pediatrics. 2003 Jan;111(1):e17–25. (PubMed PMID: 12509590. Epub 2003/01/02. eng.)
56. Mahowald MW, Schenk CH, Cramer Bornemann MA. Violent parasomnias forensic implications. Handb Clin Neurol. 2011;99:1149–59. (PubMed PMID: 21056247. Epub 2010/11/09. eng.)
57. Schenck CH, Arnulf I, Mahowald MW. Sleep and sex: what can go wrong? A review of the literature on sleep related disorders and abnormal sexual behaviors and experiences. Sleep. 2007 Jun;30(6):683–702. (PubMed PMID: 17580590. Pubmed Central PMCID: 1978350)
58. Pressman MR. Factors that predispose, prime and precipitate NREM parasomnias in adults: clinical and forensic implications. Sleep Med Rev. 2007 Feb;11(1):5–30; discussion 1–3. (PubMed PMID: 17208473)
59. Bornemann MA, Mahowald MW, Schenck CH. Parasomnias: clinical features and forensic implications. Chest. 2006 Aug;130(2):605–10. (PubMed PMID: 16899867. Epub 2006/08/11. eng.)
60. Ohayon MM, Caulet M, Priest RG. Violent behavior during sleep. J Clin Psychiatry. 1997;58:369–76.
61. Camfield P, Gordon K, Camfield C, Tibbles J, Dooley J, Smith B. EEG results are rarely the same if repeated within six months in childhood epilepsy. Can J Neurol Sci. 1995 Nov;22(4):297–300. (PubMed PMID: 8599774.
62. Gilbert DL, Gartside PS. Factors affecting the yield of pediatric EEGs in clinical practice. Clin Pediatr (Phila). 2002 Jan-Feb;41(1):25–32. (PubMed PMID: 11866362)
63. Aydin K, Okuyaz C, Serdaroglu A, Gucuyener K. Utility of electroencephalography in the evaluation of common neurologic conditions in children. J Child Neurol. 2003 Jun;18(6):394–6. (PubMed PMID: 12886973)
64. Bozorg AM, Lacayo JC, Benbadis SR. The yield of routine outpatient electroencephalograms in the veteran population. J Clin Neurophysiol. 2010 Jun;27(3):191–2. (PubMed PMID: 20461015. Epub 2010/05/13. eng.)
65. Gilbert DL. Interobserver reliability of visual interpretation of electroencephalograms in children with newly diagnosed seizures. Dev Med Child Neurol. 2006 Dec;48(12):1009–10; author reply 10–1. (PubMed PMID: 17109796)
66. Gilbert DL, DeRoos S, Bare MA. Does sleep or sleep deprivation increase epileptiform discharges in pediatric electroencephalograms? Pediatrics. 2004 Sep;114(3):658–62. (PubMed PMID: 15342836)
67. Eisermann M, Kaminska A, Berdougo B, Brunet ML. Melatonin: experience in its use for recording sleep EEG in children and review of the literature. Neuropediatrics. 2010 Aug;41(4):163–6. (PubMed PMID: 21086220. Epub 2010/11/19. eng.)
68. Leach JP, Stephen LJ, Salveta C, Brodie MJ. Which electroencephalography (EEG) for epilepsy? The relative usefulness of different EEG protocols in patients with possible epilepsy. J Neurol Neurosurg Psychiatry. 2006 Sep;77(9):1040–2. (PubMed PMID: 16801353. Pubmed Central PMCID: 2077738. Epub 2006/06/28. eng.)
69. Roupakiotis SC, Gatzonis SD, Triantafyllou N, Mantouvalos V, Chioni A, Zournas C, et al. The usefulness of sleep and sleep deprivation as activating methods in electroencephalographic recording: contribution to a long-standing discussion. Seizure. 2000 Dec;9(8):580–4. (PubMed PMID: 11162756. Epub 2001/02/13. eng.)
70. Oldani A, Zucconi M, Smirne S, Ferini-Strambi L. The neurophysiological evaluation of nocturnal frontal lobe epilepsy. Seizure. 1998 Aug;7(4):317–20. (PubMed PMID: 9733408. Epub 1998/09/11. eng.)
71. Chen LS, Mitchell WG, Horton EJ, Snead OC 3rd. Clinical utility of video-EEG monitoring. Pediatr Neurol. 1995 Apr;12(3):220–4. (PubMed PMID: 7619188)

72. Provini F, Plazzi G, Tinuper P, Vandi S, Lugaresi E, Montagna P. Nocturnal frontal lobe epilepsy. A clinical and polygraphic overview of 100 consecutive cases. Brain. 1999 Jun;122(Pt 6):1017–31. (PubMed PMID: 10356056. Epub 1999/06/04. eng.)
73. Bye AM, Kok DJ, Ferenschild FT, Vles JS. Paroxysmal non-epileptic events in children: a retrospective study over a period of 10 years. J Paediatr Child Health. 2000 Jun;36(3):244–8. (PubMed PMID: 10849225)
74. Mohan KK, Markand ON, Salanova V. Diagnostic utility of video EEG monitoring in paroxysmal events. Acta Neurol Scand. 1996 Nov;94(5):320–5. (PubMed PMID: 8947283)
75. Foldvary-Schaefer N, De Ocampo J, Mascha E, Burgess R, Dinner D, Morris H. Accuracy of seizure detection using abbreviated EEG during polysomnography. J Clin Neurophysiol. 2006 Feb;23(1):68–71. (PubMed PMID: 16514353)
76. Foldvary N, Caruso AC, Mascha E, Perry M, Klem G, McCarthy V, et al. Identifying montages that best detect electrographic seizure activity during polysomnography. Sleep. 2000 Mar 15;23(2):221–9. (PubMed PMID: 10737339)
77. Marzec ML, Malow BA. Approaches to staging sleep in polysomnographic studies with epileptic activity. Sleep Med. 2003 Sep;4(5):409–17. (PubMed PMID: 14592282. Epub 2003/11/01. eng.)
78. Frauscher B, Gschliesser V, Brandauer E, Ulmer H, Peralta CM, Muller J, et al. Video analysis of motor events in REM sleep behavior disorder. Mov Disord. 2007 Jul 30;22(10):1464–70. (PubMed PMID: 17516467. Epub 2007/05/23. eng.)
79. Chesson AL Jr, Ferber RA, Fry JM, Grigg-Damberger M, Hartse KM, Hurwitz TD, et al. The indications for polysomnography and related procedures. Sleep. 1997 Jun;20(6):423–87. (PubMed PMID: 9302726. Epub 1997/06/01. eng.)
80. Aldrich MS, Jahnke B. Diagnostic value of video-EEG polysomnography. Neurology. 1991 Jul;41(7):1060–6. (PubMed PMID: 2067634)
81. Zhang J, Lam SP, Ho CK, Li AM, Tsoh J, Mok V, et al. Diagnosis of REM sleep behavior disorder by video-polysomnographic study: is one night enough? Sleep. 2008 Aug 1;31(8):1179–85. (PubMed PMID: 18714790. Pubmed Central PMCID: 2542964. Epub 2008/08/22. eng.)
82. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW. A polysomnographic and clinical report on sleep-related injury in 100 adult patients. Am J Psychiatry. 1989 Sep;146(9):1166–73. (PubMed PMID: 2764174)
83. Blatt I, Peled R, Gadoth N, Lavie P. The value of sleep recording in evaluating somnambulism in young adults. Electroencephalogr Clin Neurophysiol. 1991 Jun;78(6):407–12. (PubMed PMID: 1712276)
84. Zadra A, Pilon M, Joncas S, Rompre S, Montplaisir J. Analysis of postarousal EEG activity during somnambulistic episodes. J Sleep Res. 2004 Sep;13(3):279–84. (PubMed PMID: 15339264)
85. Schenck CH, Pareja JA, Patterson AL, Mahowald MW. Analysis of polysomnographic events surrounding 252 slow-wave sleep arousals in thirty-eight adults with injurious sleepwalking and sleep terrors. J Clin Neurophysiol. 1998 Mar;15(2):159–66. (PubMed PMID: 9563584. Epub 1998/05/01. eng.)
86. Allison KC, Lundgren JD, O'Reardon JP, Geliebter A, Gluck ME, Vinai P, et al. Proposed diagnostic criteria for night eating syndrome. Int J Eat Disord. 2010 Apr;43(3):241–7. (PubMed PMID: 19378289. Epub 2009/04/21. eng.)
87. Mahowald MW, Schenck CH, Goldner M, Bachelder V, Cramer-Bornemann M. Parasomnia pseudo-suicide. J Forensic Sci. 2003 Sep;48(5):1158–62. (PubMed PMID: 14535686. Epub 2003/10/11. eng.)
88. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep. 1986 Jun;9(2):293–308. (PubMed PMID: 3505730)
89. Schenck CH, Bundlie SR, Patterson AL, Mahowald MW. Rapid eye movement sleep behavior disorder. A treatable parasomnia affecting older adults. JAMA. 1987 Apr 3;257(13):1786–9. (PubMed PMID: 3820495. Epub 1987/04/03. eng.)

90. Sorensen GL, Kempfner J, Zoetmulder M, Sorensen HB, Jennum P. Attenuated heart rate response in REM sleep behavior disorder and Parkinson's disease. Mov Disord. 2012 Jun;27(7):888–94. (PubMed PMID: 22555939)
91. Iranzo A, Santamaria J, Tolosa E. The clinical and pathophysiological relevance of REM sleep behavior disorder in neurodegenerative diseases. Sleep Med Rev. 2009 Dec;13(6):385–401. (PubMed PMID: 19362028. Epub 2009/04/14. eng.)
92. Manni R, Terzaghi M, Glorioso M. Motor-behavioral episodes in REM sleep behavior disorder and phasic events during REM sleep. Sleep. 2009 Feb 1;32(2):241–5. (PubMed PMID: 19238811. Pubmed Central PMCID: 2635588. Epub 2009/02/26. eng.)
93. AASM. REM sleep behavior disorder (including parasomnia overlap disorder and status dissociatus). In: Sateia MJ, editor. The International Classification of Sleep Disorders, 2nd edn., diagnostic and coding manual. Westchester, IL: American Academy of Sleep Medicine; 2005. pp. 148–52.
94. Oudiette D, Leu-Semenescu S, Roze E, Vidailhet M, De Cock VC, Golmard JL, et al. A motor signature of REM sleep behavior disorder. Mov Disord. 2012 Mar;27(3):428–31. (PubMed PMID: 22173891)
95. Oudiette D, De Cock VC, Lavault S, Leu S, Vidailhet M, Arnulf I. Nonviolent elaborate behaviors may also occur in REM sleep behavior disorder. Neurology. 2009 Feb 10;72(6):551–7. (PubMed PMID: 19204265. Epub 2009/02/11. eng.)
96. De Cock VC, Vidailhet M, Leu S, Texeira A, Apartis E, Elbaz A, et al. Restoration of normal motor control in Parkinson's disease during REM sleep. Brain. 2007 Feb;130(Pt 2):450–6. (PubMed PMID: 17235126. Epub 2007/01/20. eng.)
97. D'Agostino A, Manni R, Limosani I, Terzaghi M, Cavallotti S, Scarone S. Challenging the myth of REM sleep behavior disorder: no evidence of heightened aggressiveness in dreams. Sleep Med. 2012 Jun;13(6):714–9. (PubMed PMID: 22503942)
98. Aurora RN, Zak RS, Maganti RK, Auerbach SH, Casey KR, Chowdhuri S, et al. Best practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin Sleep Med. 2010 Feb 15;6(1):85–95. (PubMed PMID: 20191945. Pubmed Central PMCID: 2823283. Epub 2010/03/03. eng.)
99. Iber C, Ancoli-Israel S, Chesson A, Quan SF, for the American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications, 1st edn. Westchester, IL: American Academy of Sleep Medicine; 2007.
100. Walters AS, Lavigne G, Hening W, Picchietti DL, Allen RP, Chokroverty S, et al. The scoring of movements in sleep. J Clin Sleep Med. 2007 Mar 15;3(2):155–67. (PubMed PMID: 17557425. Epub 2007/06/15. eng.)
101. Medicine AAoS. International Classification of Sleep Disorders, 2nd edn., diagnostic and coding manual (ICSD-2). Westchester, IL: American Academy of Sleep Medicine; 2005.
102. Frauscher B, Iranzo A, Hogl B, Casanova-Molla J, Salamero M, Gschliesser V, et al. Quantification of electromyographic activity during REM sleep in multiple muscles in REM sleep behavior disorder. Sleep. 2008 May 1;31(5):724–31. (PubMed PMID: 18517042. Pubmed Central PMCID: 2398742. Epub 2008/06/04. eng.)
103. Bliwise DL, Rye DB. Elevated PEM (phasic electromyographic metric) rates identify rapid eye movement behavior disorder patients on nights without behavioral abnormalities. Sleep. 2008 Jun 1;31(6):853–7. (PubMed PMID: 18548830. Pubmed Central PMCID: 2442408. Epub 2008/06/14. eng.)
104. Burns JW, Consens FB, Little RJ, Angell KJ, Gilman S, Chervin RD. EMG variance during polysomnography as an assessment for REM sleep behavior disorder. Sleep. 2007 Dec 1;30(12):1771–8. (PubMed PMID: 18246986. Pubmed Central PMCID: 2276138. Epub 2008/02/06. eng.)
105. Mayer G, Kesper K, Ploch T, Canisius S, Penzel T, Oertel W, et al. Quantification of tonic and phasic muscle activity in REM sleep behavior disorder. J Clin Neurophysiol. 2008 Feb;25(1):48–55. (PubMed PMID: 18303560. Epub 2008/02/28. eng.)

106. Ferri R, Manconi M, Plazzi G, Bruni O, Vandi S, Montagna P, et al. A quantitative statistical analysis of the submentalis muscle EMG amplitude during sleep in normal controls and patients with REM sleep behavior disorder. J Sleep Res. 2008 Mar;17(1):89–100. (PubMed PMID: 18275559. Epub 2008/02/16. eng.)
107. Fantini ML, Ferini-Strambi L, Montplaisir J. Idiopathic REM sleep behavior disorder: toward a better nosologic definition. Neurology. 2005 Mar 8;64(5):780–6. (PubMed PMID: 15753409. Epub 2005/03/09. eng.)
108. Sforza E, Krieger J, Petiau C. REM sleep behavior disorder: clinical and physiopathological findings. Sleep Med Rev. 1997 Nov;1(1):57–69. (PubMed PMID: 15310524. Epub 2004/08/18. eng.)
109. Montplaisir J, Gagnon JF, Fantini ML, Postuma RB, Dauvilliers Y, Desautels A, et al. Polysomnographic diagnosis of idiopathic REM sleep behavior disorder. Mov Disord. 2010 Oct 15;25(13):2044–51. (PubMed PMID: 20818653. Epub 2010/09/08. eng.)
110. Consens FB, Chervin RD, Koeppe RA, Little R, Liu S, Junck L, et al. Validation of a polysomnographic score for REM sleep behavior disorder. Sleep. 2005 Aug 1;28(8):993–7. (PubMed PMID: 16218083. Epub 2005/10/13. eng.)
111. Iranzo A, Luca Ratti P, Casanova-Molla J, Serradell M, Vilaseca I, Santamaria J. Excessive muscle activity increases over time in idiopathic REM sleep behavior disorder. Sleep. 2009 Sep 1;32(9):1149–53. (PubMed PMID: 19750919. Epub 2009/09/16. eng.)
112. Montagna P. Nocturnal paroxysmal dystonia and nocturnal wandering. Neurology. 1992 Jul;42(7 Suppl 6):61–7. (PubMed PMID: 1630641)
113. Meierkord H, Fish DR, Smith SJ, Scott CA, Shorvon SD, Marsden CD. Is nocturnal paroxysmal dystonia a form of frontal lobe epilepsy? Mov Disord. 1992;7(1):38–42. (PubMed PMID: 1557065. Epub 1992/01/01. eng.)
114. Lugaresi E, Cirignotta F, Montagna P. Nocturnal paroxysmal dystonia. Epilepsy Res Suppl. 1991;2:137–40. (PubMed PMID: 1760084. Epub 1991/01/01. eng.)
115. Hughes JR. A review of sleepwalking (somnambulism): the enigma of neurophysiology and polysomnography with differential diagnosis of complex partial seizures. Epilepsy Behav. 2007 Dec;11(4):483–91. (PubMed PMID: 17931980)
116. Derry CP, Duncan JS, Berkovic SF. Paroxysmal motor disorders of sleep: the clinical spectrum and differentiation from epilepsy. Epilepsia. 2006 Nov;47(11):1775–91. (PubMed PMID: 17116016. Epub 2006/11/23. eng.)
117. Guilleminault C, Leger D, Philip P, Ohayon MM. Nocturnal wandering and violence: review of a sleep clinic population. J Forensic Sci. 1998 Jan;43(1):158–63. (PubMed PMID: 9456536. Epub 1998/02/11. eng.)
118. Nobili L. Nocturnal frontal lobe epilepsy and non-rapid eye movement sleep parasomnias: differences and similarities. Sleep Med Rev. 2007 Aug;11(4):251–4. (PubMed PMID: 17628315. Epub 2007/07/14. eng.)
119. Silvestri R, Bromfield E. Recurrent nightmares and disorders of arousal in temporal lobe epilepsy. Brain Res Bull. 2004 Jun 30;63(5):369–76. (PubMed PMID: 15245763)
120. Oldani A, Zucconi M, Asselta R, Modugno M, Bonati MT, Dalpra L, et al. Autosomal dominant nocturnal frontal lobe epilepsy. A video-polysomnographic and genetic appraisal of 40 patients and delineation of the epileptic syndrome. Brain. 1998 Feb;121(Pt 2):205–23. (PubMed PMID: 9549500. Epub 1998/04/29. eng.)
121. Mai R, Sartori I, Francione S, Tassi L, Castana L, Cardinale F, et al. Sleep-related hyperkinetic seizures: always a frontal onset? Neurol Sci. 2005 Dec;26 Suppl 3:s220–4. (PubMed PMID: 16331400)
122. Nobili L, Cossu M, Mai R, Tassi L, Cardinale F, Castana L, et al. Sleep-related hyperkinetic seizures of temporal lobe origin. Neurology. 2004 Feb 10;62(3):482–5. (PubMed PMID: 14872038)
123. Ryvlin P, Minotti L, Demarquay G, Hirsch E, Arzimanoglou A, Hoffman D, et al. Nocturnal hypermotor seizures, suggesting frontal lobe epilepsy, can originate in the insula. Epilepsia. 2006 Apr;47(4):755–65. (PubMed PMID: 16650142. Epub 2006/05/03. eng.)

124. Terzaghi M, Sartori I, Mai R, Tassi L, Francione S, Cardinale F, et al. Sleep-related minor motor events in nocturnal frontal lobe epilepsy. Epilepsia. 2007 Feb;48(2):335–41. (PubMed PMID: 17295628. Epub 2007/02/14. eng.)
125. Tinuper P, Provini F, Bisulli F, Lugaresi E. Hyperkinetic manifestations in nocturnal frontal lobe epilepsy. Semeiological features and physiopathological hypothesis. Neurol Sci. 2005 Dec;26 Suppl 3:s210–4. (PubMed PMID: 16331398. Epub 2005/12/07. eng.)
126. Combi R, Dalpra L, Tenchini ML, Ferini-Strambi L. Autosomal dominant nocturnal frontal lobe epilepsy—a critical overview. J Neurol. 2004 Aug;251(8):923–34. (PubMed PMID: 15316796. Epub 2004/08/19. eng.)
127. Provini F, Montagna P, Plazzi G, Lugaresi E. Nocturnal frontal lobe epilepsy: a wide spectrum of seizures. Mov Disord. 2000 Nov;15(6):1264. (PubMed PMID: 11104218. Epub 2000/12/05. eng.)
128. Zucconi M, Oldani A, Ferini-Strambi L, Bizzozero D, Smirne S. Nocturnal paroxysmal arousals with motor behaviors during sleep: frontal lobe epilepsy or parasomnia? J Clin Neurophysiol. 1997 Nov;14(6):513–22. (PubMed PMID: 9458058. Epub 1998/02/11. eng.)
129. Tai P, Poochikian-Sarkissian S, Andrade D, Valiante T, del Campo M, Wennberg R. Postictal wandering is common after temporal lobe seizures. Neurology. 2010 Mar 16;74(11):932–3. (PubMed PMID: 20231671. Epub 2010/03/17. eng.)
130. Plazzi G, Vetrugno R, Provini F, Montagna P. Sleepwalking and other ambulatory behaviours during sleep. Neurol Sci. 2005 Dec;26 Suppl 3:s193–8. (PubMed PMID: 16331395. Epub 2005/12/07. eng.)
131. Nobili L, Francione S, Cardinale F, Lo Russo G. Epileptic nocturnal wanderings with a temporal lobe origin: a stereo-electroencephalographic study. Sleep. 2002 Sep 15;25(6):669–71. (PubMed PMID: 12224845)
132. Vignatelli L, Bisulli F, Provini F, Naldi I, Pittau F, Zaniboni A, et al. Interobserver reliability of video recording in the diagnosis of nocturnal frontal lobe seizures. Epilepsia. 2007 Aug;48(8):1506–11. (PubMed PMID: 17484750)
133. Vignatelli L, Bisulli F, Naldi I, Ferioli S, Pittau F, Provini F, et al. Excessive daytime sleepiness and subjective sleep quality in patients with nocturnal frontal lobe epilepsy: a case-control study. Epilepsia. 2006;47 Suppl 5:73–7. (PubMed PMID: 17239111. Epub 2007/01/24. eng.)
134. Derry CP, Davey M, Johns M, Kron K, Glencross D, Marini C, et al. Distinguishing sleep disorders from seizures: diagnosing bumps in the night. Arch Neurol. 2006 May;63(5):705–9. (PubMed PMID: 16682539)
135. Manni R, Terzaghi M, Repetto A. The FLEP scale in diagnosing nocturnal frontal lobe epilepsy, NREM and REM parasomnias: data from a tertiary sleep and epilepsy unit. Epilepsia. 2008 Sep;49(9):1581–5. (PubMed PMID: 18410366. Epub 2008/04/16. eng.)
136. Woody RC. Home videorecording of "spells" in children. Pediatrics. 1985 Oct;76(4):612–3. (PubMed PMID: 4047806)
137. Sheth RD, Bodensteiner JB. Effective utilization of home-video recordings for the evaluation of paroxysmal events in pediatrics. Clin Pediatr (Phila). 1994 Oct;33(10):578–82. (PubMed PMID: 7813135)
138. Sartori S, Vecchi M, Toldo I, Boniver C, Dalla Bernardina B, Maria Laverda A. Benign nocturnal alternating hemiplegia of childhood: the first clinical report with paroxysmal events home-video recordings. Mov Disord. 2008 Aug 15;23(11):1605–8. (PubMed PMID: 18618665. Epub 2008/07/12. eng.)
139. Stephenson J, Breningstall G, Steer C, Kirkpatrick M, Horrocks I, Nechay A, et al. Anoxic-epileptic seizures: home video recordings of epileptic seizures induced by syncopes. Epileptic Disord. 2004 Mar;6(1):15–9. (PubMed PMID: 15075063. Epub 2004/04/13. eng.)
140. Beun AM, Gutter T, Overweg J. Home EEG and video monitoring in epilepsy: first experiences. Clin Neurol Neurosurg. 1994 Aug;96(3):257–60. (PubMed PMID: 7988097. Epub 1994/08/01. eng.)
141. Stiasny-Kolster K, Mayer G, Schafer S, Moller JC, Heinzel-Gutenbrunner M, Oertel WH. The REM sleep behavior disorder screening questionnaire—a new diagnostic instrument. Mov Disord. 2007 Dec;22(16):2386–93. (PubMed PMID: 17894337. Epub 2007/09/27. eng.)

142. Naismith SL, Rogers NL, Mackenzie J, Hickie IB, Lewis SJ. The relationship between actigraphically defined sleep disturbance and REM sleep behaviour disorder in Parkinson's disease. Clin Neurol Neurosurg. 2010 Jun;112(5):420–3. (PubMed PMID: 20303647. Epub 2010/03/23. eng.)
143. Miyamoto T, Miyamoto M, Iwanami M, Kobayashi M, Nakamura M, Inoue Y, et al. The REM sleep behavior disorder screening questionnaire: validation study of a Japanese version. Sleep Med. 2009 Dec;10(10):1151–4. (PubMed PMID: 19604719. Epub 2009/07/17. eng.)
144. Nomura T, Inoue Y, Kagimura T, Uemura Y, Nakashima K. Utility of the REM sleep behavior disorder screening questionnaire (RBDSQ) in Parkinson's disease patients. Sleep Med. 2011 Aug;12(7):711–3. (PubMed PMID: 21700495)

Part II
Clinical Characteristics of Arousal Disorders

Chapter 5
Sleepwalking and Its Variants in Adults

Frank M. Ralls and Madeleine M. Grigg-Damberger

Introduction

Somnambulism (from the Latin *somnus* for sleep and ambulare meaning to walk around) or sleepwalking (SW) is a parasomnia that emerges as a partial arousal typically from non-rapid eye movement (NREM) 3 sleep. SW is one of a family of NREM arousal disorders (DoA) that begin as sudden partial awakenings from NREM 3 sleep [1]. These include confusional arousals, sleep terrors (STs), sleep-related eating disorder (SRED) [2, 3], sexual behaviors during sleep (sleep sex or sexsomnia) [4–6], sleep driving [7–9], and parasomnia overlap syndrome when in combination with rapid eye movement (REM) sleep behavior disorder (RBD) [10].

Parasomnias are unusual motor behaviors or experiences that occur during the entry into sleep, during sleep, or during arousals from sleep. A parasomnia becomes a sleep disorder if it is potentially injurious or causes injury to the patient or others, fragments sleep, causes daytime sleepiness or insomnia, or other adverse health effects and negative psychosocial effects.

SW was recognized by Hippocrates: "people groaning and shouting in their sleep, some who choke; others jump from their bed and run outside and remain out of their mind till they wake, when they are as healthy and sane as they were before" [11]. In the Middle Ages, SW was closely tied to religious beliefs, exciting "religious veneration and awe" when believed to be a "consequence of Divine appointment," less appreciated when thought due to "diabolical agency" [12].

Physicians of the late nineteenth century debated at length whether somnambulism, catalepsy, chorea, vertigo, or hysteria represented variants of epilepsy.

M. M. Grigg-Damberger (✉)
Department of Neurology, University of New Mexico, MSC10 5620,
One University of NM, Albuquerque, NM 87131-0001, USA
e-mail: MGriggD@salud.unm.edu

F. M. Ralls
Division of Pulmonary, Critical Care, and Sleep Medicine,
Department of Internal Medicine, University of New Mexico,
1101 Medical Arts Ave., ND, Bldg. #2, Albuquerque, NM 87102, USA
e-mail: fralls@salud.unm.edu

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias*
DOI 10.1007/978-1-4614-7627-6_5, © Springer Science+Business Media New York 2013

Restricted to clinical observations alone, James Pritchard (a nineteenth century English physician) thought SW, epilepsy, nightmares, and ecstatic states were similar afflictions for "Where they do not coexist with epilepsy, they often seem to stand in place of it" [13]. Johannes Müller (a nineteenth century professor of anatomy and physiology at the University of Berlin) in 1843 wrote how a sleepwalker "rises and performs all acts of life" … and when "attended with danger, he is unconscious of it; he crosses for example, narrow planks, as a child would do, that is not aware of the danger" [14]. The advent of electroencephalography (EEG) and video-polysomnography (video-PSG) in the twentieth century has taught us that SW has a neurobiological basis and can be distinguished from sleep-related epilepsy [15, 16] and other parasomnias [17].

SW in adults has rarely been associated with acts of violence or inadvertent homicide [3, 4, 18–22], indecent exposure [23, 24], pseudo-suicide [25], or impulsive behaviors [26]. These rare occurrences have fostered much of the never-ending fascination SW has fostered in folklore, novels, operas, and film [27, 28]. Most recently, Harry Potter in the 2004 film "Harry Potter and the Prisoner of Azkaban" uses SW as an excuse for being out of bed after hours [29]. In the 2010 movie, "In My Sleep," a man who sleepwalks finds himself covered in blood after waking, with a knife at his side and the police banging at his door, and learns that the wife of his best friend was stabbed to death [30]. In a 2005 episode "Role Model" of the television series House, a woman finds she is pregnant after having sexual intercourse with her ex-husband while sleeping [31].

NREM DoA are thought to represent examples of *state dissociation*, in which the physiological markers of one sleep/wake state intrude into another [32, 33]. Sleep/wake state cycling or synchronization between the primary states of being (wakefulness, NREM sleep, and REM sleep) is often remarkably seamless and rapid, but when states oscillate rapidly, the components of one state of being may intrude or become admixed with another. When this happens, behavioral markers of waking (such as walking, talking, complex motor behaviors) may be associated with those of sleep (high arousal threshold, amnesia, automatic behavior, dream imagery) [33].

The repetitive motor behaviors of many parasomnias and some epileptic seizures may represent release or expression of central pattern generators (CPGs) during sleep [34]. CPGs are species-specific neural networks in the brain stem and spinal cord of humans, which can produce repetitive motor sequences without neocortical input. Release or lack of inhibition of CPGs during sleep is likely to permit SW, STs, confusional arousals, sleep bruxism, periodic limb movements (PLMs) during sleep, sleep-related expiratory groaning, sleep-related eating, faciomandibular myoclonus, and nocturnal frontal lobe seizures.

Ontogeny (the study of how a living organism develops from conception to birth and across its lifespan) may contribute to the appearance and/or disappearance of both normal and abnormal parasomnias in humans. Unihemispheric sleep in NREM is a phylogenetic adaptation observed in some marine mammals and birds. Sleeping with only one-half of their brain at a time allows dolphins, seals, and whales to surface to breathe. The eye contralateral to the wake hemisphere is kept open and out of the water to monitor the environment while they continue to swim, whereas the eye

contralateral to the sleeping hemisphere is closed. Mallard ducks will sleep standing in a line with a duck on each end sleeping with the eye to outside kept open to guard the flock from invaders. The sentinel ducks have more unihemispheric sleep than those who sleep in the middle of the flock, and they can react to threatening stimuli seen through the one open eye. Parasomnias in humans may represent a protective role of sleeping by sleeping with only parts of our brains at one time.

Clinical Features of NREM Arousal Disorders in Adults

NREM DoA usually begin at the transition out of the first NREM 3 period, 60–90 min after sleep onset. Usually only one event occurs in a night, but if a second occurs, it is usually 60–90 min later and milder. An adult when SW typically (1) appears confused, disoriented, often misperceives objects and persons, perceives threats when none are present; (2) may perform complex, coordinated, and semipurposeful routine or nonsensical behaviors in inappropriate places and times; (3) is difficult to arouse from an episode, but if aroused, may recall fragmentary images; (4) exhibits signs of sympathetic autonomic activation (tachycardia, tachypnea); and (5) has limited or no recall of the events the following day.

SW episodes often begin with the individual sitting up in bed, fumbling with bedclothes, looking about in a confused manner before getting out of bed and slowly beginning to walk around [1, 35]. The eyes are usually open, often wide open with a confused "glassy" stare; whereas the eyes are typically closed during episodes of RBD [1]. The person often walks toward sound, light, or a particular room. Complex motor behaviors such as dressing or undressing, opening drawers or doors, and going to the bathroom or outside can be observed and typically vary from one event to another (i.e., not stereotyped as in epileptic seizures). Inappropriate behaviors and impaired judgment such as climbing out windows, urinating in a closet, a corner, or next to the toilet, or moving furniture are not uncommon. Visual inspection functions but the walker often misidentifies objects (e.g., lifting a glass of water at the bedside to the ear as though it was a telephone receiver). The SW episode typically ends spontaneously within several minutes with a return to sleep in the person's bed or less inappropriate places (couch, someone else's bed, outdoors).

Adults who sleepwalk often also have STs and/or confusional arousals, beginning as one and evolving to another. *Confusional arousals* in adults are characterized by moaning, whimpering, and/or incoherent vocalization; aimless thrashing, flailing, or kicking; looking "possessed," not in terror, but remaining in bed; when spoken to, acting confused and slow to respond, if at all; and exhibiting moderate degrees of sympathetic activation. *Sleep terrors* are heralded by a blood-curdling scream or cry, followed by confusion, intense vocalization, motor agitation, and severe sympathetic activation (profuse sweating, mydriasis, tachycardia, and tachypnea) [35].

Unlike children, adult sleepwalkers often recall fragments, thoughts, and images of many or most of their SW episodes, and some of their behaviors represent enactment of recent events/concerns/stimuli in their sleep environment [36]. Zadra et al.

reported 78 % of 68 adult chronic sleepwalkers remember parts of their SW episodes (16 % always, 37 % often, and 25 % sometimes) and 69 % said that fragmentary images or thoughts often or always accompanied their SW [37]. Oudiette et al. (2009) recorded overnight PSG in 38 adults with chronic severe SW and/or STs and found that (1) 71 % recalled at least one dreamlike mentation related to an in-laboratory SW or ST episode; (2) the dreamlike mentation action corresponded with some of the motor behaviors observed (reenactment); (3) 95 % of mentations were a single visual scene; and (4) mentations were frequently unpleasant, creating feelings of apprehension in 84 %, misfortune in 54 %, and aggression in 24 % (with the sleepwalker being the victim) [38]. Case reports of complex dream-enacting behaviors in chronic sleepwalkers have been reported [39].

Epidemiology and Risk Factors for Sleepwalking

SW is most common in children and decreases with age. A longitudinal study of child development reported an overall prevalence of 40 % for STs and 14.5 % for SW in children aged 2.5–6 years [40]. The peak incidence of STs is between 5 and 7 years, whereas SW peaks later between 8 and 12 years [41]. An earlier study found 40 % of children (ages 6–16 years) have at least one episode of SW (most between ages 11 and 12 years) but only 2–3 % have more than one per month [42]. The majority of children who sleepwalk stop sleepwalking by the age of 13 years, but SW persists in 24 % of frequent sleepwalkers [42].

SW and other DoA is far less common in adults [41] and epidemiological studies even fewer. Forty to 60 % of SW episodes after late adolescence occur in individuals who had them in childhood, sometimes recurring after having none for several years [42, 43]. A telephone survey of a large representative sample of 4,972 adults in the UK found that 2 % reported SW, 2.2 % STs, and 4.2 % confusional arousals [41]. SW was reported in 3.9 % of men and 3.1 % of women of 11,220 subjects in the Finnish Twin Cohort, but occurred weekly in only 0.4 % of either gender [44]. Of the adults who did sleepwalk, 89 % of men and 84 % of women reported SW in childhood. The proportion who reported never having walked in their sleep in childhood and did so as adults was 0.6 % in both men and women.

A large prospective cross-sectional study found 29 % of 19,136 US adults ($\geq$ 18 years) reported a lifetime history of "nocturnal wandering" (NW), 3.6 % within the previous year [45]. Only 0.2 % had $\geq$ 1 episode per week, 1 % $\geq$ 2 per month, and 2.6 % 1–12 across the year. NW decreased with age, excepting those who report $\geq$ 1 episode per week. NW was not associated with gender. Twenty-six percent reported having had NW as a child or adolescent but without any episodes within the prior year. Individuals who self-reported NW in the previous year were twice as likely to report a family history of NW compared with those who denied NW (30.5 % vs. 17.2 %, odds ratio [OR] 2.12). NW when present that year was most often chronic: 7.2 % reported episodes had been present for less than 6 months, 5.8 % for 6–12 months, 6.2 % for 1–5 years, and 80.5 % for > 5 years.

Logistic regression analysis demonstrated that the risk for frequent NW (≥ 2 episodes per month) increased significantly if the individual who also reported obstructive sleep apnea (OSA) syndrome (OR 3.9), circadian rhythm sleep disorder (OR 3.4), insomnia disorder (OR 2.1), alcohol abuse or dependence (OR 3.5), major depressive disorder (OR 3.5), obsessive-compulsive disorder (OR 3.9), or use of over-the-counter sleeping pills (OR 2.5) or selective serotonin reuptake inhibitor antidepressants (OR 3.0). They found a higher risk for having at least 1 NW episode in the previous year in individuals sleeping less than 7 h per night after adjusting for possible confounding factors such as age, sleep, and mental disorder. The association between NW and major depressive disorder or obsessive compulsive disorder could not be attributed to the use of psychotropic medication(s).

Another recent large prospective cross-sectional study of 1,000 Norwegian adults (≥ 18 years) found that 22.4 % reported a history of SW but only 1.7 % reported SW within the past 3 months [46]. The lifetime and current prevalence of STs was 10.4 % and 2.7 %, confusional arousal 18.5 % and 6.9 %, self-injury during sleep 4.3 % and 0.9 %, injuring someone else during sleep 3.8 % and 0.4 %, sexual acts during sleep 7.1 % and 2.7 %, and sleep-related eating 4.5 % and 2.2 %, respectively [46]. About 12 % reported ≥ 5 parasomnias. The lifetime prevalence of SW among a random sample of 276 young adult Nigerians was 23 % and an adult prevalence of 1.42 % [47]. The prevalence of SW in > 1,000 Brazilian adults (ages 20–80 years) in 2007 was 2.8 % [48].

Familial or Genetic Predisposition to NREM Arousal Disorders

A family history is one of the strongest risk factors for DoA in children and adults. The first (and perhaps the most spectacular) report of familial SW by Clerici in 1930 described a family of six members (husband, wife (who was also his cousin), and their four children), all of whom gathered one night at 3 AM around a table in their servants' quarters [49]. A landmark study by Kales et al. (1980) found 80 % of 25 sleepwalkers and 27 with STs had one or more relative who was affected by SW, STs, or both [50]. The Finnish Twin Cohort mentioned earlier found no difference in the concordance rate for SW between 1,045 monozygotic or 1,899 dizygotic twin pairs with concordance rates of 0.55 and 0.35 for monozygotic and dizygotic childhood twin pairs and 0.32 and 0.06 for monozygotic and dizygotic adult pairs, respectively. Genetic influences predicted that 66 % of the total phenotypic variance for SW in men and boys, 36 % in women, and 57 % in girls [44].

Guilleminault et al. have long emphasized how underlying primary sleep disorders (most often obstructive sleep-disordered breathing (OSDB), less often restless legs syndrome (RLS)) trigger SW or other DoA in children and adults; treating them often eliminates the DoA [41, 51–54]. Most recently, a report found that craniofacial risk factors for sleep-disordered breathing (SDB; particularly maxillary and/or mandibular deficiencies) were often present in families of adults referred for SW

[55]. They argue that these inherited craniofacial abnormalities predispose to OSDB and lead to sleep fragmentation and DoA.

A prospective case-control study found a higher incidence of parasomnias in children with idiopathic epilepsy compared with their siblings or healthy controls [56], but parasomnias were not more common in a prospective study of adults with a wide variety of different epilepsies and seizure types compared with healthy controls [57]. However, DoA and sleep-related bruxism is more common in patients and their relatives with nocturnal frontal lobe epilepsy (NFLE) [58]. The lifetime prevalence of DoA was 6-fold higher in patients with NFLE and 4.7 times greater in their relatives compared with controls.

Lecendreux et al. (2003) performed HLA-DQB1 typing in 60 Caucasian subjects with SW and their families and 60 ethnically-matched controls without any diagnosed sleep disorder [59]. Licis et al. (2011) collected DNA samples and performed parametric linkage analysis on 9 affected and 13 unaffected family members in a 4-generation SW family. They found that (1) 35 % of the sleepwalkers tested positive for DQB1*0501 compared with 13.3 % of the controls (OR 3.5); (2) SW was inherited as an autosomal dominant disorder with reduced penetrance and the genetic locus for it was at chromosome 20q12-113.12; and (3) SW in a first degree relative increased the chances of developing this disorder by a factor of 10 [60]. More research is needed to confirm whether SW is a mono- or polygenetic inherited disorder and to confirm the connection with inherited craniofacial abnormalities.

Factors Which Predispose, Prime, or Precipitate Sleepwalking

SW or STs in adults is most likely to occur when priming factors (such as sleep deprivation or situational stress) are coupled with provoking triggers (noise, light, sound) in individuals who have a familial or genetic predisposition for it [61]. The frequency of DoA episodes can be lessened by identifying and eliminating these. Genetic susceptibility or family history predispose to DoA [44, 50, 55, 60, 62, 63]. *Priming* factors include conditions and substances that increase NREM 3 sleep or make arousal from sleep more difficult: sleep deprivation/restriction, alcohol, certain medications, situational or emotional stress, and fever [61, 64] Noise, touch, or forced awakenings from NREM sleep can precipitate SW in predisposed adults [43].

New onset or recurrence of SW in adults warrants consideration of other primary sleep disorders, including OSDB, RLS, periodic limb movement disorder (PLMD), RBD, jet lag, and/or shift work [52, 55, 64–68]. Other stressors that can precipitate SW in predisposed adults are stressful life events, changes in sleep environment, family or workplace conflicts, emotional stress, infections, extreme fatigue, pain, or changes in exercise pattern [61, 69–73].

A plethora of small and/or single-case reports demonstrate that SW and its variants can be triggered by nonbenzodiazepine hypnotics, neuroleptics, antidepressants, lithium, sodium oxybate, and beta-blockers in predisposed individuals [7, 9, 61, 74–96]. In summary, SW in adults is most likely to occur when priming factors

(such as sleep deprivation or situational stress) are coupled with provoking triggers (noise, light, sound) in individuals who have a familial or genetic predisposition for it [61]. When these occur, a "perfect storm" for SW occurs [97]. Box 5.1 summarizes factors that predispose, prime, or perpetuate DoA.

Adult Sleepwalking Common in Psychiatric Populations

The majority of adult sleepwalkers does not have a Diagnostic and Statistical Manual of Mental Disorders (DSM)-based psychiatric disorder or highly disturbed personality traits, [5, 52, 61, 97, 98] but SW and/or STs are common in certain adult psychiatric populations [99]. A coexisting bipolar or adjustment disorder increased the risk for confusional arousals 13.0 and 3.1 times, respectively, among 4,972 UK adults [41]. Major depressive or obsessive compulsive disorders were major risk factors for ≥ 2 episodes of NW in US adults [45]. Panic or anxiety disorders, simple phobias, or suicidal thoughts were more likely to be reported in a case-control study of 21 adolescents who reported SW and/or STs in the prior year compared with 30 healthy controls [100]. SW (along with trance, possession, and paranormal experiences) were more frequently reported in patients with dissociative disorders than healthy controls [101]. Adult-onset SW was thought to contribute to delusions, aggression, and accidental death in some patients with schizophrenia [99].

Nonbenzodiazepine hypnotic (with or without concomitant psychotropic) use may contribute to the higher incidence of DoA in patients with psychiatric problems. Five percent of 255 Taiwanese adults (average age 42 years, 54 % females) taking zolpidem (average dose 10 mg) reported SW and/or amnesic sleep-related behavioral problems [102]. All had concomitant psychiatric problems, including schizophrenia, anxiety, and affective or adjustment disorders. Complex sleep-related behaviors among these patients included watching television, telephone use, eating, or conversation with their family. A recent prospective cross-sectional study of 66 psychiatric patients with childhood-onset (56 %, $n = 37$) or adult-onset (44 %, $n = 29$) SW found that lifetime use of zolpidem was associated with adult-onset SW [89]. Adult-onset sleepwalkers had more frequent SW episodes and sleep-related eating than child-onset walkers and were 5.4 times more likely to complain of frequent insomnia. SW recurred in only 40 % of childhood-onset walkers when comorbid psychiatric problems developed.

Sleepwalking Variants

Adults while sleeping rarely exhibit episodes of eating, drinking, driving a motor vehicle, or injure or murder individuals who attempt to help them. Often these complex motor behaviors emerge from NREM 3 sleep.

Sleep-Related Violent Behavior

The most common sleep disorders that can result in injurious or violent behaviors are DoA and RBD; less often OSDB, nocturnal seizures, narcolepsy with cataplexy, psychogenic or dissociative disorders, and malingering [18, 20, 27, 103]. Violent behavior during sleep (VBS) was self-reported by 1.6 % of 19,961 adults (aged 15 years or older) from multiple European Union countries [20]. During VBS episodes, 79 % report vivid dreams and 31 % hurt themselves or someone else. The greatest risk factor for VBS is to have a family member with VBS (OR 9.0), although SW (OR 2.0) and STs (OR 4.2) in the family increased the risk of VBS [20]. Only 12 % of people who had VBS had consulted a physician.

Violent behavior during SW tends to occur when the episode is already underway and the individual is approached by another person (often one trying to help), occurs more in males, and is associated with more stressors, disturbed sleep, and excessive use of caffeine and drug abuse [21, 27, 39, 104]. VBS attributed to DoA in 32 cases from the medical or legal literature were present in 100 % of the confusional arousal, 81 % of STs, and 40–90 % of the SW episodes [21].

Dramatic reports of somnambulistic violent behavior and/or homicide still gain considerable attention in the media [22] and often prompt a referral to sleep specialists [39, 105]. VBS during an episode of SW or STs have resulted in attempted or completed homicide, suicide, or inappropriate sexual behaviors. Clinical features of historical cases of VBS attributed to DoA are summarized in Box 5.2.

A number of criminal cases have claimed that SW or its variant was induced by alcohol intoxication [90]. Alcohol-induced SW as a criminal defense has been based upon the concept that alcohol increases NREM 3 sleep. Some studies have shown that alcohol modestly increases the percent of NREM 3 sleep in the first 2–4 h of a night [90]. However, the amount and percentage of NREM 3 sleep is often reduced or absent in those who regularly abuse alcohol. It is possible for an individual to perform violent acts without conscious awareness while sleeping, but whether SW occurred at the time of the crime remains uncertain. Guidelines developed for determining a putative role of sleep disorder in a violent act are summarized in Box 5.3 [106].

Sleep Driving and Drug-Impaired Driving Overlap Syndromes

A rare variant of SW in adults is driving a motor vehicle for long distances without conscious awareness while sleeping (so-called sleep driving) [7]. Episodes of driving a motor vehicle have been rarely reported in individuals with SW. These must be distinguished from the far more common reports of adults driving under the influence of nonbenzodiazepine hypnotics often coupled with other substances. Sleep driving in a sleepwalker is very rare: the US Federal Drug Administration (FDA) found only 14 cases of sleep driving between 1992 and 2006, which were *not* due to the use or misuse of nonbenzodiazepine hypnotics.

Bizarre, dangerous, or socially inappropriate behaviors have been associated with the more often inappropriate use or abuse of nonbenzodiazepine hypnotics (zolpidem, zopiclone, or zaleplon) [7, 9, 107]. Alcohol, a Z-drug, or other substances in patients with a history of SW can be a priming factor for SW [86] and zolpidem at higher doses is more likely to cause SW [108]. Nevertheless, these so-called "Z-drugs" can precipitate a sleepwalker to walk. The majority of media and police reports of "sleep driving" occur in individuals with no prior history of DoA. Impaired driving (or inappropriate eating or sexual behavior) associated with sedative/hypnotic use is often misattributed to SW (and better called drug-impaired driving). Zolpidem was the major intoxicant in 2.3 % of 8,121 driving while intoxicated (DWI) arrests in Wisconsin from 1999 to 2005; higher than prescribed levels were found in 35 % cases and 23 % of the arrests were between 0800 and 1200 hours.

Z-drug-impaired driving bears only superficial resemblance to the behavior presented as characteristic of "true" sleep driving [109]. Sleepwalkers when sleep driving without medication, alcohol, or other substance use are able to stand and walk unaided but are unable to interact with police. However, drivers who have been prosecuted for driving under the influence of Z-drugs (1) appear drowsy, tired, confused, and disoriented and have unsteady gait, slowed speech, impaired coordination, and short-term memory loss [7]; (2) are often severely physically impaired, unable to stand up or maintain balance, but able to understand or interact with police; (3) have often failed to take the medication at the correct time or remain in bed for sufficient time and/or have combined Z-drugs with other central nervous system depressants and/or alcohol; and (4) often have blood levels of Z-drugs that exceed therapeutic ranges [7, 8].

Nocturnal Eating and Sleep-Related Eating Disorder

SRED was originally described in 1991 [110], but diagnostic criteria for it continue to evolve [111–116]. It is a parasomnia that is characterized by recurrent episodes of involuntary or compulsive eating after awakening typically from NREM 2 or 3 sleep, which have adverse health consequences [111–113, 117] SRED is a dysfunctional nocturnal eating (NE) behavior diagnosed if a patient reports one or more of the following: (1) ingestion of unusual, inedible or toxic substances; (2) difficulty falling back to sleep or report nonrestorative sleep; (3) sleep-related injury or potentially injurious behaviors; (4) morning anorexia; or (5) adverse health consequences.

Sleep clinicians have been asked to distinguish SRED from nocturnal eating syndrome (NES), clinical features of which are summarized in Table 5.1. However, the distinction is often near to impossible because of symptom overlap between them. NES is a primary eating disorder characterized by evening hyperphagia (≥ 25 % of daily caloric intake after the evening meal and/or ≥ 2 nighttime awakenings with ingestions per week), frequent nocturnal awakenings from sleep with conscious compulsive eating, morning anorexia, and a circadian delay in meal timing [118, 119].

Table 5.1 Clinical features that may help distinguish sleep-related eating disorder from nocturnal eating syndrome

Sleep-related eating disorder (SRED): a parasomnia	Nocturnal eating syndrome (NES): a primary eating disorder
Recurrent episodes of involuntary eating and drinking during the main sleep period associated with little or no awareness of these	Evening hyperphagia: consuming $\geq 25\,\%$ of daily food intake after the evening meal and/or awakening to eat ≥ 2 nights per week for ≥ 3 months
Consumption of inedible or toxic substances	And 3 of the 5 features Morning anorexia Strong urge to eat between dinner and sleep onset and/or nocturnal awakenings Insomnia ≥ 4 nights per week Belief that eating is necessary to fall asleep or return to sleep Mood frequently depressed or mood worsens in the evening
Dangerous behaviors performed in the pursuit of food or while cooking it	Awareness and recall of the evening and nocturnal eating episodes
Eating foods in combinations, amounts, and/or raw states they would have never been prepared or eaten when awake	
May exhibit dangerous and/or atypical behaviors when cooking (stove left on, kitchen a mess)	Associated with significant distress and/or impaired functioning
Can cause morning anorexia, weight gain, and/or other adverse health consequences from this	
Adverse health consequences from recurrent binge eating of high caloric food	Not secondary to substance abuse/dependence, medication(s), a general medical, and/or psychiatric disorder
Not associated with anorexia nervosa, bulimia, binge-eating, or other daytime eating disorders	

NE is associated with obesity, binge eating, and psychological distress [120]. A recent study by Vinai et al. (2012) had eating disorder and sleep specialists evaluate 28 consecutive adults (mean age 44.5 ± 12.5 years, 57 % females) with SRED [111]. They found 79 % also met diagnostic criteria for NES [111]. All of these patients with SRED also complained of evening hyperphagia, morning anorexia, insomnia, and mood disorders. Video-PSG findings did not distinguish between groups.

Three case series have reported comorbid SW in 48–65 % of patients with SRED [110, 114, 116]. SW without SRED may precede SRED and then it often becomes the predominant SW behavior [110]. Amnesia for SRED episodes most often occurs with concomitant sedative-hypnotic use (especially zolpidem). Several case series or single-case reports describe SRED provoked by sedative-hypnotics or other medications, most often zolpidem, but also zopiclone, zaleplon, quetiapine, risperidone, olanzapine, and sodium oxybate [87, 121–127]. SRED is associated with psychiatric disorders, especially depression and dissociation.

NE and SRED are very common in patients with RLS [128, 129]. Thirty-three percent of 100 patients with RLS endorsed symptoms of SRED compared with 1 % of 100 age-matched normal controls [129]. A prospective study by Howell and Schneck (2012) evaluated how often 88 patients presenting with RLS and 42 with psychophysiological insomnia reported either NE or SRED [129]. They found that (1) 61 % of the RLS and 36 % of SRED patients complained of NE compared with 12 % of psychophysiological insomnia patients; (2) NE could not be attributed to arousal because the patients with insomnia were more likely to report prolonged nocturnal awakenings (93 %) than the patients with RLS (64 %); (3) the frequency of amnestic SW and SRED was far greater among RLS patients taking sedative-hypnotics than those with insomnia (80 vs. 8 %, respectively); and (4) the frequency of NE decreased from 68 to 34 % after the RLS patients were treated with dopaminergic agents. They concluded that NE is common in RLS and often lessens with dopaminergic therapy. Amnestic SRED and SW occur primarily when RLS patients take sedative-hypnotics. Most of the few video-PSG studies on SRED have been done on drug-free subjects. Vertugno et al. (2006) recorded 45 episodes of NE in 22 of 35 consecutive drug-free patients and found that (1) eating episodes always occurred after *complete* awakenings from NREM 1, 2, or 3 sleep (and REM sleep in 1 patient) with an EEG background consistent with normal wakefulness; (2) patients interviewed during the eating episodes were fully conscious, remembered the events the following morning, and reported a compulsion to eat (but denied feeling hungry or thirsty); (3) awakenings were not closely related to PLMs or respiratory-related arousals; and (4) the mean time delay from awakening to food intake was 7 min (range 0.3–81 min), eating duration 6 min (0.4–20 min), and return to sleep after returning to bed was 14 min (0.5–107 min). Elevated PLM indexes in 63 % and RLS dyskinesias in 14 % (and SRED are particularly common in patients with RLS) of the patients were observed. A peculiar video-PSG feature in 29 (83 %) of their patients was periodic recurring chewing and swallowing movements throughout all stages of sleep, but especially NREM 1 and 2. It resembled rhythmic masticatory muscle activity (RMMA) seen during sleep in patients with sleep bruxism (and less often normal controls). Half of these oral movements were linked to EEG arousals and often existent with PLMs. The authors speculated that the high prevalence of RMMA and PLMs during sleep in patients with SRED coupled with compulsory food-seeking behavior and reported efficacy of dopaminergic medications argue for a dopaminergic dysfunction underlying the pathogenesis of SRED.

A case-control video-PSG study by Brion et al. (2012) compared clinical histories and PSG findings in 15 patients with SRED, 21 sleepwalkers, and 20 age- and sex-matched healthy volunteers [112]. They found that (1) patients with SRED were mainly women, had disease onset in adulthood, suffered nightly episodes and insomnia, and had more frequent eating problems in childhood and higher current anorexia scores than sleepwalkers and controls; (2) unlike controls, 66 % of patients with SRED had a past or current history of SW; (3) SRED episodes typically occurred during the first half of the night; (4) SRED patients had frequent arousals from NREM 3 (not seen in controls); (5) SRED patients had higher awareness during their parasomnias than sleepwalkers; and (6) only 10 % of sleepwalkers ate during

their SW episodes. On video-PSG, eating episodes occurred mostly within 1 min after awakening from NREM 2 ($n = 9$) or NREM 3 ($n = 6$) sleep. The frequencies of RLS, PLM, and sleep apnea were similar across the three groups. The authors concluded that patients with SRED share several clinical commonalities with sleepwalkers (although their level of awareness is higher) with having prior or current eating behavior problems.

Treatment strategies for SRED include eliminating medications that contribute to it and correcting comorbid sleep disorders (e.g., RLS and rarely OSA). The majority of patients with drug-induced SRED improve. If symptoms persist, the patients, especially those with RLS, should consider dopaminergic agents (such as pramipexole) [130, 131]. SRED in some patients with SW were controlled with clonazepam [110]. Preliminary studies show that topiramate may be effective, but larger randomized controlled trials are needed [132–134].

Parasomnia Overlap Disorder and Status Dissociatus

Parasomnia overlap disorder (POD) refers to a particularly rare sleep disorder characterized by the combination of injurious SW, STs, and RBD [5, 135]. The original case series of 33 patients by Schenck et al. [5] reported two subgroups: idiopathic ($n = 22$, mean age 9 ± 7 years) and symptomatic ($n = 11$, mean age 27 ± 23 years). POD was regarded as symptomatic when parasomnia began with a neurologic (e.g., narcolepsy, brain tumor, multiple sclerosis) or psychiatric disorder (major depression, schizophrenia, post-traumatic stress disorder, or chronic ethanol/amphetamine abuse and withdrawal). Little has been published since on POD: clinical and video-PSG findings of POD in 40-year-old woman following an acute inflammatory encephalitis where neuroimaging showed a lesion in the pontine tegmentum as a possible anatomic cause for it [136] and two small case reports of POD with sexual behaviors during sleep [10, 137]. These describe persistence of muscle tone during REM sleep and sudden transitions from NREM 3 sleep to partial wakefulness with accompanying complex motor behaviors. Parasomnia overlap syndrome may be found in some patients with Parkinson's disease (PD). A recent prospective prevalence study found that 36 (9 %) of 417 patients with PD reported SW, adult-onset SW in 22 (5 %) patients; sleepwalkers were more likely to have higher scores on a RBD- validated questionnaire, hallucinations, and nightmares [138].

Status dissociatus (SD) is a condition in which sleep/wake state differentiation is completely uncertain [139]. SD has been observed in patients with fatal familial insomnia [140–144], Morvan's syndrome [145, 146], and perhaps delirium tremens. Isolated case reports of its occurrence in individuals with multiple system atrophy, brainstem lesions, or Guillain–Barre syndrome have been reported [147–149]. Complex motor behaviors emerge from indeterminate EEG and other biophysiological markers of sleep and wake. A most interesting paper by Stamelou et al. (2012) argues that the twilight state of paradoxical unresponsiveness and complex nonepileptic repetitive stereotyped perioral, eye, and limb movements are seen in the majority of patients with anti-N-methyl-D-aspartate-receptor encephalitis [150].

Sleep-Related Sexual Behaviors

Sleep-related sexual behavior (SRSB) is inappropriate sexual behavior occurring without conscious awareness when sleeping [4, 10, 137, 151–153]. Alves et al. (1999) reported a 27-year-old man with a history of SW since the age of 9 years. Sleep-related violent behavior began at age 20 years and amnestic episodes of complete sexual orgasm with his wife beginning at age 23 years. A literature review in 2007 detailed 31 cases (mean age 32 years, 81 % males) from sexual vocalizations or body movements, fondling, masturbation, sexual intercourse (with or without orgasm), and sexual assault/rape. PSG recorded in 26 (35 % for forensic concerns) captured sexual vocalization (moaning) from NREM 3 sleep in 3 and sexual intercourse provoked by the bed partner from NREM 1/wakefulness in one. A video-PSG study of three men with SRSB found OSDB in one, DoA in another, and RBD in the third [151]. SRSB with video-PSG was recently reported in a 60-year-old woman with parasomnia overlap syndrome [10]. Diagnosing SRSB especially when forensic issues are concerned requires corroborated history, video-PSG with extended EEG, and electromyography (EMG) montages (to identify other sleep disorders such as OSDB, sleep-related seizures, RBD, POD, and psychogenic or dissociative disorders), neuropsychological assessment (primarily to identify the presence of psychiatric comorbidities) and urine drug screen.

Indications for Video-Polysomnography in Adult Sleepwalkers

Comprehensive in-laboratory video-PSG is not routinely indicated for "typical" SW or STs in prepubertal children [154–157]. However, video-PSG is usually warranted to evaluate parasomnias in older adolescents or adults that (1) begin or recur in adulthood; (2) occur more than 2–3 times per week; (3) are potentially injurious or have caused injury to the patient or others; (4) are accompanied by symptoms suggestive of SDB, PLMD, suspected or known epilepsy, and/or excessive daytime sleepiness; or (5) could be seizure-related but the initial clinical evaluation and a standard EEG was inconclusive [154]. Video-PSG is occasionally requested to evaluate forensic cases where parasomnias and/or other sleep disorders or drugs are a contributing factor [4, 19, 61, 106].

Video-Polysomnographic Features of Disorders of Arousal

Unfortunately, only a third of patients with paroxysmal nocturnal events will have one of their habitual events on a single night of in-laboratory video-PSG [158, 159]. Aldrich et al. (1991) found that 1–2 consecutive nights of video-PSG provided valuable diagnostic information in 69 % of 41 patients whose paroxysmal motor behaviors were "prominent," 41 % of 11 referred for "minor motor activity in sleep," and 78 %

of 36 patients with known epilepsy [158]. Video-PSG was diagnostic in 65 % and "helpful" in another 26 % of 100 consecutive adults referred for frequent sleep-related injuries, identifying DoA in 54, RBD in 36, sleep-related dissociative disorders in 7, nocturnal seizures in 2, and OSA in 1 [98].

V-PSG recordings confirm that the majority (> 90 %) of DoA arise from NREM 3 sleep (occasionally from NREM 2 sleep), but not always in the first third of the night [160, 161]. Occasionally, a sudden run of rhythmic high-voltage delta EEG activity lasting 10–30 s may herald the onset of a DoA episode. This EEG pattern is called hypersynchronous delta activity (HSD). Initially misconstrued as diagnostic for DoA events, it is now regarded as a nonspecific EEG arousal pattern, observed in healthy controls during spontaneous arousals from NREM 3 sleep or in arousals from NREM sleep due to obstructive respiratory events.

Onset of a DoA on video-PSG is typically heralded by the abrupt onset of tachycardia (severity of it varies: ST > SW > confusional arousal). Tachycardia accompanies NFLE seizures, but change in heart rate is often absent in RBD events. The EEG following onset of a DoA most often shows either high-amplitude delta intermixed with beta or alpha activity or hypersynchronous theta or delta activity [162]. Often, muscle artifact obscures part or most of the DoA event; worse yet, the patient may pull off the electrodes and run from the bed. Less often, scorable epochs of NREM 2 sleep or repeated microsleeps are observed. Figure 5.1 shows the onset of a confusional arousal from NREM 3 sleep. Wakefulness or REM sleep should prompt consideration of other parasomnias.

Sleep researchers from Montreal have published an elegant series of experimental studies evaluating how to increase the likelihood of recording a typical SW or ST event in a single night of in-laboratory video-PSG [69, 163, 164]. Twenty-five hours of total sleep deprivation in 40 adult sleepwalkers increased the frequency and complexity of SW events recorded in the laboratory, resulting in ≥ 1 event in 90 % of the patients and none of the controls [163]. Many of the DoA behaviors recorded were mild: playing with the bed sheets or electrodes, turning and resting on one's hands while staring about looking confused, resting on one's knees, or trying to get out of the bed [36]. To ensure 25 h of total sleep deprivation, subjects were asked to arrive in the laboratory at their customary bedtime but remain awake until 1 h later than their usual wake time.

To further provoke DoA events, 10 adult sleepwalkers and 10 controls underwent two consecutive nights of video-PSG. After a normal night of baseline recording in the laboratory, patients and controls were deprived of sleep for 25 h and then presented with recurring 3-s blasts of 1000 Hz pure sounds in ascending intensities of 10 dB from 40 dB to 90 dB via earphones with a minimum of 1 min between two stimuli during NREM 3 sleep and the first and second NREM–REM sleep cycles. Auditory stimuli were presented in the targeted sleep stage after at least 1 min of stable EEG and EMG until an EEG arousal, a behavioral episode, or a maximum of six auditory stimuli was reached [36]. The majority of DoA events occurred from NREM 3 sleep, a few from NREM 2 sleep, and none from REM sleep. Using these techniques, the investigators found that they could trigger 1–3 SW events in 100 % of their subjects (and none of their controls). The mean intensity of auditory

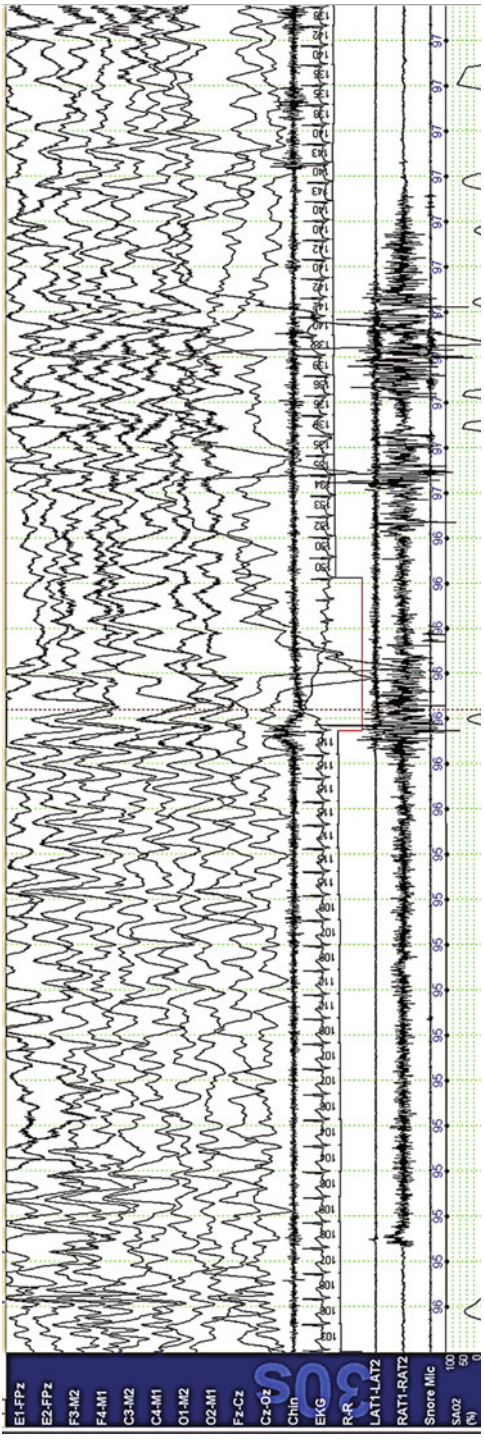


Fig. 5.1 Confusional arousal from NREM 3 sleep in a 6-year-old child (note the tachycardia)

stimulus needed to induce DoA episodes was similar to that needed to induce non-DoA arousals in sleepwalkers and controls (approximately 50 dB). These findings suggest that sleepwalkers are neither more easy nor more difficult to awaken from NREM 3 sleep than controls, but the sleepwalkers suffer from an atypical and distinct arousal reaction [36, 69].

Most studies have failed to find meaningful or consistent differences in sleep macroarchitecture in children or adults with DoA, except for a greater number of arousals selectively from NREM 3 sleep in those with DoA, even on nights without SW/STs [69, 159, 165–167]. Sleep researchers have found differences in sleep microarchitecture and EEG power in adults with SW or STs compared with controls: a slower decay of EEG delta power of NREM 3 sleep across recurring cycles of NREM sleep and nonspecific alterations in cyclic alternating pattern during NREM sleep consistent with increased NREM 3 sleep instability [51, 168, 169]. More work is needed to see if individuals with DoA can be identified by abnormalities in their sleep microarchitecture.

Differential Diagnosis of Sleepwalking in Adults Usually Requires Confirmation by Video-Polysomnography

Video-PSG is usually required to confirm the particular parasomnia in adults with frequent NW and identify if there are other primary sleep disorders contributing to it. The differential diagnosis for NW in adults is summarized in Box 5.4. Most often, DoA in adults needs to be distinguished from sleep-related hypermotor seizures, RBD, pseudo-RBD due to severe OSDB, and rarely dissociative events or malingering.

The clinical features of sleep-related hypermotor seizures are summarized in Box 5.5. Figure 5.2 shows an example of a nocturnal frontal lobe seizure unexpectedly recorded in a 16-year-old patient, which began from NREM 3 sleep. Longer lasting nocturnal frontal lobe seizures can lead to "episodic nocturnal wandering," but more often, postictal wandering is associated with seizures that are temporal lobe in origin [170–174]. Nocturnal temporal lobe seizures tend to be *less* frequent, do *not* cluster, and usually do *not* have the hyperkinetic motor activity of NFLE.

RBD is usually identified by the presence of REM sleep without atonia with or without RBD behaviors. The timing of RBD episodes is quite different from DoA. RBD episodes usually appear in the first 90 min after sleep onset, typically last 1–5 min, and recur 3–5 times at 90–120 min intervals across an entire night of sleep during recurring periods of REM sleep. As opposed to DoA, patients with RBD are easily aroused from an event. Once aroused, they are able to recount dreams (if not too demented) that correspond to the observed behaviors [175, 176]. Their eyes are typically closed during events. Their heart rates do *not* increase during RBD events (perhaps reflecting loss of sympathetic autonomic regulation).

RBD motor behaviors can be simple (talking, shouting, excessive jerking of limbs or body) or complex (arm flailing, slapping, kicking, sitting up, leaping from bed, running, crawling, gesturing, swearing) [135]. Because many of the RBD motor

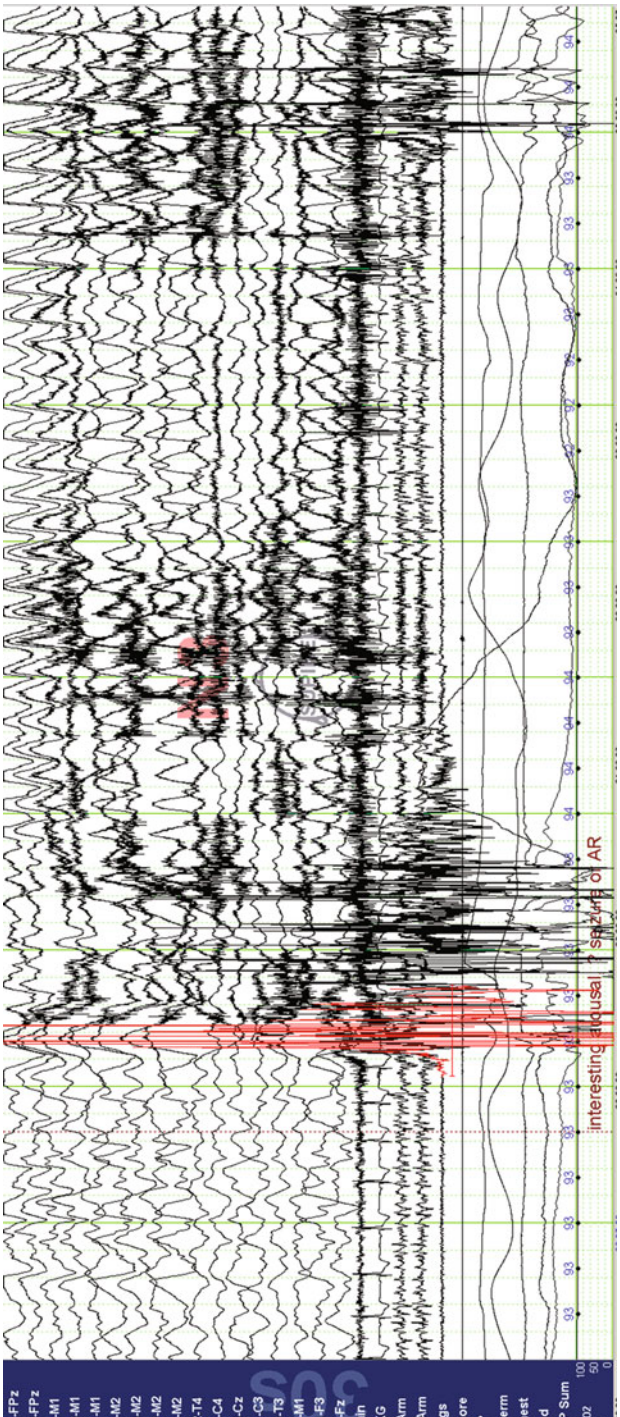


Fig. 5.2 Stereotyped rhythmic activity accompanied by hypermotor leg movements, chewing, vocalization, and complete awakening in a 16-year-old patient with developmental delay

and/or vocal behaviors usually last only a few seconds, we have found it particularly useful to review carefully the epochs of REM sleep in the video-PSG when the excessive phasic motor activity is observed, confirming clinical manifestations of RBD that are easily missed. Figure 5.3 shows a 60-s epoch recorded on a video-PSG in a 79-year-old man with severe OSDB and occasional dream enactment behavior. Note the excessive tonic activity in the chin EMG, excessive phasic activity in the leg EMG channels, atrial fibrillation in the electrocardiogram (EKG), and an obstructive apnea that lasts for 31 s and causes desaturation to 64 % but no arousal.

Violent behaviors from any stage of sleep can be observed in patients with severe OSA. In 2005, Iranzo et al. reported 16 adults who presented with dream-enacting behaviors and unpleasant dreams [177]. Severe OSA (mean apnea–hypopnea index (AHI) 68 per hour) but no REM sleep without atonia was found on video-PSG. Abnormal sleep behaviors occurred only during apnea-induced arousals. Continuous positive airway pressure (CPAP) therapy eliminated the abnormal behaviors, unpleasant dreams, snoring, and daytime hypersomnolence. We recently recorded video-EEG for VBS in a 45-year-old boxer in whom apnea triggered recurring violent arousals from NREM 2 sleep in which the 45-year-old traumatized boxer who would assume boxing postures, loud vocalization, and fierce expression, but he regained consciousness within seconds and the EEG within 1 min was consistent with wakefulness (Fig. 5.4 a and b).

Treatment Strategies for Adult Sleepwalkers

Treatment of SW in adults (summarized in Box 5.6) consists of reassurance, education of the patient and family, setting up a safe sleep environment, and reducing or avoiding priming or precipitating factors [178, 179]. Identifying and treating other primary sleep disorders (OSDB, RLS) may lessen or eliminate DoA. A prospective case-control study of 50 young adults with chronic SW and compared with an equal number of age-matched controls found that many of the sleepwalkers also had OSDB [52]. Treating them with CPAP or surgery controlled their SW (whereas benzodiazepines or psychotherapy did not). Nonadherent CPAP patients continued to have episodes of SW.

Pharmacotherapy may be appropriate for frequent chronic and/or potentially injurious SW or STs in adults when these are (1) potentially injurious or have caused injury or sleep disturbance to the individual or others; (2) chronic and frequent; (3) capable of causing legal issues regarding violent or sexual behavior (although nocturnal sleep-related violence is rarely, if ever, recurrent); (4) chronic and causing individual or family distress; and (5) associated with secondary consequences (e.g., weight gain, social embarrassment, excessive daytime sleepiness). For some adult sleepwalkers, clonazepam can be taken only on “predictable” nights or nightly for several months, then gradually discontinued or reinstituted if behaviors recur. In patients with POD, clonazepam with/without melatonin may be effective.

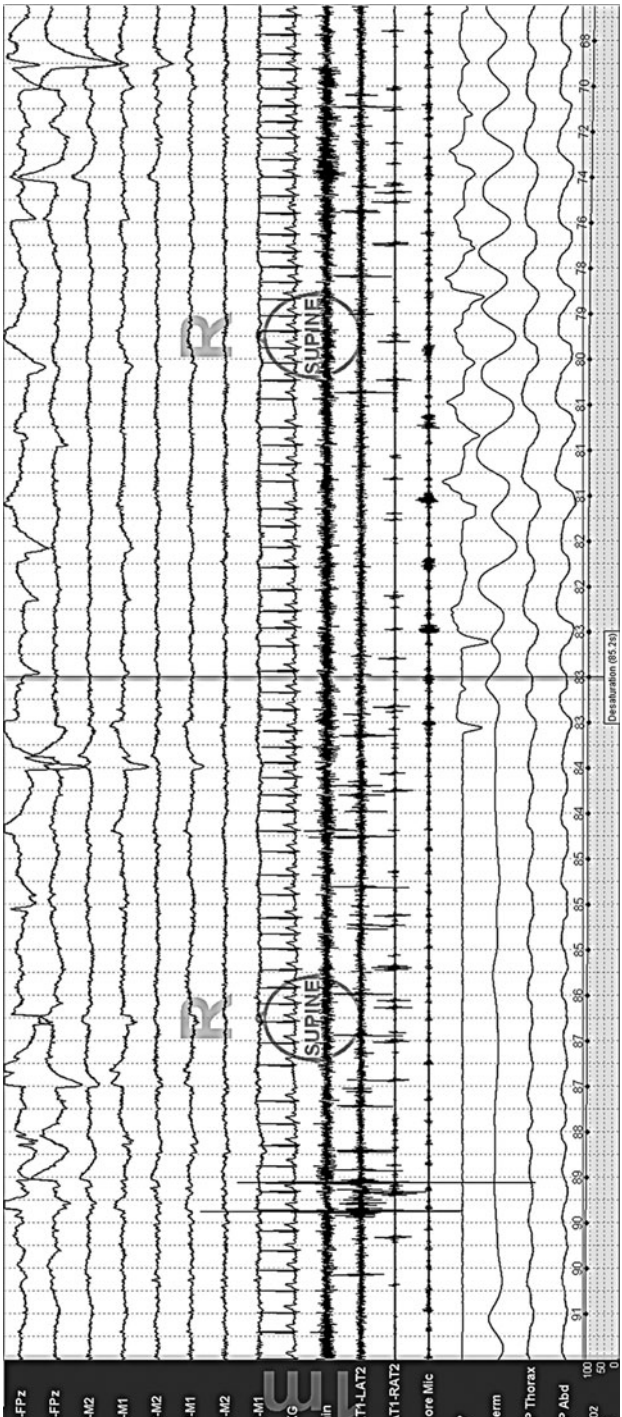


Fig. 5.3 PSG during REM sleep recorded on 79-year-old patients with symptoms suggestive of OSA and RBD. Note excessive tonic activity in the chin EMG, excessive phasic activity in the leg EMG channels, a prolonged obstructive apnea lasting for 31 s and causing desaturation to 64 % (but no arousal), and atrial fibrillation in the EKG channel

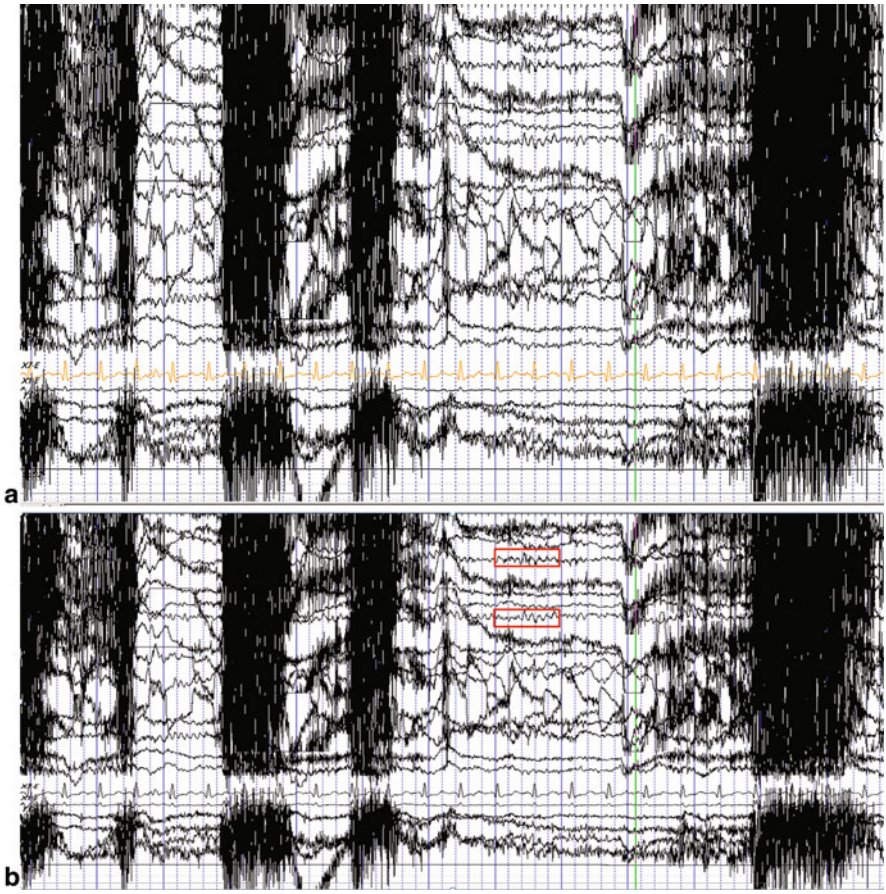


Fig. 5.4 **a** Abrupt arousal from NREM 2 sleep: 45-year-old patient sits up, cries out, and assumes boxing posture. **b** An epoch of 15 s of violent arousal from NREM 2 sleep in a boxer: EEG background in between muscle artifact 1.5 min later shows normal 9-Hz dominant alpha rhythm of wakefulness (*boxes*)

Clonazepam (0.5–2 mg QHS) has been used for many years with good results in adults with frequent and potentially injurious DoA (or RBD) [35, 180]. The value of clonazepam to suppress frequent DoA in adults is based on five small case series, which together show that 83 % of 61 sleepwalkers responded to it [178, 181]. A single-blinded prospective trial found 10 mg diazepam in adult sleepwalkers often, but not always, suppressed SW [182]. Two large case series have found clonazepam dosed only at bed provided complete or substantial control of injurious sleep behaviors (most often DoA or RBD) with a relatively low risk of adverse effects, dosage tolerance or dependency [98, 183].

Clonazepam has an elimination half-life of 30–40 h, and maximum plasma concentrations occur within 1–4 h after oral ingestion [184]. Clonazepam used to treat DoA, RBD, or other injurious parasomnias in adults is often limited by side effects: sedation especially upon awakening, early morning clumsiness, impotence, and confusion [183, 185, 186]. Clonazepam taken only at night can cause memory or word-finding difficulties, depression, disinhibition, and if the dose is too low, it may trigger SW/ST or confusional arousals, especially in older adults with or without dementia. Clonazepam (1) is relatively contraindicated in patients with a history of substance or alcohol abuse, untreated sleep disordered breathing, cognitive or motor dysfunction, or a nocturnal dissociative disorder and (2) should be used with caution in patients with dementia, gait disorders, or concomitant OSA [187].

Conclusion

Adult SW most often occurs in individuals with a past history of SW as a child. Adult SW most often arises when priming, precipitating, and provoking factors trigger them in an individual with an inherent, familial, and/or genetic tendency for deep sleep. New onset or recurrence of chronic or injurious SW in adult requires a comprehensive clinical and diagnostic evaluation to differentiate NW from other parasomnias and to identify other treatable primary sleep disorders. SW is more common in patients with neurodegenerative diseases and is often associated with RBD or parasomnia overlap syndrome. Treatment remains conservative by providing a safe environment, avoiding triggers, and reserving pharmacologic intervention for extremely disruptive behavior.

Case Example

A 31-year-old woman presented following an episode of waking up in the street in front of her home in her nightgown, with a knife in one hand and an unopened package of deli ham in the other. Her partner stated that the patient would infrequently (1–2 times per year) perform unusual behaviors after falling asleep for 1–2 h. Sometimes she would move objects around on a desk, sit at the table sipping from an empty cup, or walk around the house and return to bed. She would wake up on the living room sofa, having gone to bed the night before. If awake, her partner would gently redirect her back to bed and she would sleep the remainder of the night without further incident. Upon awakening, the patient did not remember anything that occurred while SW. Since starting her new job, the episodes increased to 1–3 times per week, and the most recent episode of leaving the house raised special concern. Further questioning revealed that she had numerous episodes of SW as a child. However, these decreased to 1–2 per year during her teenage years.

Review of her medical history was notable for recently starting thyroid replacement therapy, otherwise her medications included an antihypertensive and oral

contraception. Social history was significant for starting a new job that had been stressful and required that she start work at 4 AM. The physical examination was remarkable for a bone-mass index (BMI) of 35 and a neck circumference of 17 cm. The partner reported that the patient snored but did not witness any pauses in breathing. Due to symptoms suggestive of sleep disordered breathing (OSA), the patient underwent PSG (sleep study), which demonstrated moderate OSA. Other hematologic parameters were normal. She was prescribed continuous positive airway pressure (CPAP) therapy and was instructed to increase her sleep time by 1–2 h in order to sleep 7–9 h per night. Follow-up at 1, 3, and 6 months demonstrated complete resolution of the SW behaviors.

Comments

This case demonstrates classic findings in the adult sleepwalker. She has a history of SW as a child. SW events were increased by sleep deprivation, stress, and OSA, causing arousals from sleep. Treatment consisted of treating medical issues, in this case OSA, improving sleep hygiene, providing a safe environment, and reassurance.

Practical Points

- SW occurs in 2 % of adults but occurs weekly in less than 0.5 %.
- SW in adults is typically associated with a past history or family history of SW.
- Common precipitating factors for adult SW include sleep restriction/deprivation, emotional or situational stress, and use of certain medications.
- Video-PSG is usually needed to differentiate adult SW from NFLE, RBD, parasomnia overlap syndrome, pseudo-RBD due to severe OSA, psychogenic or dissociative events, or malingering.
- A secondary cause should be sought in de novo sleepwalking in adults (e.g., medication changes, psychiatric disorders, SDB, untreated medical disorders, neurodegenerative disease).
- Treatment for SW should focus on providing a safe environment and reassurance and pharmacotherapy should be reserved only for cases where the behavior poses a risk to safety.

Box 5.1: Factors Which Prime, Predispose, or Precipitate Sleepwalking or Sleep Terrors in Adults
- Genetic predisposition = strongest factor;
- Cumulative partial sleep deprivation or sleep restriction;
- Situational, mental, or emotional stress;
- Extreme exercise, fatigue, or exhaustion;

- Environmental stimuli (noise, light, touch, attempts to arouse);
- Circadian rhythm disorders (shift work, jet lag, night shift);
- Other primary sleep disorders: obstructive sleep-disordered breathing, restless legs syndrome, periodic limb movements during sleep, narcolepsy with cataplexy;
- Drugs (nonbenzodiazepine hypnotics, alcohol, antidepressants, antipsychotics, antihistamines, other sedative-hypnotics, sodium oxybate);
- Fever or infections.

Box 5.2: Summary of the Clinical Features of Historical Cases of Violence Attributed to Sleepwalking and Its Variants [21]

- Majority were male, most between ages 17–35 years;
- The provocation was quite minor and the violent response greatly exaggerated;
- Most violence began following direct provocation or close proximity to the sleepwalker;
- Most often, the victims encountered or sought out the sleepwalker;
- Violence was more often inaccurately directed, but was precisely delivered in other cases;
- Violence most often directed at the bed partner, occasionally a child or a subject's mother;
- Implements employed included guns, hammers, shovels, scissors, axes, razors, a bayonet, or throwing a child or baby out the window or against a wall;
- During the episode, the individual fails to recognize the victim but exhibits feelings of horror or fear upon awakening after the event and recognizing what has occurred;
- Most lack recall of the event, but two were aware that they had shot someone but uncertain who;
- Immediate triggers were physical stimulation or loud noises, and often occurred when the individual had been under psychological stress, or had a recent quarrel, argument, or threatened attack;
- Most but not all had a previous history of SW.

Box 5.3: Guidelines for Determining a Putative Role of Sleep Disorder in a Violent Act

- Episode typically brief, lasting < few minutes;
- Spatial orientation and fine motor coordination intact but no facial recognition or memory of event;

- Upon return of consciousness, perplexity, horror, or remorse without attempt to escape, conceal, or cover-up the action; pain perception for wounds often delayed;
- History of parasomnias;
- Usually some degree of amnesia for the event; however, islands of partial memory may remain;
- Victim may be someone who merely happened to be present but may have been the stimulus for the arousal;
- Acts of violence usually follow periods of poor sleep, some related to obstructive sleep-disordered breathing, and/or insomnia related to anxiety or depression;
- Recurrence of violent behaviors during sleep are rare.

Box 5.4: Differential Diagnosis for Nocturnal Wandering in Adults
- NREM arousal disorder (confusional arousal, sleepwalking, sleep terror);
- Sleep-related epilepsy;
- REM sleep behavior disorder (RBD) and pseudo-RBD due to obstructive sleep apnea;
- Sleep-related panic attacks;
- Nightmare disorder;
- Sleep-related dissociative disorder;
- Sleep-related choking, laryngospasm, or gastroesophageal reflux;
- Sleep-related rhythmic movement disorder with vocalization;
- Sleep-related expiratory groaning (catathrenia);
- Post-traumatic stress disorder (PTSD);
- Sudden death when sleeping due to myocardial infarction, Brugada syndrome, untreated OSA, sudden unexpected death in epilepsy, and trauma.

Box 5.5: Clinical Characteristics That Suggest Sleep-Related Hypermotor Seizures
- An abrupt, often explosive, onset awakening the patient from grossly undisturbed NREM 2 sleep;
- Asymmetric dystonic or tonic postures;
- Thrashing, pedaling, and kicking of the lower extremities;
- Tend to be "fairly" stereotyped in appearance for the individual patient;
- Brief (typically lasting 20–30 s, less than 1–2 min);
- Patients are often aware during the seizure, but say they cannot control their movements or vocalizations;

- No postictal confusion or amnesia;
- 20 % have no scalp-recorded ictal EEG activity accompanying them.

Box 5.6: Treating Sleepwalking and Sleep Terrors in Adults
- Present the diagnosis to patient and family and educate them about the nature of these;
- Allow episodes to run their course:
  - Interfere only to prevent injury;
  - May try gently redirecting the individual back to bed and resist waking the person;
- Secure the bedroom and home to prevent injury:
  - Nightlights; window and door locks;
  - Motion detectors in hallways;
  - Alarms or barriers at door/stairs;
  - Remove sharp objects from bedroom floor;
  - Consider ground floor bedrooms and moving the bed partner;
  - Secure hazardous objects such as kitchen knives and guns;
- Regular bed- and wake-times with adequate amounts of sleep;
- Decrease noise, light, pain, nocturia, stress, and dyspnea, which may contribute to partial arousal;
- Avoid visual, auditory, or tactile stimuli especially during the first third of the night, which may trigger an event;
- Avoid sleep restriction/deprivation, jet lag, night/shift work, extreme exercise, fatigue, and emotional or situational stress;
- Identify and treat other primary sleep disorders (sleep apnea, restless legs, narcolepsy RBD, sleep-related epilepsy, parasomnia overlap syndrome, insomnia, nocturnal eating, and gastroesophageal reflux);
- Avoid precipitating medications or substances: alcohol, antipsychotics, antidepressants, antihistamines, sedative-hypnotics, and benzodiazepines;
- Clonazepam is potentially injurious and may cause excessive daytime sleepiness or daytime stress.

References

1. Medicine AAoS. International classification of sleep disorders, 2nd ed., diagnostic & coding manual (ICSD-2). Westchester, IL: American Academy of Sleep Medicine; 2005.
2. Allison KC, Lundgren JD, O'Reardon JP, Geliebter A, Gluck ME, Vinai P, et al. Proposed diagnostic criteria for night eating syndrome. Int J Eat Disord. 2010 Apr;43(3):241–7. (PubMed PMID: 19378289. Epub 2009/04/21. eng.)
3. Schenck CH, Mahowald MW. Review of nocturnal sleep-related eating disorders. Int J Eat Disord. 1994 May;15(4):343–56. (PubMed PMID: 8032349. Epub 1994/05/01. eng.)

4. Schenck CH, Arnulf I, Mahowald MW. Sleep and sex: what can go wrong? A review of the literature on sleep related disorders and abnormal sexual behaviors and experiences. Sleep. 2007 Jun 1;30(6):683–702. (PubMed PMID: 17580590. Pubmed Central PMCID: 1978350. Epub 2007/06/22. eng.)
5. Schenck CH, Boyd JL, Mahowald MW. A parasomnia overlap disorder involving sleepwalking, sleep terrors, and REM sleep behavior disorder in 33 polysomnographically confirmed cases. Sleep. 1997 Nov;20(11):972–81. (PubMed PMID: 9456462. Epub 1998/02/11. eng.)
6. Bejot Y, Juenet N, Garrouty R, Maltaverne D, Nicolleau L, Giroud M, et al. Sexsomnia: an uncommon variety of parasomnia. Clin Neurol Neurosurg. 2010 Jan;112(1):72–5. (PubMed PMID: 19765888. Epub 2009/09/22. eng.)
7. Pressman MR. Sleep driving: sleepwalking variant or misuse of z-drugs? Sleep medicine. reviews. 2011 Oct;15(5):285–92. (PubMed PMID: 21367628)
8. Poceta JS. Zolpidem ingestion, automatisms, and sleep driving: a clinical and legal case series. J Clin Sleep Med. 2011 Dec 15;7(6):632–8. (PubMed PMID: 22171202. Pubmed Central PMCID: 3227709)
9. Daley C, McNiel DE, Binder RL. "I did what?" Zolpidem and the courts. J Am Acad Psychiatry Law. 2011;39(4):535–42. (PubMed PMID: 22159981)
10. Cicolin A, Tribolo A, Giordano A, Chiarot E, Peila E, Terreni A, et al. Sexual behaviors during sleep associated with polysomnographically confirmed parasomnia overlap disorder. Sleep Med. 2011 May;12(5):523–8. (PubMed PMID: 21493137. Epub 2011/04/16. eng)
11. Hippocrates. The sacred disease. In: Lloyd GER, editor. Hippocratic writings. Boston, MA: Penguin; 1983. pp. 237–51.
12. Wienholt A. Introduction. Seven lectures on somnambulism (trans: Colquhoun JC). Edinburgh, Scotland: Adam and Charles Back; 1845.
13. Temkin O. The falling sickness: a history of epilepsy from the Greeks to the beginnings of modern neurology. 2nd ed. Baltimore, MD: Johns Hopkins Press; 1994.
14. Müller JB. Elements of physiology, vol. 2 (trans: Baly W). Cambridge: Lea and Blanchard; 1843. p. 813.
15. Derry C. Nocturnal frontal lobe epilepsy vs parasomnias. Curr Treat Options Neurol. 2012 Oct;14(5):451–63. (PubMed PMID: 22865379. Epub 2012/08/07. eng.)
16. Derry CP, Harvey AS, Walker MC, Duncan JS, Berkovic SF. NREM arousal parasomnias and their distinction from nocturnal frontal lobe epilepsy: a video EEG analysis. Sleep. 2009 Dec 1;32(12):1637–44. (PubMed PMID: 20041600. Pubmed Central PMCID: 2786048. Epub 2010/01/01. eng.)
17. Grigg-Damberger M, Ralls F. Primary sleep disorders and paroxysmal nocturnal nonepileptic events in adults with epilepsy from the perspective of sleep specialists. J Clin Neurophysiol. 2011 Apr;28(2):120–40. (PubMed PMID: 21399519. Epub 2011/03/15. eng.)
18. Ebrahim I, Fenwick P. Sleep related violence, alcohol and sleepwalking. Brain; 2012 Nov;135(Pt 11):e219. (PubMed PMID: 22734126)
19. Mahowald MW, Schenk CH, Cramer Bornemann MA. Violent parasomnias forensic implications. Handb Clin Neurol. 2011;99:1149–59. 2011;99:1149–59. (PubMed PMID: 21056247. Epub 2010/11/09. eng.)
20. Ohayon MM, Schenck CH. Violent behavior during sleep: prevalence, comorbidity and consequences. Sleep Med. 2010 Oct;11(9):941–6. (PubMed PMID: 20817553. Pubmed Central PMCID: 2939252)
21. Pressman MR. Disorders of arousal from sleep and violent behavior: the role of physical contact and proximity. Sleep. 2007 Aug;30(8):1039–47. (PubMed PMID: 17702274. Pubmed Central PMCID: 1978391)
22. Cartwright R. Sleepwalking violence: a sleep disorder, a legal dilemma, and a psychological challenge. Am J Psychiatry. 2004 Jul;161(7):1149–58. (PubMed PMID: 15229043)
23. Schenck CH, Mahowald MW. Sleepwalking and indecent exposure. Med Sci Law. 1992 Jan;32(1):86–7. (PubMed PMID: 1740990. Epub 1992/01/01. eng.)
24. Thomas TN. Sleepwalking disorder and mens rea: a review and case report. Maricopa County Superior Court. J Forensic Sci. 1997 Jan;42(1):17–24. (PubMed PMID: 8988570)

25. Mahowald MW, Schenck CH, Goldner M, Bachelder V, Cramer-Bornemann M. Parasomnia pseudo-suicide. J Forensic Sci. 2003 Sep;48(5):1158–62. (PubMed PMID: 14535686. Epub 2003/10/11. eng.)
26. Bonkalo A. Impulsive acts and confusional states during incomplete arousal from sleep: crinimological and forensic implications. Psychiatr Q. 1974;48(3):400–9. (PubMed PMID: 4463401)
27. Umanath S, Sarezky D, Finger S. Sleepwalking through history: medicine, arts, and courts of law. J Hist Neurosci. 2011 Oct;20(4):253–76. (PubMed PMID: 22003856)
28. Riva MA, Sironi VA, Tremolizzo L, Lombardi C, De Vito G, Ferrarese C, et al. Sleepwalking in Italian operas: a window on popular and scientific knowledge on sleep disorders in the 19th century. Eur Neurol. 2010;63(2):116–21. (PubMed PMID: 20110713)
29. Rowling JK. Harry Potter and the prisoner of Azkaban: IGN Entertainment, Inc.; 2004.
30. In My Sleep 2010.
31. Role Model 2005.
32. Mahowald MW, Cramer Bornemann MA, Schenck CH. State dissociation, human behavior, and consciousness. Curr Top Med Chem. 2011;11(19):2392–402. (PubMed PMID: 21906025. Epub 2011/09/13. eng.)
33. Mahowald MWB, Schenck CH. State dissociation: implications for sleep and wakefulness, consciousness, and culpability. Sleep Med Clin. 2011;6(4):393–400.
34. Tassinari CA, Cantalupo G, Hogl B, Cortelli P, Tassi L, Francione S, et al. Neuroethological approach to frontolimbic epileptic seizures and parasomnias: The same central pattern generators for the same behaviours. Rev Neurol (Paris). 2009 Oct;165(10):762–8. (PubMed PMID: 19733874. Epub 2009/09/08. eng.)
35. Provini F, Tinuper P, Bisulli F, Lugaresi E. Arousal disorders. Sleep Med. 2011 Dec;12 Suppl 2:S22–6. (PubMed PMID: 22136894)
36. Zadra A, Pilon M. Non-rapid eye movement parasomnia: diagnostic methods. In: Pressman M, editor. Parasomnias. Sleep medicine clinics, vol. 6. Philadelphia: W.B. Saunders; 2011. pp. 447–58.
37. Zadra A, Pilon M, Montplaisir J. Phenomenological experiences in adult sleepwalkers: towards a science of consciousness. Research Abstracts. 2008:128.
38. Oudiette D, Leu S, Pottier M, Buzare MA, Brion A, Arnulf I. Dreamlike mentations during sleepwalking and sleep terrors in adults. Sleep. 2009 Dec;32(12):1621–7. (PubMed PMID: 20041598. Pubmed Central PMCID: 2786046)
39. Pillmann F. Complex dream-enacting behavior in sleepwalking. Psychosom Med. 2009 Feb;71(2):231–4. (PubMed PMID: 19073753. Epub 2008/12/17. eng.)
40. Petit D, Touchette E, Tremblay RE, Boivin M, Montplaisir J. Dyssomnias and parasomnias in early childhood. Pediatrics. 2007 May;119(5):e1016–25. (PubMed PMID: 17438080)
41. Ohayon MM, Guilleminault C, Priest RG. Night terrors, sleepwalking, and confusional arousals in the general population: their frequency and relationship to other sleep and mental disorders. J Clin Psychiatry. 1999 Apr;60(4):268–76; quiz 77. (PubMed PMID: 10221293. Epub 1999/04/30. eng.)
42. Klackenberg G. Somnambulism in childhood—prevalence, course and behavioral correlations. A prospective longitudinal study (6–16 years). Acta Paediatr Scand. 1982 May;71(3):495–9. (PubMed PMID: 7136663)
43. Tinuper P, Bisulli F, Provini F. The parasomnias: mechanisms and treatment. Epilepsia. 2012 Dec;53 Suppl 7:12–9. (PubMed PMID: 23153205)
44. Hublin C, Kaprio J, Partinen M, Heikkila K, Koskenvuo M. Prevalence and genetics of sleepwalking: a population-based twin study. Neurology. 1997 Jan;48(1):177–81. (PubMed PMID: 9008515)
45. Ohayon MM, Mahowald MW, Dauvilliers Y, Krystal AD, Leger D. Prevalence and comorbidity of nocturnal wandering in the U.S. adult general population. Neurology. 2012 May 15;78(20):1583–9. (PubMed PMID: 22585435. Epub 2012/05/16. eng.)
46. Bjorvatn B, Gronli J, Pallesen S. Prevalence of different parasomnias in the general population. Sleep Med. 2010 Dec;11(10):1031–4. (PubMed PMID: 21093361. Epub 2010/11/26. eng.)

47. Oluwole OS. Lifetime prevalence and incidence of parasomnias in a population of young adult Nigerians. J Neurol. 2010 Jul;257(7):1141–7. (PubMed PMID: 20143107. Epub 2010/02/10. eng.)
48. Santos-Silva R, Bittencourt LR, Pires ML, de Mello MT, Taddei JA, Benedito-Silva AA, et al. Increasing trends of sleep complaints in the city of Sao Paulo, Brazil. Sleep Med. 2010 Jun;11(6):520–4. (PubMed PMID: 20494615)
49. Clerici A. Sonnabulismo. Gazz Osp. 1930;51:361–3.
50. Kales A, Soldatos CR, Bixler EO, Ladda RL, Charney DS, Weber G, et al. Hereditary factors in sleepwalking and night terrors. Br J Psychiatry. 1980 Aug;137:111–8. (PubMed PMID: 7426840)
51. Guilleminault C, Lee JH, Chan A, Lopes MC, Huang YS, da Rosa A. Non-REM-sleep instability in recurrent sleepwalking in pre-pubertal children. Sleep Med. 2005 Nov;6(6):515–21. (PubMed PMID: 15994122. Epub 2005/07/05. eng.)
52. Guilleminault C, Kirisoglu C, Bao G, Arias V, Chan A, Li KK. Adult chronic sleepwalking and its treatment based on polysomnography. Brain. 2005 May;128(Pt 5):1062–9. (PubMed PMID: 15817520. Epub 2005/04/09. eng.)
53. Remulla A, Guilleminault C. Somnambulism (sleepwalking). Expert Opin PharmacPeriodical. 2004 Oct;5(10):2069–74. (PubMed PMID: 15461542. Epub 2004/10/06. eng.)
54. Guilleminault C, Palombini L. Pelayo R, Chervin RD. Sleepwalking and sleep terrors in prepubertal children: what triggers them? Pediatrics. 2003 Jan;111(1):e17–25. (PubMed PMID: 12509590. Epub 2003/01/02. eng.)
55. Cao M, Guilleminault C. Families with sleepwalking. Sleep Med. 2010 Aug;11(7):726–34. (PubMed PMID: 20598633. Epub 2010/07/06. eng.)
56. Cortesi F, Giannotti F, Ottaviano S. Sleep problems and daytime behavior in childhood idiopathic epilepsy. Epilepsia. 1999 Nov;40(11):1557–65. (PubMed PMID: 10565583. Epub 1999/11/24. eng.)
57. Khatami R, Zutter D, Siegel A, Mathis J, Donati F, Bassetti CL. Sleep-wake habits and disorders in a series of 100 adult epilepsy patients—a prospective study. Seizure. 2006 Jul;15(5):299–306. (PubMed PMID: 16546407. Epub 2006/03/21. eng.)
58. Bisulli F, Vignatelli L, Naldi I, Licchetta L, Provini F, Plazzi G, et al. Increased frequency of arousal parasomnias in families with nocturnal frontal lobe epilepsy: a common mechanism? Epilepsia. 2010 Sep 5;51(9):1852–60. (PubMed PMID: 20477848. Epub 2010/05/19. eng.)
59. Lecendreux M, Bassetti C, Dauvilliers Y, Mayer G, Neidhart E, Tafti M. HLA and genetic susceptibility to sleepwalking. Mol Psychiatry. 2003 Jan;8(1):114–7. (PubMed PMID: 12556916. Epub 2003/01/31. eng.)
60. Licis AK, Desruisseau DM, Yamada KA, Duntley SP, Gurnett CA. Novel genetic findings in an extended family pedigree with sleepwalking. Neurology. 2011 Jan 4;76(1):49–52. (PubMed PMID: 21205695. Pubmed Central PMCID: 3030226)
61. Pressman MR. Factors that predispose, prime and precipitate NREM parasomnias in adults: clinical and forensic implications. Sleep Med Rev. 2007 Feb;11(1):5–30; discussion 1–3. (PubMed PMID: 17208473)
62. Hublin C, Kaprio J. Genetic aspects and genetic epidemiology of parasomnias. Sleep Med Rev. 2003 Oct;7(5):413–21. (PubMed PMID: 14573377. Epub 2003/10/24. eng.)
63. Hublin C, Kaprio J, Partinen M, Koskenvu M. Parasomnias: co-occurrence and genetics. Psychiatr Genet. 2001 Jun;11(2):65–70. (PubMed PMID: 11525419)
64. Zadra A, Pilon M. NREM parasomnias. Handb Clin Neurol. 2011;99:851–68. (PubMed PMID: 21056232. Epub 2010/11/09. eng.)
65. Casez O, Dananchet Y, Besson G. Migraine and somnambulism. Neurology. 2005 Oct 25;65(8):1334–5. (PubMed PMID: 16247080)
66. Yalvac HD, Emul M, Karlidag R, Ozcan C, Unal S. Sleepwalking in multiple sclerosis: a case report. J Neuropsychiatry Clin Neurosci. 2010 Fall;22(4):451-r.e32–e32. (PubMed PMID: 21037150)
67. Sillesen NH, Nielsen LT, Bonde C. [Complex injuries associated with somnambulism]. Ugeskr Laeger. 2010 Dec 13;172(50):3489–90. (PubMed PMID: 21156113. Komplekse skader i forbindelse med sovngaengeri.)

68. Alonso-Navarro H, Jimenez-Jimenez FJ. Restless legs syndrome associated with narcolepsy and somnambulism. Parkinsonism Relat Disord. 2010 Feb;16(2):146–7. (PubMed PMID: 19703790)
69. Pilon M, Montplaisir J, Zadra A. Precipitating factors of somnambulism: impact of sleep deprivation and forced arousals. Neurology. 2008 Jun 10;70(24):2284–90. (PubMed PMID: 18463368)
70. Guilleminault C, Kirisoglu C, da Rosa AC, Lopes C, Chan ASleepwalking, a disorder of. NREM sleep instability. Sleep Med. 2006 Mar;7(2):163–70. (PubMed PMID: 16459139. Epub 2006/02/07. eng.)
71. Pressman MR, Meyer TJ, Kendrick-Mohamed J, Figueroa WG, Greenspon LW, Peterson DD. Night terrors in an adult precipitated by sleep apnea. Sleep. 1995 Nov;18(9):773–5. (PubMed PMID: 8638070)
72. Pressman MR. Hypersynchronous delta sleep EEG activity and sudden arousals from slow-wave sleep in adults without a history of parasomnias: clinical and forensic implications. Sleep. 2004 Jun 15;27(4):706–10. (PubMed PMID: 15283006)
73. Pilon M, Desautels A, Montplaisir J, Zadra A. Auditory arousal responses and thresholds during REM and NREM sleep of sleepwalkers and controls. Sleep Med. 2012 May;13(5):490–5. (PubMed PMID: 22341611)
74. Yeh YW, Chen CH, Feng HM, Wang SC, Kuo SC, Chen CK. New onset somnambulism associated with different dosage of mirtazapine: a case report. Clin Neuropharmacol. 2009 Jul-Aug;32(4):232–3. (PubMed PMID: 19644232)
75. Oulis P, Kokras N, Papadimitriou GN, Masdrakis VG. Bupropion-induced sleepwalking. J Clin Psychopharmacol. 2010 Feb;30(1):83–4. (PubMed PMID: 20075658)
76. Lange CL. Medication-associated somnambulism. J Am Acad Child Adolesc Psychiatry. 2005 Mar;44(3):211–2. (PubMed PMID: 15725964)
77. Huapaya LV. Seven cases of somnambulism induced by drugs. Am J Psychiatry. 1979 Jul;136(7):985–6. (PubMed PMID: 453369)
78. Siddiqui F, Osuna E, Chokroverty S. Writing emails as part of sleepwalking after increase in Zolpidem. Sleep Med. 2009 Feb;10(2):262–4. (PubMed PMID: 19059805. Epub 2008/12/09. eng.)
79. Hoque R, Chesson AL Jr. Zolpidem-induced sleepwalking sleep related eating disorder and sleep-driving: fluorine-18-flourodeoxyglucose positron emission tomography analysis and a literature review of other unexpected clinical effects of zolpidem. J Clin Sleep Med. 2009 Oct 15;5(5):471–6. (PubMed PMID: 19961034. Pubmed Central PMCID: 2762721. Epub 2009/12/08. eng.)
80. Ferentinos P, Paparrigopoulos T. Zopiclone and sleepwalking. Int J Neuropsychopharmacol. 2009 Feb;12(1):141–2. (PubMed PMID: 18925983. Epub 2008/10/18. eng.)
81. Hensel J, Pillmann F. Late-life somnambulism after therapy with metoprolol. Clin Neuropharmacol. 2008 Jul-Aug;31(4):248–50. (PubMed PMID: 18670251)
82. Khazaal Y, Krenz S, Zullino DF. Bupropion-induced somnambulism. Addict Biol. 2003 Sep;8(3):359–62. (PubMed PMID: 13129839)
83. von Vigier RO, Vella S, Bianchetti MG. Agitated sleepwalking with fluoroquinolone therapy. Pediatr Infect Dis J. 1999 May;18(5):484–5. (PubMed PMID: 10353533)
84. Landry P, Warnes H, Nielsen T, Montplaisir J. Somnambulistic-like behaviour in patients attending a lithium clinic. Int Clin Psychopharmacol. 1999 May;14(3):173–5. (PubMed PMID: 10435770)
85. Harazin J, Berigan TR. Zolpidem tartrate and somnambulism. Mil Med. 1999 Sep;164(9):669–70. (PubMed PMID: 10495642)
86. Mendelson WB. Sleepwalking associated with zolpidem. J Clin Psychopharmacol. 1994 Apr;14(2):150. (PubMed PMID: 8195460)
87. Tamanna S, Ullah MI, Pope CR, Holloman G, Koch CA. Quetiapine-induced sleep-related eating disorder-like behavior: a case series. J Med Case Reports. 2012 Nov 6;6(1):380. (PubMed PMID: 23130910)

88. Mathew T, Sarma GR, Nadig R, Varghese R. Topiramate-induced somnambulism in a migraineur: a probable idiosyncratic adverse effect. J Clin Sleep Med. 2012 Apr 15;8(2):197–8. (PubMed PMID: 22505867. Pubmed Central PMCID: 3311419)
89. Lam SP, Fong SY, Yu MW, Li SX, Wing YK. Sleepwalking in psychiatric patients: comparison of childhood and adult onset. Aust N Z J Psychiatry. 2009 May;43(5):426–30. (PubMed PMID: 19373703. Epub 2009/04/18. eng.)
90. Pressman MR, Mahowald MW, Schenck CH, Bornemann MC. Alcohol-induced sleepwalking or confusional arousal as a defense to criminal behavior: a review of scientific evidence, methods and forensic considerations. J Sleep Res. 2007 Jun;16(2):198–212. (PubMed PMID: 17542950)
91. Zolpidem: sleepwalking and automatic behaviours. Prescrire Int. 2007 Oct;16(91):200. (PubMed PMID: 17929383)
92. Liskow B, Pikalov A. Zaleplon overdose associated with sleepwalking and complex behavior. J Am Acad Child Adolesc Psychiatry. 2004 Aug;43(8):927–8. (PubMed PMID: 15266187)
93. Kunzel HE, Schuld A, Pollmacher T. Sleepwalking associated with reboxetine in a young female patient with major depression–a case report. Pharmacopsychiatry. 2004 Nov;37(6):307–8. (PubMed PMID: 15551201)
94. Sattar SP, Ramaswamy S, Bhatia SC, Petty F. Somnambulism due to probable interaction of valproic acid and zolpidem. Ann Pharmacother. 2003 Oct;37(10):1429–33. (PubMed PMID: 14519043)
95. Iruela LM. Zolpidem and sleepwalking. J Clin Psychopharmacol. 1995 Jun;15(3):223. (PubMed PMID: 7636001)
96. Charney DS, Kales A, Soldatos CR, Nelson JC. Somnambulistic-like episodes secondary to combined lithium-neuroleptic treatment. Br J Psychiatry. 1979 Nov;135:418–24. (PubMed PMID: 44211)
97. Pressman MR Preface: Common misconceptions about sleepwalking and other parasomnias. In: Pressman MR, editor. Parasomnias. Sleep medicine clinics, vol. 6. Philadelphia: W. B. Saunders; 2011. pp. xiii–xvii.
98. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW. A polysomnographic and clinical report on sleep-related injury in 100 adult patients. Am J Psychiatry. 1989 Sep;146(9):1166–73. (PubMed PMID: 2764174)
99. Seeman MV. Sleepwalking, a possible side effect of antipsychotic medication. Psychiatr Q. 2011 Mar;82(1):59–67. (PubMed PMID: 20734137)
100. Gau SF, Soong WT. Psychiatric comorbidity of adolescents with sleep terrors or sleepwalking: a case-control study. Aust N Z J Psychiatry. 1999 Oct;33(5):734–9. (PubMed PMID: 10544999)
101. Ross CA. Possession experiences in dissociative identity disorder: a preliminary study. J Trauma Dissociation. 2011;12(4):393–400. (PubMed PMID: 21667381)
102. Tsai JH, Yang P, Chen CC, Chung W, Tang TC, Wang SY, et al. Zolpidem-induced amnesia and somnambulism: rare occurrences? Eur Neuropsychopharmacol. 2009 Jan;19(1):74–6. (PubMed PMID: 18819779)
103. Ingravallo F, Schenck CH, Plazzi G. Injurious REM sleep behaviour disorder in narcolepsy with cataplexy contributing to criminal proceedings and divorce. Sleep Med. 2010 Oct;11(9):950–2. (PubMed PMID: 20810310. Epub 2010/09/03. eng.)
104. Szelenberger W, Niemcewicz S, Dabrowska AJ. Sleepwalking and night terrors: psychopathological and psychophysiological correlates. Int Rev Psychiatry. 2005 Aug;17(4):263–70. (PubMed PMID: 16194798)
105. Viana Bde M, Bawden FC, Valladares Neto Dde C, Caramelli P. Violent sleepwalking in a general hospital ward: a case report. Rev Bras Psiquiatr. 2009 Sep;31(3):281–2. (PubMed PMID: 19784495. Epub 2009/09/29. eng.)
106. Bornemann MA, Mahowald MW, Schenck CH. Parasomnias: clinical features and forensic implications. Chest. 2006 Aug;130(2):605–10. (PubMed PMID: 16899867. Epub 2006/08/11. eng.)

107. Southworth MR, Kortepeter C, Hughes A. Nonbenzodiazepine hypnotic use and cases of "sleep driving". Ann Intern Med. 2008 Mar 18;148(6):486–7. (PubMed PMID: 18347361)
108. Hwang TJ, Ni HC, Chen HC, Lin YT, Liao SC. Risk predictors for hypnosedative-related complex sleep behaviors: a retrospective, cross-sectional pilot study. J Clin Psychiatry. 2010 Oct;71(10):1331–5. (PubMed PMID: 20441722)
109. Marshall NS, Buchanan PR. Z drug zombies: parasomnia, drug effect or both? Sleep Med Rev. 2011 Oct;15(5):283–4. (PubMed PMID: 21641242. Epub 2011/06/07. eng.)
110. Schenck CH, Hurwitz TD, Bundlie SR, Mahowald MW. Sleep-related eating disorders: polysomnographic correlates of a heterogeneous syndrome distinct from daytime eating disorders. Sleep. 1991 Oct;14(5):419–31. (PubMed PMID: 1759095. Epub 1991/10/01. eng.)
111. Vinai P, Ferri R, Ferini-Strambi L, Cardetti S, Anelli M, Vallauri P, et al. Defining the borders between sleep-related eating disorder and night eating syndrome. Sleep Med. 2012 Jun;13(6):686–90. (PubMed PMID: 22456111)
112. Brion A, Flamand M, Oudiette D, Voillery D, Golmard JL, Arnulf I. Sleep-related eating disorder versus sleepwalking: a controlled study. Sleep Med. 2012 Sep;13(8):1094–101. (PubMed PMID: 22841035)
113. Winkelman JW, Johnson EA, Richards LM. Sleep-related eating disorder. Handb Clin Neurol. 2011;98:577–85. (PubMed PMID: 21056212)
114. Vetrugno R, Manconi M, Ferini-Strambi L, Provini F, Plazzi G, Montagna P. Nocturnal eating: sleep-related eating disorder or night eating syndrome? A videopolysomnographic study. Sleep. 2006 Jul 1;29(7):949–54. (PubMed PMID: 16895263. Epub 2006/08/10. eng.)
115. Auger RR. Sleep-related eating disorders. Psychiatry. 2006 Nov;3(11):64–70. (PubMed PMID: 20877520. Pubmed Central PMCID: 2945843)
116. Winkelman JW. Clinical and polysomnographic features of sleep-related eating disorder. J Clin Psychiatry. 1998 Jan;59(1):14–9. (PubMed PMID: 9491060)
117. Winkelman JW. Sleep-related eating disorder and night eating syndrome: sleep disorders, eating disorders, or both? Sleep. 2006 Jul;29(7):876–7. (PubMed PMID: 16895252)
118. Milano W, De Rosa M, Milano L, Capasso A. Night eating syndrome: an overview. J Pharm Pharmacol. 2012 Jan;64(1):2–10. (PubMed PMID: 22150667)
119. Stunkard AJ, Allison KC, Geliebter A, Lundgren JD, Gluck ME, O'Reardon JP. Development of criteria for a diagnosis: lessons from the night eating syndrome. Compr Psychiatry. 2009 Sep–Oct;50(5):391–9. (PubMed PMID: 19683608)
120. Striegel-Moore RH, Rosselli F, Wilson GT, Perrin N, Harvey K, DeBar L. Nocturnal eating: association with binge eating, obesity, and psychological distress. Int J Eat Disord. 2010 Sep;43(6):520–6. (PubMed PMID: 19708071. Pubmed Central PMCID: 2891279)
121. Wallace DM, Maze T, Shafazand S. Sodium oxybate-induced sleep driving and sleep-related eating disorder. J Clin Sleep Med. 2011 Jun 15;7(3):310–1. (PubMed PMID: 21677903. Pubmed Central PMCID: 3113972)
122. Yun CH, Ji KH. Zolpidem-induced sleep-related eating disorder. J Neurol Sci. 2010 Jan 15;288(1–2):200–1. (PubMed PMID: 19822330)
123. Wing YK, Lam SP, Li SX, Zhang J, Yu MW. Sleep-related eating disorder and zolpidem: an open interventional cohort study. J Clin Psychiatry. 2010 May;71(5):653–6. (PubMed PMID: 20492858)
124. Molina SM, Joshi KG. A case of zaleplon-induced amnestic sleep-related eating disorder. J Clin Psychiatry. 2010 Feb;71(2):210–1. (PubMed PMID: 20193650)
125. Mahowald MW, Cramer Bornemann MA, Schenck CH. A case of reversible restless legs syndrome (RLS) and sleep-related eating disorder relapse triggered by acute right leg herpes zoster infection: literature review of spinal cord and peripheral nervous system contributions to RLS. Sleep Med. 2010 Jun;11(6):583–5. (PubMed PMID: 20129821. Epub 2010/02/05. eng.)
126. Dang A, Garg G, Rataboli PV. Zolpidem induced Nocturnal Sleep-Related Eating Disorder (NSRED) in a male patient. Int J Eat Disord. 2009 May;42(4):385–6. (PubMed PMID: 19107832)

127. Morgenthaler TI, Silber MH. Amnestic sleep-related eating disorder associated with zolpidem. Sleep Med. 2002 Jul;3(4):323–7. (PubMed PMID: 14592194)
128. Howell MJ, Schenck CH. Restless nocturnal eating: a common feature of Willis-Ekbom syndrome (RLS). J Clin Sleep Med. 2012;8(4):413–9. (PubMed PMID: 22893772. Pubmed Central PMCID: 3407260)
129. Provini F, Antelmi E, Vignatelli L, Zaniboni A, Naldi G, Calandra-Buonaura G, et al. Association of restless legs syndrome with nocturnal eating: a case-control study. Mov Disord. 2009 Apr 30;24(6):871–7. (PubMed PMID: 19199358)
130. Provini F, Albani F, Vetrugno R, Vignatelli L, Lombardi C, Plazzi G, et al. A pilot double-blind placebo-controlled trial of low-dose pramipexole in sleep-related eating disorder. Eur J Neurol. 2005 Jun;12(6):432–6. (PubMed PMID: 15885046. Epub 2005/05/12. eng.)
131. Kobayashi N, Yoshimura R, Takano M. Successful treatment with clonazepam and pramipexole of a patient with sleep-related eating disorder associated with restless legs syndrome: a case report. Case Report Med. 2012;2012:893681. (PubMed PMID: 22481958. Pubmed Central PMCID: 3312196)
132. Cooper-Kazaz R. Treatment of night eating syndrome with topiramate: dawn of a new day. J Clin Psychopharmacol. 2012 Feb;32(1):143–5. (PubMed PMID: 22217954)
133. Winkelman JW. Efficacy and tolerability of open-label topiramate in the treatment of sleep-related eating disorder: a retrospective case series. J Clin Psychiatry. 2006 Nov;67(11):1729–34. (PubMed PMID: 17196052)
134. Winkelman JW. Treatment of nocturnal eating syndrome and sleep-related eating disorder with topiramate. Sleep Med. 2003 May;4(3):243–6. (PubMed PMID: 14592329)
135. AASM. REM sleep behavior disorder (including parasomnia overlap disorder and status dissociatus. In: Sateia MJ, editor. The international classification of sleep disorders, 2nd ed., diagnostic & coding manual. Westchester, IL: American Academy of Sleep Medicine; 2005. pp. 148–52.
136. Limousin N, Dehais C, Gout O, Heran F, Oudiette D, Arnulf I. A brainstem inflammatory lesion causing REM sleep behavior disorder and sleepwalking (parasomnia overlap disorder). Sleep Med. 2009 Oct;10(9):1059–62. (PubMed PMID: 19345142. Epub 2009/04/07. eng.)
137. Alves R, Aloe F, Tavares S, Vidrio S, Yanez L, Aguilar-Roblero R, et al. Sexual behavior in sleep, sleepwalking and possible REM behavior disorder: a case report. Sleep Res Online. 1999;2(3):71–2. (PubMed PMID: 11382885. Epub 2001/05/31. eng.)
138. Oberholzer M, Poryazova R, Bassetti CL. Sleepwalking in Parkinson's disease: a questionnaire-based survey. J Neurol. 2011 Jul;258(7):1261–7. (PubMed PMID: 21293874)
139. Mahowald MW, Schenck CH. Status dissociatus–a perspective on states of being. Sleep. 1991 Feb;14(1):69–79. (PubMed PMID: 1811323. Epub 1991/02/01. eng.)
140. Raggi A, Perani D, Giaccone G, Iannaccone S, Manconi M, Zucconi M, et al. The behavioural features of fatal familial insomnia: a new Italian case with pathological verification. Sleep Med. 2009 May;10(5):581–5. (PubMed PMID: 18824410. Epub 2008/10/01. eng.)
141. Krasnianski A, Bartl M, Sanchez Juan PJ, Heinemann U, Meissner B, Varges D, et al. Fatal familial insomnia: Clinical features and early identification. Ann Neurol. 2008 May;63(5):658–61. (PubMed PMID: 18360821)
142. Montagna P. Fatal familial insomnia: a model disease in sleep physiopathology. Sleep Med Rev. 2005 Oct;9(5):339–53. (PubMed PMID: 16109494)
143. Montagna P, Cortelli P, Avoni P, Tinuper P, Plazzi G, Gallassi R, et al. Clinical features of fatal familial insomnia: phenotypic variability in relation to a polymorphism at codon 129 of the prion protein gene. Brain Pathol. 1998 Jul;8(3):515–20. (PubMed PMID: 9669701)
144. Sforza E, Montagna P, Tinuper P, Cortelli P, Avoni P, Ferrillo F, et al. Sleep-wake cycle abnormalities in fatal familial insomnia. Evidence of the role of the thalamus in sleep regulation. Electroencephalogr Clin Neurophysiol. 1995 Jun;94(6):398–405. (PubMed PMID: 7607093)
145. Loukaides P, Schiza N, Pettingill P, Palazis L, Vounou E, Vincent A, et al. Morvan's syndrome associated with antibodies to multiple components of the voltage-gated potassium channel complex. J Neurol Sci. 2012 Jan 15;312(1–2):52–6. (PubMed PMID: 21906755)

146. Serratrice G, Serratrice J. Continuous muscle activity, Morvan's syndrome and limbic encephalitis: ionic or non ionic disorders? Acta Myol. 2011 Jun;30(1):32–3. (PubMed PMID: 21842591. Pubmed Central PMCID: 3185830)
147. Vetrugno R, Alessandria M, D'Angelo R, Plazzi G, Provini F, Cortelli P, et al. Status dissociatus evolving from REM sleep behaviour disorder in multiple system atrophy. Sleep Med. 2009 Feb;10(2):247–52. (PubMed PMID: 18396457)
148. Cochen V, Arnulf I, Demeret S, Neulat ML, Gourlet V, Drouot X, et al. Vivid dreams, hallucinations, psychosis and REM sleep in Guillain-Barre syndrome. Brain. 2005 Nov;128(Pt 11):2535–45. (PubMed PMID: 16000335. Epub 2005/07/08. eng.)
149. Provini F, Vetrugno R, Pastorelli F, Lombardi C, Plazzi G, Marliani AF, et al. Status dissociatus after surgery for tegmental ponto-mesencephalic cavernoma: a state-dependent disorder of motor control during sleep. Mov Disord. 2004;19(6):719–23.
150. Stamelou M, Plazzi G, Lugaresi E, Edwards MJ, Bhatia KP. The distinct movement disorder in anti-NMDA receptor encephalitis may be related to status dissociatus: A hypothesis. Mov Disord. 2012 Sep 15;27(11):1360–3. (PubMed PMID: 22700398)
151. Della Marca G, Dittoni S, Frusciante R, Colicchio S, Losurdo A, Testani E, et al. Abnormal sexual behavior during sleep. J Sex Med. 2009 Dec;6(12):3490–5. (PubMed PMID: 19570043)
152. Ebrahim IO. Somnambulistic sexual behaviour (sexsomnia). J Clin Forensic Med. 2006 May;13(4):219–24. (PubMed PMID: 16564199)
153. Guilleminault C, Moscovitch A, Yuen K, Poyares D. Atypical sexual behavior during sleep. Psychosom Med. 2002 Mar-Apr;64(2):328–36. (PubMed PMID: 11914450. Epub 2002/03/27. eng.)
154. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J Jr, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep. 2005 Apr 1;28(4):499–521. (PubMed PMID: 16171294)
155. Wise MS, Nichols CD, Grigg-Damberger MM, Marcus CL, Witmans MB, Kirk VG, et al. Executive summary of respiratory indications for polysomnography in children: an evidence-based review. Sleep. 2011 Mar;34(3):389–98AW. (PubMed PMID: 21359088. Pubmed Central PMCID: 3041716)
156. Aurora RN, Zak RS, Karippot A, Lamm CI, Morgenthaler TI, Auerbach SH, et al. Practice parameters for the respiratory indications for polysomnography in children. Sleep. 2011 Mar;34(3):379–88. (PubMed PMID: 21359087. Pubmed Central PMCID: 3041715)
157. Kotagal S, Nichols CD, Grigg-Damberger MM, Marcus CL, Witmans MB, Kirk VG, et al. Non-respiratory indications for polysomnography and related procedures in children: an evidence-based review. Sleep. 2012;35(11):1451–66. (PubMed PMID: 23115394. Pubmed Central PMCID: 3466792)
158. Aldrich MS, Jahnke B. Diagnostic value of video-EEG polysomnography. Neurology. 1991 Jul;41(7):1060–6. (PubMed PMID: 2067634)
159. Blatt I, Peled R, Gadoth N, Lavie P. The value of sleep recording in evaluating somnambulism in young adults. Electroencephalogr Clin Neurophysiol. 1991 Jun;78(6):407–12. (PubMed PMID: 1712276)
160. Gastaut H, Broughton R. A clinical and polygraphic study of episodic phenomena during sleep. In: Wortis J, editor. Recent advances in biological psychiatry. New York City, NY: Plenum Press; 1965. pp. 197–221.
161. Kavey NB, Whyte J. Resor SR, Jr., Gidro-Frank S. Somnambulism in adults. Neurology. 1990 May;40(5):749–52. (PubMed PMID: 2330099)
162. Schenck CH, Pareja JA, Patterson AL, Mahowald MW. Analysis of polysomnographic events surrounding 252 slow-wave sleep arousals in thirty-eight adults with injurious sleepwalking and sleep terrors. J Clin Neurophysiol. 1998 Mar;15(2):159–66. (PubMed PMID: 9563584. Epub 1998/05/01. eng.)
163. Zadra A, Pilon M, Montplaisir J. Polysomnographic diagnosis of sleepwalking: effects of sleep deprivation. Ann Neurol. 2008 Apr;63(4):513–9. (PubMed PMID: 18351640. Epub 2008/03/21. eng.)

164. Joncas S, Zadra A, Paquet J, Montplaisir J. The value of sleep deprivation as a diagnostic tool in adult sleepwalkers. Neurology. 2002 Mar 26;58(6):936–40. (PubMed PMID: 11914411)
165. Halasz P, Ujszaszi J, Gadoros J. Are microarousals preceded by electroencephalographic slow wave synchronization precursors of confusional awakenings? Sleep. 1985;8(3):231–8. (PubMed PMID: 4048739)
166. Espa F, Ondze B, Deglise P, Billiard M, Besset A. Sleep architecture, slow wave activity, and sleep spindles in adult patients with sleepwalking and sleep terrors. Clin Neurophysiol. 2000 May;111(5):929–39. (PubMed PMID: 10802466)
167. Gaudreau H, Joncas S, Zadra A, Montplaisir J. Dynamics of slow-wave activity during the NREM sleep of sleepwalkers and control subjects. Sleep. 2000 Sep 15;23(6):755–60. (PubMed PMID: 11007442)
168. Zucconi M, Oldani A, Ferini-Strambi L, Smirne S. Arousal fluctuations in non-rapid eye movement parasomnias: the role of cyclic alternating pattern as a measure of sleep instability. J Clin Neurophysiol. 1995 Mar;12(2):147–54. (PubMed PMID: 7797629)
169. Bruni O, Ferri R, Novelli L, Finotti E, Miano S, Guilleminault C. NREM sleep instability in children with sleep terrors: the role of slow wave activity interruptions. Clin Neurophysiol. 2008 May;119(5):985–92. (PubMed PMID: 18313981. Epub 2008/03/04. eng.)
170. Tai P, Poochikian-Sarkissian S, Andrade D, Valiante T, del Campo M, Wennberg R. Postictal wandering is common after temporal lobe seizures. Neurology. 2010 Mar 16;74(11):932–3. (PubMed PMID: 20231671. Epub 2010/03/17. eng.)
171. Plazzi G, Vetrugno R, Provini F, Montagna P. Sleepwalking and other ambulatory behaviours during sleep. Neurol Sci. 2005 Dec;26 Suppl 3:s193–8. (PubMed PMID: 16331395. Epub 2005/12/07. eng.)
172. Mai R, Sartori I, Francione S, Tassi L, Castana L, Cardinale F, et al. Sleep-related hyperkinetic seizures: always a frontal onset? Neurol Sci. 2005 Dec;26 Suppl 3:s220–4. (PubMed PMID: 16331400.
173. Nobili L, Cossu M, Mai R, Tassi L, Cardinale F, Castana L, et al. Sleep-related hyperkinetic seizures of temporal lobe origin. Neurology. 2004 Feb 10;62(3):482–5. (PubMed PMID: 14872038)
174. Nobili L, Francione S, Cardinale F, Lo Russo G. Epileptic nocturnal wanderings with a temporal lobe origin: a stereo-electroencephalographic study. Sleep. 2002 Sep 15;25(6):669–71. (PubMed PMID: 12224845)
175. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep. 1986 Jun;9(2):293–308. (PubMed PMID: 3505730)
176. Schenck CH, Bundlie SR, Patterson AL, Mahowald MW. Rapid eye movement sleep behavior disorder. A treatable parasomnia affecting older adults. JAMA. 1987 Apr 3;257(13):1786–9. (PubMed PMID: 3820495. Epub 1987/04/03. eng.)
177. Iranzo A, Santamaria J. Severe obstructive sleep apnea/hypopnea mimicking REM sleep behavior disorder. Sleep. 2005 Feb 1;28(2):203–6. (PubMed PMID: 16171244. Epub 2005/09/21. eng.)
178. Harris M, Grunstein RR. Treatments for somnambulism in adults: assessing the evidence. Sleep Med Rev. 2009 Aug;13(4):295–7. (PubMed PMID: 19046651. Epub 2008/12/03. eng.)
179. Kotagal S. Parasomnias in childhood. Sleep Med Rev. 2009 Apr;13(2):157–68. (PubMed PMID: 19064329. Epub 2008/12/10. eng.)
180. Aurora RN, Zak RS, Maganti RK, Auerbach SH, Casey KR, Chowdhuri S, et al. Best practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin Sleep Med. 2010 Feb 15;6(1):85–95. (PubMed PMID: 20191945. Pubmed Central PMCID: 2823283. Epub 2010/03/03. eng.)
181. Leu-Semenescu S, Arnulf I. Disruptive nocturnal behavior in elderly subjects: could it be a parasomnia? Psychol Neuropsychiatr Vieil. 2010 Jun;8(2):97–109. (PubMed PMID: 20525541. Epub 2010/06/09. Agitation nocturne chez la personne agee: et si c'etait une parasomnie? fre.)

182. Reid WH, Haffke EA, Chu CC. Diazepam in intractable sleepwalking: a pilot study. Hillside J Clin Psychiatry. 1984;6(1):49–55. (PubMed PMID: 6400570)
183. Schenck CH, Mahowald MW. Long-term, nightly benzodiazepine treatment of injurious parasomnias and other disorders of disrupted nocturnal sleep in 170 adults. Am J Med. 1996 Mar;100(3):333–7. (PubMed PMID: 8629680. Epub 1996/03/01. eng.)
184. Anderson KN, Shneerson JM. Drug treatment of REM sleep behavior disorder: the use of drug therapies other than clonazepam. J Clin Sleep Med. 2009 Jun 15;5(3):235–9. (PubMed PMID: 19960644. Pubmed Central PMCID: 2699168. Epub 2009/12/08. eng.)
185. Schenck CH, Mahowald MW. A polysomnographic, neurologic, psychiatric, and clinical outcome report on 70 consecutive cases with REM sleep behavior disorder (RBD): sustained clonazepam efficacy in 89.5% of 57 treated patients. Clev Clin J Med. 1990;57(Suppl):S9–23.
186. Olson EJ, Boeve BF, Silber MH. Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. Brain. 2000 Feb;123(Pt 2):331–9. (PubMed PMID: 10648440)
187. Ferman TJ, Boeve BF, Smith GE, Silber MH, Kokmen E, Petersen RC, et al. REM sleep behavior disorder and dementia: cognitive differences when compared with AD. Neurology. 1999 Mar 23;52(5):951–7. (PubMed PMID: 10102411. Epub 1999/04/02. eng.)

Chapter 6
Sleepwalking in Children and Adolescents

Ravindra Arya and Sejal V. Jain

Introduction

Sleepwalking or somnambulism is a non-rapid eye movement (NREM) parasomnia characterized by apparently purposive complex motor behavior during N3 sleep. It is of interest to clinicians as a differential diagnosis of partial-onset seizures and other sleep disorders and to neuroscientists as a model that may provide insight into the regulation of N3 sleep. It is also of importance to evolutionary biologists, as it is not observed in nonhuman primates and is regarded as an acquired behavioral response associated with humanoid differentiation [1].

Sleepwalking is reported to have a prevalence of 2–14 % in children [2–5] and 1.6–2.4 % in adults [6] in mixed clinic and community based samples. Some of these patients outgrow their affliction if the onset is before 10 years of age [7]; however, up to 25 % have been documented to continue sleepwalking in adulthood [8].

Etiological Associations

The exact etiology of sleepwalking is not delineated. However, there are several known associations that may partially contribute to causation.

Genetic Factors

Evidence for a genetic basis of sleepwalking comes from multiple different sources including epidemiologic and cytogenetic studies. A small study ($n = 37$) including

S. V. Jain (✉) · R. Arya
Department of Neurology, Cincinnati Children's Hospital Medical Center,
3333 Burnet Ave, MLC 2015, Cincinnati, OH 45229, USA
e-mail: Sejal.Jain@cchmc.org

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_6, © Springer Science+Business Media New York 2013

children whose one or both parents had sleepwalked during childhood found that such children are more likely to manifest sleepwalking by 8 years of age as compared with controls [9]. A large population-based Finnish study ($n = 11,220$) with 1,045 monozygotic and 1,899 dizygotic twins found that for childhood-onset sleepwalking, the concordance rate for probands was 0.55 for monozygotic and 0.35 for dizygotic pairs [8]. For adult-onset sleepwalkers, the corresponding values were 0.32 and 0.06, respectively. The authors calculated that the proportion of total phenotypic variance attributable to genetic influence was 66 % in males and 57 % in females in childhood-onset sleepwalking and 80 % in males and 36 % in females in adult-onset sleepwalking [8]. In the human leukocyte antigen (HLA) studies, 35 % of sleepwalkers were found to be positive for HLA-DQB1-050 as compared with 13 % controls (odds ratio 3.5, 95 % confidence interval 1.4–8.7) in a study including 60 sleepwalkers with matched controls [10]. Excess transmission was noted for DQB1-05 and DQB1-04 alleles in familial cases [10]. Recently, autosomal dominant inheritance with reduced penetrance was reported in family members with sleepwalking for a genetic locus at chromosome 20q12-q13.12 [11]. Hence, it is hypothesized that although genetic factors may not be sufficient for expression of sleepwalking phenotype by themselves, they likely have a predisposing influence.

Acquired Factors

Most of the acquired factors are believed to cause partial arousals or poor quality sleep, which precipitate sleepwalking episodes.

Other Sleep Disorders Sleep-disordered breathing has been observed in up to 58 % of children with sleepwalking, with about half of them also having a family history of respiratory problems. Successful treatment of disordered breathing was further noted to alleviate sleepwalking in all patients in this series [12]. In another study, comorbid obstructive sleep apnea (OSA) or upper airway resistance syndrome (UARS) was noted in all sleepwalkers [13]. On the other end, 54 % of children with OSA reported sleepwalking on a questionnaire [14]. It has been proposed that abnormal respiratory events trigger frequent arousals contributing to sleepwalking behavior [15]. Restless legs syndrome (RLS) and periodic limb movement syndrome (PLMS) has also been reported to precipitate parasomnia [12].

Sleep Deprivation Sleep deprivation has been tried as an activation procedure to produce sleepwalking in controlled circumstances, possibly because it is known to increase slow-wave sleep [16]. In a study ($n = 10$), 38 h of sleep deprivation was noted to increase frequency and complexity of sleepwalking episodes and the number of arousals from slow-wave sleep [17]. However, another study ($n = 10$) found no increase in sleepwalking with sleep deprivation, although complex stereotypical sleep behaviors were noted to increase and were considered by authors as preliminary stage of sleepwalking [16]. Forced arousal produced by auditory stimulation in slow-wave sleep during first and second NREM–rapid eye movement (REM) cycles, during

a recovery following 25 h of sleep deprivation, was shown to precipitate greater somnambulistic episodes as compared with normal sleep [18].

Drugs Several different drugs have been observed to produce new-onset sleepwalking behavior as well as reactivation of dormant sleepwalking in patients with past or family history of this disorder. It has been proposed that the possible pathogenesis may be due to increased slow-wave sleep [19]. Most of the evidence for drug-induced sleepwalking exists for lithium and zolpidem. In one of the earliest reports on sleepwalking, 9 % of psychiatric patients on lithium and neuroleptic comedication were found to have sleepwalking behavior [20]. Since then, the association between lithium therapy and sleepwalking has been reported often, and also in patients on other psychotropic medications [21, 22]. Reactivation of childhood sleepwalking in up to 27 % of patients with lithium-induced parasomnia has also been reported [22, 23]. Similarly, there have been isolated reports of both new-onset and reactivation sleepwalking with the use of zolpidem [24–26]. At least in some of these patients, there were other possible factors that could have contributed to precipitation of sleepwalking, e.g., previous brain injury [26] and concomitant use of valproate [27]. However, in one patient, sleepwalking disappeared after discontinuing zolpidem [24]. Additionally, there has been a report of a patient developing sleepwalking after initiation of bupropion that is a centrally acting dopaminergic stimulant [28].

Hyperthyroidism A case series with eight patients of new-onset sleepwalking coinciding with onset of thyrotoxicosis has been reported [29]. In this report, sleepwalking disappeared in all patients as they attained a euthyroid state and relapsed in two whose hyperthyroidism became poorly controlled because of lack of compliance with treatment. Interestingly, the authors hypothesized that the fatigue associated with thyrotoxicosis may contribute to onset of sleepwalking [29].

Other Associations Several other factors have been associated with onset or relapse of sleepwalking in isolated reports. Other reported possible risk factors include herpes simplex encephalitis, alcohol abuse, and even a trial of continuous positive airway pressure, where two episodes of sleepwalking were seen during a period of delta rebound [30–32].

Clinical Features, Polysomnography (PSG), and Video-Electroencephalogram (EEG)

Sleepwalking represents episodes of partial arousal occurring out of slow-wave sleep. These are characterized by ambulatory behaviors during altered state of consciousness and impaired judgment. Episodes may begin with sitting up in bed with eyes open. Complex behavior of change in body position, turning, playing with sheets, and eventually getting out of the bed may occur. Behaviors such as walking around the house, going to kitchen or bathroom, and going downstairs are associated. Complex behaviors such as cooking, cleaning, eating, and even driving have been reported.

These semipurposeful movements are performed with some dexterity. Typically, the child is calm, but if awakened, agitation and confusion can occur along with prolongation of the episode. Child often returns to bed and has no recollection of the event in the morning. Due to altered awareness and ambulation, there is risk of injury from falling on stairs, jumping out of windows, going out of house, and running into closed doors. Inappropriate behaviors such as urinating in unusual places and violence are also seen especially in men [33–36]. In an adult, atypical presentation with multiple episodes in a night is reported [37].

Some of the clinical features of sleepwalking have been best observed during PSG. Sleepwalking episodes occur most frequently during first 3 h of sleep, when N3 sleep is most abundant. The episodes can last for 1–30 min [38]. PSG findings consistently reported in sleepwalkers include reduced sleep efficiency and decreased N2 sleep, but increased N3 sleep [39]. Although duration of N3 sleep is increased, it has an abnormal architecture and is characterized by increased fragmentation and frequent arousals [39, 40].

During the few minutes preceding sleepwalking-related arousal, increased slow-wave activity has been reported as compared with baseline [39, 41]. Specifically, a study found greater slow-wave activity 2 min before a sleepwalking episode as compared with other samples obtained 10 min before the same episode and at the actual arousal [39]. This finding has been confirmed with analysis of power spectrum, with increased delta power being noted to be temporally related to arousal resulting in sleepwalking. At the same time, there was decreased physiologic slow-wave activity or delta power during other periods of N2–N3 sleep [41]. These suggest the inability to sustain slow-wave sleep. These features were more prominent during first or initial few sleep cycles [40]. During the actual sleepwalking episode, diffuse alpha frequency activity has been reported to be superimposed on delta rhythm, thought to be reflecting incomplete arousal [42, 43]. Diffuse rhythmic delta activity and, less frequently, alpha and beta activity are also reported as postarousal EEG activities [43]. For some time, the hypersynchronous delta activity was considered as a hallmark of sleepwalking, but it is disputed as a non-specific marker probably reflecting arousal activity [44].

Cyclic alternating patterns (CAP) are phenomena characterized by sequences of transient EEG events (phase A) with relatively stable background activity (phase B), with a periodicity of less than 1 min. Phase A is a marker of cortical activity and arousal, whereas phase B represents rebound deactivation [45]. A higher CAP rate has been documented in sleepwalkers [13, 46]. In one study, increase in CAP rates was similar to that in patients with UARS [13]. Hence, there is increased instability in NREM sleep in sleep walkers. Along with PSG and video-EEG, assessment of daytime sleepiness, sleep time, sleep quality, OSA, RLS, and PLMS, should also be performed.

Coexistent Conditions

Psychological Conditions

Children with sleepwalking were noted to have higher separation anxiety and high hyperactivity–inattention score [47]. Family or personal history of panic disorder has been reported in sleepwalkers [48]. In a study, 85 % of the teenagers with sleepwalking or sleep terrors had a psychiatric comorbidity. These included panic disorder, overanxious disorder, alcohol or cigarette use, suicidal ideation, and simple phobia. Increased fatigue, dysmenorrhea, and low mood in patients were also observed [49]. A study based on Rorschach tests noted inhibited aggression in sleepwalkers, which was hypothesized by the authors as a mature defense mechanism against anxiety [2]. In another study, experience of a recent stressful event along with higher prevalence of mood and anxiety disorders were noted in adult sleepwalkers [6]. In adults, aggression, anxiety, hysteria, panic disorder and phobias, and profiles similar to post-traumatic stress disorder have been reported with sleepwalking [19, 50, 51]. Patients with later age of onset and persistent sleepwalking in adulthood display active, outward behavioral patterns, which suggest difficulties in handling aggression [7]. However, in another study in adults, prevalence of Axis I psychiatric disorders was not increased in sleepwalkers [52]. It is unclear whether sleepwalking and coexistent psychopathology stem from common neurochemical disturbance or whether at least some of the psychomorbidity is just an epiphenomenon partially due to social stigmatization.

Other Sleep Disorders

Sleepwalking is known to be associated with other parasomnias. In a study exploring hereditary aspects of sleepwalking, it was observed that 80 % of sleepwalking pedigrees and 96 % of night terror pedigrees included other individuals, besides proband, who were affected by sleepwalking, night terrors, or both [53]. It was proposed that sleepwalking and night terrors probably share a common genetic predisposition [19, 53]. Among persistent sleepwalkers at 6 years of age, 92 % had somniloquy and 41 % had night terrors [47].

Excessive daytime sleepiness has been reported both subjectively and on multiple sleep latency test (MSLT). Increased automobile accidents are also reported that may be due to excessive daytime sleepiness [54]. Children with parasomnia also have bedtime resistance, sleep onset delay, inappropriate sleep duration, and increased night waking [55].

Neurological Diseases

Two unrelated entities, migraine and Tourette syndrome, have been reported in childhood-onset sleepwalking. In a study looking at this association, 19 % of children with Tourette syndrome had sleepwalking [56]. The authors proposed that probably both the conditions share a common neurochemical basis and result from disturbed brainstem serotonin metabolism [56].

There are several reports of association between migraine headaches and sleepwalking. In one study, up to 30 % of children with migraine had sleepwalking and 67 % of childhood-onset sleepwalkers suffered from migraine [57]. Another subsequent study also found high frequency of sleepwalking in migraine patients, although not to this degree. In patients with childhood-onset sleepwalking, migraine episodes usually had prominent visual symptoms at onset and occipital localization of headache [58].

Differential Diagnosis

Partial-Onset Seizures

The major consideration in any paroxysmal disorder is to rule out an epileptic basis for the episodes. Both hypermotor behaviors observed in autosomal dominant nocturnal frontal lobe epilepsy and complex automatisms of some temporal lobe seizures can mimic sleepwalking episodes [59]. However, there are certain clinical and EEG features that can help in differentiating sleepwalking from seizures. Usually, sleepwalking episodes occur during first few cycles of N3 sleep as compared with seizures, which often occur during drowsiness of N2 sleep anytime during the night. Vocalizations including screaming and distal upper extremity automatisms are also more indicative of a seizure episode. By definition, sleepwalking is an NREM parasomnia and does not result in clinical arousal, whereas awakening and postictal confusion are fairly common in seizures. Frontal lobe seizures are brief, occur multiple times in night, occur mostly out of N2, and have highly stereotypic semiology [60–62]. Frontal Lobe Epilepsy and Parasomnias (FLEP) scale was validated in studies for differential diagnoses [63, 64].

An overnight video-EEG is often helpful to exclude seizures and is indicated for this purpose in a patient being thought to have sleepwalking. Previously, there have been reports of abnormal interictal epileptiform activity in the EEG records of sleepwalkers [65, 66]. However, it probably represents a chance association, as up to 8 % of apparently normal subjects can have such activity [67]. Even in patients thought of as having sleepwalking, observation of evolving ictal patterns in EEG has led to the correct diagnosis [68]. In this context, “episodic nocturnal wandering” is a poorly characterized phenomenon, which probably has an epileptic basis. At least in one patient, the episode of nocturnal wandering was associated with ictal activity

originating from right temporal lobe with spread to cingulate gyrus, on prolonged video-EEG monitoring with intracranial electrodes [68, 69].

REM Behavior Disorder (RBD)

This disorder is sometimes confused with sleepwalking. However, it usually involves more violent motor activity in older men, said to represent acting out of their dreams, as compared with sleepwalking, which is more commonly seen in children and adolescents and rarely has a hypermotor character. However, RBD in association with narcolepsy may be seen in younger patients. Other differentiating feature is little autonomic activation seen in RBD as compared with marked activation in sleepwalkers. Also, memory of vivid dream leading to the motor behavior is present in RBD. There is typically a complete arousal following the event [34]. On PSG, intermittent decrease/absence in REM atonia or increase in phasic movements is seen. These features help distinguish the conditions. Parasomnia overlap disorder should also be considered if sleepwalking and RBD occur in the same individual [33].

Management

Nonpharmacologic Measures

Hypnosis

Since as late as 1990's, there has been much enthusiasm for hypnosis as a treatment for sleepwalking. In an earlier series, 4/6 patients reported complete remission with the use of hypnosis [70]. In another report by the same group, sustained improvement up to 1 year was observed in patients with sleepwalking but otherwise free of concurrent psychiatric disorders, with 6 brief sessions of hypnosis [71]. In a later adult study ($n = 27$), 74 % reported improvement with self-hypnosis practiced at home [72].

Anticipatory Awakening There are a few reports of successful treatment of sleepwalking with anticipatory awakening. An 8-year-old boy was woken up just before the anticipated time of sleepwalking episode for five consecutive nights. This was reported to later eliminate the sleepwalking behavior altogether [73]. In another family with 3 sleepwalking siblings, anticipatory awakening was reported to be curative [74].

Safety Measures

Adaptations and modifications of sleep environment are usually recommended to ensure safety of the patient. These may include removal of potentially dangerous

objects from the bedroom, clearing the floor obstructions, keeping windows and sometimes even doors closed, and allowing the patient to sleep on the ground floor, on a mattress placed directly on floor or in a sleeping bag [38]. Maintaining good sleep hygiene with regular schedule, avoidance of alcohol, stress management, and discontinuing or changing medications with adverse influence on N3 sleep architecture may sometimes be sufficient to relieve sleepwalking [38, 75]. Sleepwalkers should not be awakened but guided back to bed and allowed to fall back to sleep. Social stigmatization should be avoided at all costs and individual and family counseling may be helpful in this regard.

Drug Therapy

Occasional episodes of sleepwalking are usually managed conservatively. However, recurrent episodes with a risk of injury to self or others are usually an indication for drug treatment. There are no evidence-based recommendations for choice of drug (s), dose, or duration of treatment.

Benzodiazepines

Although there is a lack of well-designed controlled studies for any pharmacological therapy in sleepwalking, most of the anecdotal evidence supports benzodiazepines. A small double-blind, crossover, placebo-controlled study found daily bedtime 10 mg diazepam to alleviate sleepwalking in adult patients [76]. Four out of five patients reported satisfactory benefit and continued diazepam for 9 months with no serious adverse events or development of tolerance [76]. This report was consistent with uncontrolled case reports of efficacy of diazepam in adults with sleepwalking [77]. In children, efficacy of diazepam has been documented in isolated cases, with some concern for relapse on discontinuation. However, prompt recovery on resumption of treatment and lack of recurrence with 6 weeks therapy and slow taper over 4 weeks has also been documented [78].

Several case reports have documented beneficial effect of clonazepam in both children and adults with primary and neuroleptic-associated sleepwalking [79–82]. In a study extending over 12 years, 170 adults with disruptive sleep disorders, including 69 with injurious sleepwalking or sleep terrors, were treated for more than 6 months with daily benzodiazepines, including 136 patients who received clonazepam [83]. Overall, 146 patients (86 %) achieved complete or substantial control of their sleep disorders [83]. Clonazepam has longer duration of action and relatively better adverse effect profile as compared with diazepam [84]. Hence, it is the most commonly prescribed medication for sleepwalking in both children and adults [75].

Recently, isolated reports of benefit with other benzodiazepines in sleepwalking have also appeared, including triazolam and flurazepam [79, 85].

As discussed earlier, sleepwalking is associated with increased N3 sleep, and traditionally, it has been believed that benzodiazepines have their beneficial effect in

arousal parasomnias by decreasing N3 sleep. However, clonazepam has been shown to increase N3 sleep [86]. Hence, the efficacy of benzodiazepines may be related to better sleep consolidation by reducing fragmentation of N3 sleep and decreasing reactivity to triggering arousals [75].

Tricyclic Antidepressants

Imipramine has been documented to achieve effective control of sleepwalking in children receiving 10–50 mg at bedtime for 8 weeks [87]. Adults with coexisting night terrors also experienced remission with 50–300 mg given for 8 months to 1 year [48, 88]. Although there was recurrence on discontinuation of imipramine in adults, efficacy was restored on restarting the medication [88]. Two patients unresponsive to diazepam have also been documented to have remission with imipramine [48, 88]. The mechanism of action of imipramine in sleepwalking is not known but is believed to be related to increased norepinephrine and 5-hydroxytryptamine levels [89].

Selective serotonin reuptake inhibitors (SSRI) Paroxetine 20–40 mg once in the morning was used in a patient whose sleepwalking was already in remission with years of clonazepam use. After starting paroxetine, clonazepam could be successfully tapered and stopped with continued remission [90]. It is arguable if the disorder was itself active at that time or not. Although the exact mechanism of action of SSRI in sleepwalking is not known, they are known to have some efficacy in sleep-disordered breathing. This effect is mediated by mildly increased tongue muscle contractile tone due to noradrenergic influence [75]. Decreased sleep fragmentation resulting as a secondary gain contributes to the efficacy in sleepwalking.

Treatment of Associated Disorders

As discussed earlier, sleepwalking is known to exist as an epiphenomenon in several other disorders, including OSA, UARS, RLS, and PLMD. Treatment of these disorders is crucial and usually leads to resolution of sleepwalking [75]. Psychological evaluation and treatment should be considered in cases with suspicion of comorbid psychiatric conditions. Anxiety should also be addressed.

Legal Considerations

Actual or Attempted Homicide

There have been several reports where somnambulism was cited as a defense in cases of homicide or violent assault [91–94]. It has also been pointed out that sleepwalking

is usually accepted as a successful defense in homicidal cases [95]. Most of the law courts in different countries require the diagnosis of sleepwalking to have been established before the criminal event, in addition to other supporting evidence in the form of personal or family history of psychopathology [19, 94, 95]. From a clinical perspective, it is almost impossible to unequivocally say whether the episode in question was a sleepwalking phenomenon even in a known case of somnambulism.

Sexual Crimes

Several different types of sexual behaviors have been reported in sleepwalkers, often with legal implications. These behaviors have included indecent exposure, sleep sex with a lawful partner, sexual misconduct, and alleged rape [80, 96–101]. Usually, these behaviors have been reported to coexist with violent motor activity, nonsense vocalizations, and amnesia for the event [101, 102]. In this context, after a PSG confirmed case, Schenck and Mahowald coined a legal term, parasomnia with continuing danger as a noninsane automatism [98]. At least in one report, sleepwalking was used as a successful defense against three counts of rape [101].

Practical Points

- Sleepwalking is common in children and adolescents.
- The events occur out of slow-wave sleep and are associated with ambulatory behaviors.
- Genetic factors play an important role in predisposing individuals.
- OSA, RLS, and PLMS have been reported as precipitating factors.
- Separation anxiety is associated with sleepwalking in children.
- Differentiation from REM behavior disorder and nocturnal seizures is important, which can be achieved by PSG and video EEG.
- Low-dose clonazepam and safety are important measures in management.

Case Example

A 9-year-old boy was referred to the sleep clinic for evaluation of nighttime events, which started at the age of 5–6 years. He was found walking, sometimes going to the kitchen, and eating by his grandmother. He had also urinated on the kitchen floor or sink on several occasions. He would sometimes grab food and go to bed, and was found with a chicken-bone in mouth once. He had no recollection of the events the next day. He also had trouble falling asleep and staying asleep.

He usually went to bed at 8.30–9.00 pm on weeknights and weekends. He took clonidine 0.2 mg at 8.00 pm, which helped him fall asleep within next 20–30 min. He

usually woke up at 6.00 am on weekdays and 5.00 am on weekends, usually without difficulty and with the help of other family members. He was waking up four times a night for about 15–60 min, and could not return to sleep without help.

He was born at 37 weeks' gestation by spontaneous vaginal delivery. His mother was a smoker and had gestational diabetes and placental abruption. He was born healthy and was discharged after regular stay at the newborn nursery. History of nocturnal events was not present in the family; however, extended history of father's family was not available.

He had a history of bipolar disorder, oppositional defiant disorder, depression, and attention deficit hyperactivity disorder (ADHD). He was on aripiprazole, imipramine, sertraline, trazodone, and methylphenidate for these disorders. His physical examination was normal.

He was sent for a PSG study with extended EEG along with arm and leg electromyography (EMG) monitoring. Typical events were captured on the study. During two events, he screamed loudly. During the third event, he got out of the bed, walked around the room, and went back to sleep. Figure 6.1 shows EEG and EMG patterns during the third event. The PSG study did not show OSA or PLMD.

The patient was diagnosed with sleepwalking and sleep-related eating disorder. He was started on clonazepam 0.5 mg and was motivated to maintain strict sleep hygiene. Also, trazodone was stopped. On last follow-up, his events had reduced in frequency; however, they continue to occur.

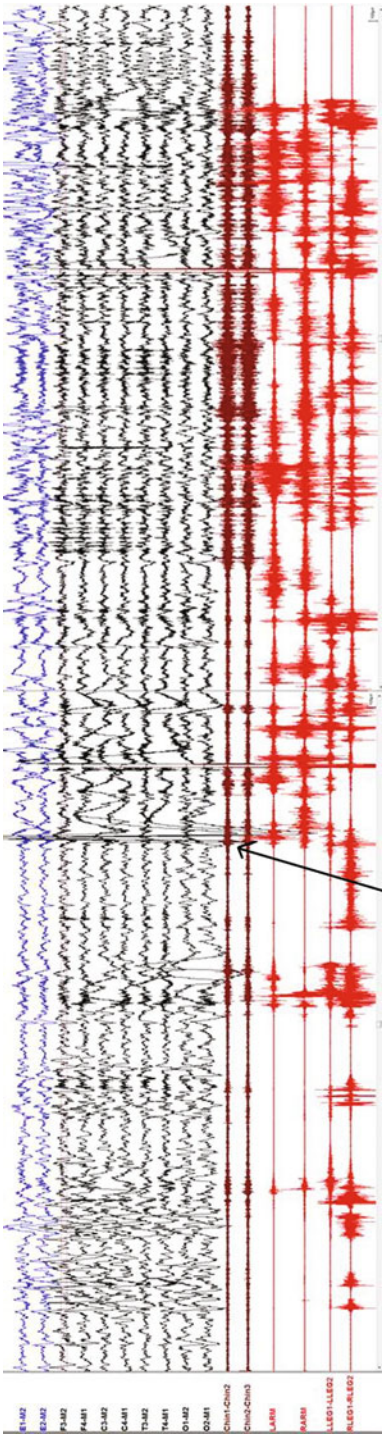


Fig. 6.1 EEG showing the sleepwalking event in the patient (the event onset is shown by the *arrow*)

References

1. Kantha SS. Is somnambulism a distinct disorder of humans and not seen in non-human primates? Med Hypotheses. 2003 Nov-Dec;61(5–6):517–8.
2. Klackenberg G. Somnambulism in childhood—prevalence, course and behavioral correlations. A prospective longitudinal study (6–16 years). Acta Paediatr Scand. 1982 May;71(3):495–9.
3. Liu X, Sun Z, Uchiyama M, Shibui K, Kim K, Okawa M. Prevalence and correlates of sleep problems in Chinese schoolchildren. Sleep. 2000 Dec 15;23(8):1053–62.
4. Neveus T, Cnattingius S, Olsson U, Hetta J. Sleep habits and sleep problems among a community sample of schoolchildren. Acta Paediatr. 2001 Dec;90(12):1450–5.
5. Archbold KH, Pituch KJ, Panahi P, Chervin RD. Symptoms of sleep disturbances among children at two general pediatric clinics. J Pediatr. 2002 Jan;140(1):97–102.
6. Ohayon MM, Guilleminault C, Priest RG. Night terrors, sleepwalking, and confusional arousals in the general population: their frequency and relationship to other sleep and mental disorders. J Clin Psychiatry. 1999 Apr;60(4):268–76; quiz 77.
7. Kales A, Soldatos CR, Caldwell AB, Kales JD, Humphrey FJ 2nd, Charney DS, et al. Somnambulism clinical characteristics and personality patterns. Arch Gen Psychiatry. 1980 Dec;37(12):1406–10.
8. Hublin C, Kaprio J, Partinen M, Heikkila K, Koskenvuo M. Prevalence and genetics of sleepwalking: a population-based twin study. Neurology. 1997 Jan;48(1):177–81.
9. Abe K, Amatomi M, Oda N. Sleepwalking and recurrent sleeptalking in children of childhood sleepwalkers. Am J Psychiatry. 1984 Jun;141(6):800–1.
10. Lecendreux M, Bassetti C, Dauvilliers Y, Mayer G, Neidhart E, Tafti M. HLA and genetic susceptibility to sleepwalking. Mol Psychiatry. 2003 Jan;8(1):114–7.
11. Licis AK, Desruisseau DM, Yamada KA, Duntley SP, Gurnett CA. Novel genetic findings in an extended family pedigree with sleepwalking. Neurology. 2011 Jan 4;76(1):49–52.
12. Guilleminault C, Palombini L, Pelayo R, Chervin RD. Sleepwalking and sleep terrors in prepubertal children: what triggers them? Pediatrics. 2003 Jan;111(1):e17–25.
13. Guilleminault C, Lee JH, Chan A, Lopes MC, Huang YS, da Rosa A. Non-REM-sleep instability in recurrent sleepwalking in pre-pubertal children. Sleep Med. 2005 Nov;6(6):515–21.
14. Owens J, Spirito A, Nobile C, Arrigan M. Incidence of parasomnias in children with obstructive sleep apnea. Sleep. 1997 Dec;20(12):1193–6.
15. Espa F, Dauvilliers Y, Ondze B, Billiard M, Besset A. Arousal reactions in sleepwalking and night terrors in adults: the role of respiratory events. Sleep. 2002;25(8):871–5.
16. Mayer G, Neissner V, Schwarzmayr P, Meier-Ewert K. Sleep deprivation in somnambulism. Effect of arousal, deep sleep and sleep stage changes. Nervenarzt. 1998 Jun;69(6):495–501.
17. Joncas S, Zadra A, Paquet J, Montplaisir J. The value of sleep deprivation as a diagnostic tool in adult sleepwalkers. Neurology. 2002 Mar 26;58(6):936–40.
18. Pilon M, Montplaisir J, Zadra A. Precipitating factors of somnambulism: impact of sleep deprivation and forced arousals. Neurology. 2008 Jun 10;70(24):2284–90.
19. Hughes JR. A review of sleepwalking (somnambulism): the enigma of neurophysiology and polysomnography with differential diagnosis of complex partial seizures. Epilepsy Behav. 2007 Dec;11(4):483–91.
20. Charney DS, Kales A, Soldatos CR, Nelson JC. Somnambulistic-like episodes secondary to combined lithium-neuroleptic treatment. Br J Psychiatry. 1979 Nov;135:418–24.
21. Glassman JN, Darko D, Gillin JC. Medication-induced somnambulism in a patient with schizoaffective disorder. J Clin Psychiatry. 1986 Oct;47(10):523–4.
22. Landry P, Montplaisir J. Lithium-induced somnambulism. Can J Psychiatry. 1998 Nov;43(9):957–8.
23. Landry P, Warnes H, Nielsen T, Montplaisir J. Somnambulistic-like behaviour in patients attending a lithium clinic. Int Clin Psychopharmacol. 1999 May;14(3):173–5.
24. Harazin J, Berigan TR. Zolpidem tartrate and somnambulism. Mil Med. 1999 Sep;164(9):669–70.

25. Tsai JH, Yang P, Chen CC, Chung W, Tang TC, Wang SY, et al. Zolpidem-induced amnesia and somnambulism: rare occurrences? Eur Neuropsychopharmacol. 2009 Jan;19(1):74–6.
26. Yang W, Dollear M, Muthukrishnan SR. One rare side effect of zolpidem—sleepwalking: a case report. Arch Phys Med Rehabil. 2005 Jun;86(6):1265–6.
27. Sattar SP, Ramaswamy S, Bhatia SC, Petty F. Somnambulism due to probable interaction of valproic acid and zolpidem. Ann Pharmacother. 2003 Oct;37(10):1429–33.
28. Khazaal Y, Krenz S, Zullino DF. Bupropion-induced somnambulism. Addict Biol. 2003 Sep;8(3):359–62.
29. Ajlouni KM, Ahmad AT, El-Zaheri MM, Ammari FL, Jarrah NS, AbuJbara MA, et al. Sleepwalking associated with hyperthyroidism. Endocr Pract. 2005 Jan-Feb;11(1):5–10.
30. Hori T, Suzuki T, Terashima Y, Kawai N, Shiraishi H, Koizumi J. Chronic herpes simplex encephalitis with somnambulism: CT, MR and SPECT findings. Jap J Psychiatry Neurol. 1990 Dec;44(4):735–9.
31. Pressman MR. Factors that predispose, prime and precipitate NREM parasomnias in adults: clinical and forensic implications. Sleep Med Rev. 2007 Feb;11(1):5–30; discussion 31–3.
32. Millman RP, Kipp GJ, Carskadon MA. Sleepwalking precipitated by treatment of sleep apnea with nasal CPAP. Chest. 1991 Mar;99(3):750–1.
33. American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic & coding manual. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
34. Avidan AY, Kaplish N. The parasomnias: epidemiology, clinical features, and diagnostic approach. Clin Chest Med. 2010;31(2):353–70.
35. Mason TB 2nd, Pack AI. Pediatric parasomnias. Sleep. 2007 Feb;30(2):141–51.
36. Provini F, Tinuper P, Bisulli F, Lugaresi E. Arousal disorders. Sleep Med. 2011;12 Suppl 2:S22–6.
37. Trajanovic NN, Shapiro CM, Ong A. Atypical presentation of NREM arousal parasomnia with repetitive episodes. Eur J Neurol. 2007 Aug;14(8):947–50.
38. Masand P, Popli AP, Weilburg JB. Sleepwalking. Am Fam Physician. 1995 Feb 15;51(3):649–54.
39. Espa F, Ondze B, Deglise P, Billiard M, Besset A. Sleep architecture, slow wave activity, and sleep spindles in adult patients with sleepwalking and sleep terrors. Clin Neurophysiol. 2000 May;111(5):929–39.
40. Gaudreau H, Joncas S, Zadra A, Montplaisir J. Dynamics of slow-wave activity during the NREM sleep of sleepwalkers and control subjects. Sleep. 2000 Sep 15;23(6):755–60.
41. Guilleminault C, Poyares D, Aftab FA, Palombini L. Sleep and wakefulness in somnambulism: a spectral analysis study. J Psychosom Res. 2001 Aug;51(2):411–6.
42. Jacobson A, Kales A, Lehmann D, Zweizig JR. Somnambulism: all-night electroencephalographic studies. Science. 1965 May 14;148(3672):975–7.
43. Schenck CH, Pareja JA, Patterson AL, Mahowald MW. Analysis of polysomnographic events surrounding 252 slow-wave sleep arousals in thirty-eight adults with injurious sleepwalking and sleep terrors. J Clin Neurophysiol. 1998 Mar;15(2):159–66.
44. Pilon M, Zadra A, Joncas S, Montplaisir J. Hypersynchronous delta waves and somnambulism: brain topography and effect of sleep deprivation. Sleep. 2006 Jan;29(1):77–84.
45. Parrino L, Halasz P, Tassinari CA, Terzano MG. CAP, epilepsy and motor events during sleep: the unifying role of arousal. Sleep Med Rev. 2006 Aug;10(4):267–85.
46. Guilleminault C, Kirisoglu C, da Rosa AC, Lopes C, Chan A. Sleepwalking, a disorder of NREM sleep instability. Sleep Med. 2006 Mar;7(2):163–70.
47. Petit D, Touchette É, Tremblay RE, Boivin M, Montplaisir J. Dyssomnias and parasomnias in early childhood. Pediatrics. 2007;119(5):e1016–25.
48. Garland EJ, Smith DH. Simultaneous prepubertal onset of panic disorder, night terrors, and somnambulism. J Am Acad Child Adolesc Psychiatry. 1991 Jul;30(4):553–5.
49. Gau SF, Soong WT. Psychiatric comorbidity of adolescents with sleep terrors or sleepwalking: a case-control study. Aust N Z J Psychiatry. 1999 Oct;33(5):734–9.

50. Crisp AH, Matthews BM, Oakey M, Crutchfield M. Sleepwalking, night terrors, and consciousness. Br Med J. 1990;300(6721):360–2.
51. Hartman D, Crisp AH, Sedgwick P, Borrow S. Is there a dissociative process in sleepwalking and night terrors? Postgrad Med J. 2001;77(906):244–9.
52. Schenck CH, Boyd JL, Mahowald MW. A parasomnia overlap disorder involving sleepwalking, sleep terrors, REM sleep behavior disorder in 33 polysomnographically confirmed cases. Sleep. 1997 Nov;20(11):972–81.
53. Kales A, Soldatos CR, Bixler EO, Ladda RL, Charney DS, Weber G, et al. Hereditary factors in sleepwalking and night terrors. Br J Psychiatry. 1980 Aug;137:111–8.
54. Zadra A, Pilon M. Non-rapid eye movement parasomnias: diagnostic methods. Sleep Med Clin. 2011;6(4):447–58.
55. Mehlenbeck R, Spirito A, Owens J, Boergers J. The clinical presentation of childhood partial arousal parasomnias. Sleep Med. 2000 Oct 1;1(4):307–12.
56. Barabas G, Matthews WS, Ferrari M. Somnambulism in children with Tourette syndrome. Dev Med Child Neurol. 1984 Aug;26(4):457–60.
57. Barabas G, Ferrari M, Matthews WS. Childhood migraine and somnambulism. Neurology. 1983 Jul;33(7):948–9.
58. Giroud M, d'Athis P, Guard O, Dumas R. Migraine and somnambulism. A survey of 122 migraine patients. Rev Neurol (Paris). 1986;142(1):42–6.
59. Plazzi G, Vetrugno R, Provini F, Montagna P. Sleepwalking and other ambulatory behaviours during sleep. Neurol Sci. 2005 Dec;26 Suppl 3:s193–8.
60. Derry CP, Duncan JS, Berkovic SF. Paroxysmal motor disorders of sleep: the clinical spectrum and differentiation from epilepsy. Epilepsia. 2006;47(11):1775–91.
61. Provini F, Plazzi G, Tinuper P, Vandi S, Lugaresi E, Montagna P. Nocturnal frontal lobe epilepsy. A clinical and polygraphic overview of 100 consecutive cases. Brain. 1999 Jun;122 (Pt 6):1017–31.
62. Tinuper P, Provini F, Bisulli F, Vignatelli L, Plazzi G, Vetrugno R, et al. Movement disorders in sleep: guidelines for differentiating epileptic from non-epileptic motor phenomena arising from sleep. Sleep Med Rev. 2007 Aug;11(4):255–67.
63. Manni R, Terzaghi M, Repetto A. The FLEP scale in diagnosing nocturnal frontal lobe epilepsy, NREM and REM parasomnias: data from a tertiary sleep and epilepsy unit. Epilepsia. 2008 Sep;49(9):1581–5.
64. Derry CP, Davey M, Johns M, Kron K, Glencross D, Marini C, et al. Distinguishing sleep disorders from seizures: diagnosing bumps in the night. Arch Neurol. 2006 May;63(5):705–9.
65. Amir N, Navon P, Silverberg-Shalev R. Interictal electroencephalography in night terrors and somnambulism. Isr J Med Sci. 1985 Jan;21(1):22–6.
66. Fehlow P. The significance of EEG findings in somnambulism. Padiatr Grenzgeb. 1990;29(1):53–7.
67. Cavazzuti GB, Cappella L, Nalin A. Longitudinal study of epileptiform EEG patterns in normal children. Epilepsia. 1980 Feb;21(1):43–55.
68. Plazzi G, Tinuper P, Montagna P, Provini F, Lugaresi E. Epileptic nocturnal wanderings. Sleep. 1995 Nov;18(9):749–56.
69. Nobili L, Francione S, Cardinale F, Lo Russo G. Epileptic nocturnal wanderings with a temporal lobe origin: a stereo-electroencephalographic study. Sleep. 2002 Sep 15;25(6):669–71.
70. Reid WH. Treatment of somnambulism in military trainees. Am J Psychother. 1975 Jan;29(1):101–6.
71. Reid WH, Ahmed I, Levie CA. Treatment of sleepwalking: a controlled study. Am J Psychother. 1981 Jan;35(1):27–37.
72. Hurwitz TD, Mahowald MW, Schenck CH, Schluter JL, Bundlie SR. A retrospective outcome study and review of hypnosis as treatment of adults with sleepwalking and sleep terror. J Nerv Ment Dis. 1991 Apr;179(4):228–33.
73. Tobin JD Jr. Treatment of somnambulism with anticipatory awakening. J Pediatr. 1993 Mar;122(3):426–7.

74. Frank NC, Spirito A, Stark L, Owens-Stively J. The use of scheduled awakenings to eliminate childhood sleepwalking. J Pediatr Psychol. 1997 Jun;22(3):345–53.
75. Remulla A, Guilleminault C. Somnambulism (sleepwalking). Expert Opin Pharmacother. 2004 Oct;5(10):2069–74.
76. Reid WH, Haffke EA, Chu CC. Diazepam in intractable sleepwalking: a pilot study. Hillside J Clin Psychiatry. 1984;6(1):49–55.
77. Chin CN. Sleep walking in adults: two case reports. Med J Malaysia. 1987 Jun;42(2):132–3.
78. Glick BS, Schulman D, Turecki S. Diazepam (Valium) treatment in childhood sleep disorders. A preliminary investigation. Dis Nerv Syst. 1971 Aug;32(8):565–6.
79. Kavey NB, Whyte J, Resor SR Jr, Gidro-Frank S. Somnambulism in adults. Neurology. 1990 May;40(5):749–52.
80. Alves R, Aloe F, Tavares S, Vidrio S, Yanez L, Aguilar-Roblero R, et al. Sexual behavior in sleep, sleepwalking and possible REM behavior disorder: a case report. Sleep Res Online. 1999;2(3):71–2.
81. Szucs A, Halasz P. Somnambulism: clinical and eletrophysiological aspects. Orv Hetil. 2005 Jun 5;146(23):1231–7.
82. Goldbloom D, Chouinard G. Clonazepam in the treatment of neuroleptic-induced somnambulism. Am J Psychiatry. 1984 Nov;141(11):1486.
83. Schenck CH, Mahowald MW. Long-term, nightly benzodiazepine treatment of injurious parasomnias and other disorders of disrupted nocturnal sleep in 170 adults. Am J Med. 1996 Mar;100(3):333–7.
84. Riss J, Cloyd J, Gates J, Collins S. Benzodiazepines in epilepsy: pharmacology and pharmacokinetics. Acta Neurol Scand. 2008 Aug;118(2):69–86.
85. Reimao R, Lefevre AB. Evaluation of flurazepam and placebo on sleep disorders in childhood. Arq Neuropsiquiatr. 1982 Mar;40(1):1–13.
86. Fritz G, Rockney R, Bernet W, Arnold V, Beitchman J, Benson RS, et al. Practice parameter for the assessment and treatment of children and adolescents with enuresis. J Am Acad Child Adolesc Psychiatry. 2004 Dec;43(12):1540–50.
87. Pesikoff RB, Davis PC. Treatment of pavor nocturnus and somnambulism in children. Am J Psychiatry. 1971 Dec;128(6):778–81.
88. Cooper AJ. Treatment of coexistent night-terrors and somnambulism in adults with imipramine and diazepam. J Clin Psychiatry. 1987 May;48(5):209–10.
89. Kotagal S. Treatment of dyssomnias and parasomnias in childhood. Curr Treat Options in Neurol. 2012;14:630–49.
90. Lillywhite AR, Wilson SJ, Nutt DJ. Successful treatment of night terrors and somnambulism with paroxetine. Br J Psychiatry. 1994 Apr;164(4):551–4.
91. Hartmann E. Two case reports: night terrors with sleepwalking—a potentially lethal disorder. J Nerv Ment Dis. 1983 Aug;171(8):503–5.
92. Oswald I, Evans J. On serious violence during sleep-walking. Br J Psychiatry. 1985 Dec;147:688–91.
93. Ovuga EB. Murder during sleep-walking. East Afr Med J. 1992 Sep;69(9):533–4.
94. Broughton R, Billings R, Cartwright R, Doucette D, Edmeads J, Edwardh M, et al. Homicidal somnambulism: a case report. Sleep. 1994;17(3):253–64.
95. Mahowald MW, Schenck CH. Parasomnias: sleepwalking and the law. Sleep Med Rev. 2000 Aug;4(4):321–39.
96. Buchanan A. Sleepwalking and indecent exposure. Med Sci Law. 1991 Jan;31(1):38–40.
97. Thomas TN. Sleepwalking disorder and mens rea: a review and case report. Maricopa County Superior Court. J Forensic Sci. 1997 Jan;42(1):17–24.
98. Schenck CH, Mahowald MW. A polysomnographically documented case of adult somnambulism with long-distance automobile driving and frequent nocturnal violence: parasomnia with continuing danger as a noninsane automatism? Sleep. 1995 Nov;18(9):765–72.
99. Rosenfeld DS, Elhajjar AJ. Sleepsex: a variant of sleepwalking. Arch Sex Behav. 1998 Jun;27(3):269–78.

100. Schenck CH, Mahowald MW. An analysis of a recent criminal trial involving sexual misconduct with a child, alcohol abuse and a successful sleepwalking defence: arguments supporting two proposed new forensic categories. Med Sci Law. 1998 Apr;38(2):147–52.
101. Ebrahim IO. Somnambulistic sexual behaviour (sexsomnia). J Clin Forensic Med. 2006 May;13(4):219–24.
102. Shapiro CM, Trajanovic NN, Fedoroff JP. Sexsomnia—a new parasomnia? Can J Psychiatry. 2003 Jun;48(5):311–7.

Chapter 7
Sleep Terrors and Confusional Arousals in Adults

Milena Pavlova and Myriam Abdennadher

Overview

Sleep terrors (STs) and confusional arousals (CAs) are types of parasomnia that emerge from nonrapid eye movement (NREM) sleep. STs occur during NREM sleep (usually slow-wave sleep), while CAs, as the name suggests, are abnormal arousals from NREM sleep (typically from slow-wave sleep).

Reasons for Evaluation

Both STs and CAs may lead to violent or injurious behavior from sleep seen in adults. Initial studies by Schenck et al. [1] reported 20 parasomnia patients who had a significant enough injury to need intensive care unit treatment. While the majority of these patients had rapid eye movement (REM) behavior disorder, 15 % had STs. These had resulted in severe injuries, including a lumbar vertebral fracture, a severe concussion, and C-spine fracture. A more recent study used a standardized interview analysis of 19,961 participants from seven European countries to determine the rate of violent behavior during sleep [2]. STs and sleepwalking were frequent causes, and the reports of 71 % of the participants suggested presence of more than one parasomnia in the same individual [2]. Factors that were significantly associated with violent behavior included STs, other parasomnias (sleepwalking, nightmares, hypnagogic hallucinations, and sleep paralysis), mood disorders, and medical illness [2]. Excessive daytime sleepiness was reported by many of the participants [2].

M. Pavlova (✉)
Department of Neurology, Brigham and Women's Hospital,
Harvard Medical School, Boston, MA, USA
e-mail: mpavlova1@partners.org

M. Abdennadher
90 St. Mary's Street, Unit 3–6, Boston, MA 02215, USA

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_7,

Provoking Factors and Associated Symptoms

In an epidemiological study of 4,972 participants [3], Ohayon et al. [3] reported several factors associated with night terrors including: subjective sense of choking or blocked breathing at night (odds ratio (OR) = 5.1), obstructive sleep apnea syndrome (OR = 4.1), alcohol consumption at bedtime (OR = 3.9), violent or injury-causing behaviors during sleep (OR = 3.2), hypnagogic hallucinations (OR = 2.2), and nightmares at least 1 night per month (OR = 4.0). CAs were associated with: younger age (OR = 4.1), shift work (OR = 2.1), hypnagogic hallucinations (OR = 3.3), deep sleep (OR = 1.6), daytime sleepiness (OR = 1.9), sleep talking (OR = 1.7), daily smoking (OR = 1.7), adjustment disorder (OR = 3.1), and bipolar disorder (OR = 13.0).

It has been clinically observed that as many other parasomnias, CAs and STs may be provoked by poor sleep. Formal polysomnographic analysis suggests that parasomnia episodes are significantly more frequent during recovering from sleep deprivation than during baseline sleep [4]. Sleep deprivation has even been proposed as a diagnostic tool to diagnose parasomnia. Joncas et al. [5] performed a study of ten patients with parasomnia and matched controls and noted a significant increase of the rate of nocturnal events during the recovery night compared with baseline in parasomnia patients, but not controls. Thus, patients with STs and CAs should be evaluated for sleep deprivation, poor sleep hygiene, shift work or other circadian rhythm disturbances, as well as sleep-fragmenting disorders (such as sleep apnea and restless legs syndrome).

Sleep Terrors (STs)

Sleep terrors (also called night terrors) are characterized by an initial sudden scream or loud cry that arise from sleep typically accompanied by sitting in bed with intense autonomic nervous system activation [6]. The patient is unresponsive to stimuli and is confused and/or disoriented if awakened. The symptomatology could sometimes evolve to sleep walking and may cause severe injury.

The events occur predominantly in the early part of the night when the highest proportion of slow-wave sleep occurs as well. They are typically briefer than other parasomnias. Full awakening emerges gradually and there is typically no associated elaborate dreaming, though a fragment can be sometimes reported.

The **diagnostic criteria** for STs per current international classification of sleep disorders (ICSD II) [6] include:

1. A sudden episode of terror occurring during sleep, usually initiated by a cry or loud scream that is accompanied by autonomic nervous system and behavioral manifestation of intense fear.
2. At least one of the following:
   (a) Difficulty arousing the person,
   (b) Mental confusion when awakening from the episode,

(c) Amnesia,
(d) Dangerous or potentially dangerous behaviors.
3. The disturbance is not better explained by another disorder.

Some authors suggest that ST emerge during the transition between deep NREM sleep (N3) and REM sleep [7]. This may explain the characteristic features of STs (the great fear, the severe autonomic system reaction) [8].

In a recent study by Ohayon et al. [2], frequency in more than half of the patients is around once per month, but 23 % had as frequent as several events per week.

Case Example 1

A 26-year-old woman presented with episodes of fear and screaming during sleep. These had started in her late adolescence. They ranged in frequency from once per month to multiple in 1 week, being more frequent during times of intense stress or sleep loss. The type of nocturnal behavior varied. Most frequently she would simply sit up in bed abruptly from sleep, often screaming or with fear or disorientation. She would gradually come to full wakefulness. There was no elaborate dream associated. On some occasions, she would leave bed, and wake up in different places in the house. Once, she attempted to go through a door, broke it with her knee and sustained a knee injury. On another occasion, she awoke next to the window, attempting to take screen down.

Practical Points

1. ST most frequently start in young adulthood (similar to other NREM parasomnias; REM behavior disorder is typically seen in older individuals).
2. Typical presentation involves abrupt screaming/sitting in bed; the patient awakes gradually (as opposed to seizures, where end is more typically abrupt).
3. There is no associated elaborate dream (as opposed to REM behavior disorders, which presents with a vivid dream recall).
4. The abnormal behaviors can lead to injury.

Differential Diagnosis

Sleep terrors must be differentiated from seizures, from other parasomnias, nocturnal panic attacks, anxiety, and psychiatric conditions including mood disorders. Less frequently, medical conditions that lead to autonomic disregulation (such as arrhythmia) or sleep apnea may present with an abrupt arousal.

Prognosis and Effect of Age

A higher prevalence of ST has been reported among individuals younger than 35 years of age. Incidence peaked in adolescence/young adulthood, though more than half of the participants did not remember the time of their first episode. In the geriatric population, the prevalence of ST is slightly less than 1 % [2].

Confusional Arousals (CAs)

Confusional arousals are characterized by an awakening in a disoriented state, vocalization, and apparent confusion. Behavior is inappropriate and sometimes aggressive. Frequently, there is amnesia.

The current **diagnostic criteria per ICSD II** [6] are as follows:

A. Recurrent mental confusion or confusional behavior occurs during an arousal or awakening from nocturnal sleep or daytime nap.
B. The disturbance is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance abuse.

Two **subtypes** are recognized:

1. Severe morning sleep inertia: unlike the typical confusional arousal which emerges from slow-wave sleep, morning sleep inertia arises in the morning, likely from lighter NREM sleep. Clinical manifestation is the same in both conditions.
2. Sleep-related abnormal sexual behaviors: these have been recently described [9] and may occur during an arousal from sleep or during sleep (as a form of sleepwalking).

Case Example 2

A 39-year-old man initially presented with symptoms of abnormal behaviors from sleep. He had these symptoms for many years; however, over time they became more frequent. At the time of presentation, they occurred nearly 2–3 times per night, 4–5 times total per week, and last for 10–15 min. His wife would find him running downstairs, trying to get out the front door, or hiding somewhere or screaming. He would generally slowly come to full awareness at the end of the episode. He was amnestic for the events, although during the event he could sometimes communicate with his wife. The events typically occurred within the first 30 min to 1 h of sleep. He had been given clonazepam 0.5 mg, which decreased the frequency of these events to once a year; however, then his wife began to notice witnessed apneas. He underwent an overnight sleep study, which demonstrated severe obstructive sleep apnea. On continuous positive airway pressure (CPAP) treatment, his daytime sleepiness,

snoring, and witnessed apneas resolved. His abnormal nocturnal behavior also resolved and clonazepam was weaned and stopped.

Several years later, he reported a new onset of stereotypical daytime events of impaired awareness. These occurred in any body position, without any apparent provocation, and lasted ~1–2 min. He would have difficulty focusing or forming complex sentences. This prompted an evaluation for epilepsy. He had an electroencephalogram (EEG), which was abnormal due to left temporal sharp waves. A subsequent continuous video-EEG captured one clinical event, in which the patient suddenly woke from non-REM sleep, jumped out of bed, and walked out of the room, and was subsequently briefly confused. Later, the patient reported that he suddenly thought someone was entering his room, so he jumped up to see what was happening. A brief period of semirhythmic left frontotemporal theta was seen at the onset; subsequently, muscle artifact obscured the recording.

Treatment with levetiracetam (an antiepileptic medication) was initiated and the need for full CPAP compliance was emphasized. After a therapeutic dose was reached, and CPAP was used nightly, the daytime events resolved, and the nocturnal events occurred only during travel, stress, or sleep disruption. Clonazepam was only used during travel.

Practical Points

1. CAs can be provoked by sleep-disrupting factors including stress, travel, and "physiological sleep disruptors." In this case, respiratory arousals from sleep apnea likely provoked more frequent events. Subsequently, the patient developed seizures. Seizures can also interrupt sleep and provoke CAs.
2. Epilepsy and CAs may coexist (the initial nocturnal events were likely CAs, as they were not very stereotypical and they resolved with treatment of sleep fragmentation and without any antiepileptic medications).
3. In some situations, epilepsy evaluation is needed for adequate diagnosis.
4. Treatment of the sleep-disrupting factors may lead to a dramatic improvement in the frequency of CAs.

There are multiple reports of CAs provoked by seizures. For example, a case series reported six patients diagnosed with NREM parasomnia—STs in three and sleepwalking in the other three, who developed exclusively nocturnal seizures later in life [10] (similar to the patient above). A subsequent study examined the frequency of parasomnias in temporal lobe epilepsy patients and found that 12 % had parasomnias—the majority had CAs (80 % of the parasomnia patients) [11]. Sleep disruption, provoked by the seizure may evolve with abnormal behavior or a "confusional arousal."

Table 7.1 Differential diagnosis of abnormal nocturnal behaviors

	Seizure	Sleep terror	Confusional arousal	RBD event
Time of occurrence during the night	From waking or NREM sleep	Typically first third	Typically first third	Typically last third
Usual duration	½ –2 min	Many minutes—variable	Many minutes—variable	Many minutes—variable
Presentation	Stereotypic	Variable	Variable	Variable
Course of individual event	Beginning—evolution—end. Versive movements or dystonic posture and **abrupt** ending favor seizure	Abrupt screaming/sitting in bed from sleep. The transition to wakefulness is **gradual**	Confusion, **gradual** transition to full wakefulness	Waxing–waning
Amnesia	Often with CPS, always with GTCS	Often	Often	Dream recall
EEG	Typically abnormal	Normal	Normal	Abnormal EMG activations during REM sleep (REM without atonia)

RBD REM behavior disorder, *NREM* nonrapid eye movement, *CPS* complex partial seizure, *GTCS* generalized tonic–clonic seizure, *EEG* electroencephalogram, *EMG* electromyogram

Differential Diagnosis

Confusional arousals must be differentiated from seizures/postictal psychosis, other parasomnias, and psychiatric disorders. Differentiation from REM behavior disorder (RBD) is also important and can be more challenging in the older patients. Both disorders can present with agitation. However, REM behavior disorder patients report a vivid dream that is consistent with the observed behavior. In addition, RBD is seen in older patients, and has a frequent association with neurodegenerative disorders, while CAs do not have such association and are seen in younger individuals. Table 7.1 summarizes features that help differentiate abnormal nocturnal events.

At this time, the most comprehensive analysis on the differentiation of parasomnia from seizures has been performed by Derry et al. [12]. A questionnaire-based scale for distinguishing frontal lobe epilepsy from parasomnia was introduced in 2006 [12]. Using this scale, Manni et al. [13], in a study of 71 patients, found that this instrument was effective in distinguishing the two disorders with a sensitivity of 71 % and specificity of 100 %. Subsequently, based on the video analysis, a decision tree was proposed to further guide the diagnostic pathway (Fig. 7.1) [14].

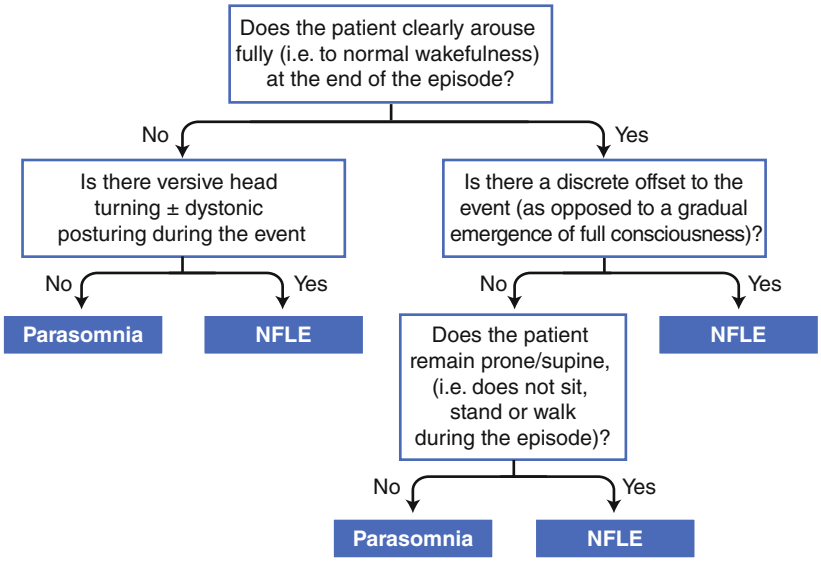


Fig. 7.1 Decision tree to help differential diagnosis of a nocturnal event. (From Derry CP.14 Used with permission of American Academy of Sleep Medicine, Darien, IL, 2012)

Prognosis

Although CAs are generally self-limited, there is a reported higher risk of mental disorders in these patients. Ohayon et al. [15] found a strong association between CAs and mental disorders.

References

1. Schenck CH, Mahowald MW. Injurious sleep behavior disorders (parasomnias) affecting patients on intensive care units. Intensive Care Med. 1991;17(4):219–24.
2. Ohayon MM, Schenck CH. Violent behavior during sleep: prevalence, comorbidity and consequences. Sleep Med. 2010 Oct;11(9):941–6.
3. Ohayon MM, Guilleminault C, Priest RG. Night terrors, sleepwalking, and confusional arousals in the general population: their frequency and relationship to other sleep and mental disorders. J Clin Psychiatry. 1999 Apr;60(4):268–76; quiz 277.
4. Zadra A, Pilon M, Joncas S, Rompré S, Montplaisir J Analysis of postarousal. EEG activity during somnambulistic episodes. J Sleep Res. 2004 Sep;13(3):279–84.
5. Joncas S, Zadra A, Paquet J, Montplaisir J. The value of sleep deprivation as a diagnostic tool in adult sleepwalkers. Neurology. 2002 Mar 26;58(6):936–40.
6. American Academy of Sleep Medicine. International classification of sleep disorders: diagnostic and coding manual. 2nd ed. Westchester: American Academy of Sleep Medicine; 2005.
7. Arkin AM. Night-terrors as anomalous REM sleep component manifestation in slow-wave sleep. Waking & Sleeping. 1978 Jul;2(3):143–7.

8. Howell MJ. Parasomnias: an updated review. Neurotherapeutics. 2012 Sep 11;9(4):753–75.
9. Schenck CH, Arnulf I, Mahowald MW. Sleep and sex: what can go wrong? A review of the literature on sleep related disorders and abnormal sexual behaviors and experiences. Sleep. 2007 Jun;30(6):683–702. Review.
10. Silvestri R, de Domenico P, Mento G, Laganà A, di Perri R. Epileptic seizures in subjects previously affected by disorders of arousal. Neurophysiol Clin. 1995;25(1):19–27.
11. Silvestri R, Bromfield E. Recurrent nightmares and disorders of arousal in temporal lobe epilepsy. Brain Res Bull. 2004 Jun 30;63(5):369–76.
12. Derry CP, Davey M, Johns M, Kron K, Glencross D, Marini C et al. Distinguishing sleep disorders from seizures: diagnosing bumps in the night. Arch Neurol. 2006 May;63(5):705–9.
13. Manni R, Terzaghi M, Repetto A. The FLEP scale in diagnosing nocturnal frontal lobe epilepsy, NREM and REM parasomnias: data from a tertiary sleep and epilepsy unit. Epilepsia. 2008 Sep;49(9):1581–5.
14. Derry CP, Harvey AS, Walker MC, Duncan JS, Berkovic SF. NREM arousal parasomnias and their distinction from nocturnal frontal lobe epilepsy: a video EEG analysis. Sleep. 2009 Dec;32(12):1637–44.
15. Ohayon MM, Priest RG, Zulley J, Smirne S. The place of confusional arousals in sleep and mental disorders: findings in a general population sample of 13,057 subjects. J Nerv Ment Dis. 2000 Jun;188(6):340–8.

Chapter 8
Sleep Terrors and Confusional Arousals in Children and Adolescents

Sejal V. Jain

Sleep Terrors

Introduction

Parasomnias are very common in 3–13-years-old children, up to 78 % in a study [1]. Confusional arousals, sleepwalking, and sleep terror are a spectrum of disorder from less to most dramatic events [2]. Sleep terrors or *pavor nocturnus* are arousals from slow-wave sleep accompanied by a cry or scream and autonomic and behavioral manifestations of intense fear [3].

Epidemiology

Sleep terrors are common in young children with peak prevalence at 5–7 years of age and spontaneous remission in adolescents [3, 4]. There is discrepancy in prevalence rates in various studies due to the differences in the definition, method, and population sample in the studies. Prevalence rates of 1–6.5 % are most commonly reported for children with relatively stable rates of 2.3–2.6 % after 15 years of age [3]. In a Canadian study, overall prevalence of 40 % was reported in children with a prevalence of 20 % in 2.5 years old dropping to 11 % at 6 years of age [5]. Prevalence of 14.7 % has been reported in children aged 3–10 years [1]. In this study, a reduction in the prevalence was seen, with only 1.2 % of the children continuing to have the night terrors at 13 years of age. In a study from Turkey, a rate of 0.9 % was reported at 7–11 years of age [6]. Furet et al. [7] studied 6–11-years-old children for parasomnia and restudied them after 5 years. Initial prevalence was 2.6 % for night

S. V. Jain (✉)
Division of Neurology, Cincinnati Children's Hospital Medical Center,
MLC 2015, 3333 Burnet Ave., Cincinnati, OH 45229, USA
e-mail: Sejal.Jain@cchmc.org

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_8,

terrors and 5 years later all children had a remission with only 0.6 % of children with newly developed sleep terrors. No gender differences have been reported in studies [5, 6].

Etiology

Predisposing Factors: Genetics

A strong familial pattern is seen suggesting genetic influences. Autosomal dominant transmission was suggested initially, with a report of three cases from three consecutive generations [8]. In another study, 96 % of the patients were found to have positive family history in first- to third- degree relatives [9]. In a twin study, out of 47 monozygotic pairs, 7 were concordant for sleep terrors, whereas none out of 7 dizygotic pairs were concordant [10]. Night terrors were found in 11 % of children with one or both parents with a history of sleepwalking as compared with 5 % of children without parental history of sleepwalking [11, 12]. In a retrospective twin study, polychoric correlation was 0.38 and 0.35 for monozygotic males and females, respectively as compared with 0.17 and 0.18 for dizygotic males and females, respectively [13]. In a prospective twin study, polychoric correlation was more than 0.60 for monozygotic twin as compared with 0.36 and 0.24 for dizygotic twins at 18 and 36 months of age, respectively. The study suggested that more than 40 % of the phenotypic variation in sleep terror was attributable to genetic influences [14]. In addition, some of the precipitating factors for sleep terrors such as restless leg syndrome (RLS) are also genetically determined and this may also be a reason for the familial tendencies for sleep terror [15].

Precipitating Factors

Sleep disorders affecting the quality and continuity of sleep may precipitate partial arousal leading to sleep terrors. In a study, 61 % of children with sleep terror and sleepwalking were found to have another sleep disorder such as sleep-disordered breathing (SDB) and restless leg syndrome-periodic limb movement disorder (RLS-PLMD). Upon successful treatment of these disorders, the parasomnia events remitted. Untreated subjects continued to have the episodes [16]. Similarly, gastroesophageal reflux can also precipitate an event [17].

Sleep deprivation alone or in combination with forced arousal has precipitated sleepwalking in experimental setting in adults [18, 19]. It is believed that following sleep deprivation, there is increased slow-wave sleep during recovery night and this may lead to increased parasomnia. Similar mechanism may occur in children and increase the frequency of sleep terrors. In addition, febrile illness, stress, several drugs including clonidine [20] and risperidone [21], and alcohol use have been

reported to be the priming factors for parasomnia [22]. Moreover, thalamic and brainstem lesions have been reported in patients with night terrors in isolated case reports [23, 24].

Pathophysiology

Sleep and wakefulness are not "all or none" states. The waking dissociated state is believed to be the cause of arousal parasomnias such as sleep terrors. Parasomnias are likely to occur during the transition states. In a patient with parasomnia, local arousal of the motor and cingulate cortices were seen with delta activity in frontoparietal association cortices [25]. This proves that sleep is not a global phenomenon and the mixture of nonrapid eye movement (NREM) sleep with wakefulness in different regions of brain can explain the occurrence of parasomnias [26, 27].

Locomotor center activation without wakefulness may explain the motor behaviors seen with the parasomnia. In a study, single-proton emission computed tomography (SPECT) scan, in a patient with parasomnia, showed activation in thalamocingulate pathway with persistent deactivation in thalamocortical arousal pathways [26].

Sleep inertia is a period of reduced vigilance during transition from sleep to wakefulness. Cerebral blood flow studies in humans have confirmed this phenomenon. Transition from NREM sleep to wakefulness may show similar pattern [26, 27].

Sleep state instability has also been suggested. Cyclic alternating pattern (CAP) represents oscillations in arousals through NREM sleep. It is divided in A phases, which are sequence of recurring transient events, followed by stable intervals or B phases, which separate these A phases. In children with sleep terror, increased total CAP rate, increased mean duration of A phases, and reduced B phase duration was seen [28]. Increased microarousals preceded by electroencephalogram (EEG) slow-wave synchronization during NREM sleep are also described in patients with parasomnia [29]. In a spectral analysis study, patients with parasomnia had higher arousals especially during first NREM–REM sleep cycle [30]. Hence, increased instability of NREM sleep is seen in patients with parasomnia [26].

Clinical Features

Sleep terrors are the most dramatic of parasomnias. An episode typically starts with a loud scream associated with extreme fear and motor manifestations. There is intense autonomic stimulation with tachycardia, tachypnea, flushing of skin, perspiration, myadriasis, and increased muscle tone [3]. The child may sit up, hit the wall, may get out of bed or room. Child is unresponsive to the attempts to console and may become more agitated. If awakened, confusion and disorientation is seen. Sometimes

incoherent vocalizations are associated. Prolonged inconsolability may also be seen. Parents may describe it as the child being "possessed" by something. The child is usually amnestic to the events, but may have incomplete memory. In adults, recall for the content associated with sleep terror or sleepwalking was seen in 58–71 % of cases [31, 32]. In addition, violent behavior is reported in adults with sleep terror [33]. Reviewing cases with history of violence, Pressman [34] identified that violent behavior was provoked by close proximity of another person in 81 % of cases with possible sleep terror. Typical duration of events is around 10 min, but longer duration may also be seen [24, 35]. The episodes typically occur out of slow-wave sleep as abrupt arousals [36], during the first third of the night or within 1–3 h of falling asleep. As slow-wave sleep reduces with age, the prevalence of night terror also decreases [3, 26].

The international classification of sleep disorders (ICSD)-2 diagnostic criteria for sleep terror are as follows [3].

A sudden episode of terror occurs during sleep, usually initiated by a cry or a loud scream that is accompanied by autonomic nervous system and behavioral manifestation of intense fear.

One of the following associated features is present:

- Difficulty in arousing the person.
- Mental confusion when wakened from an episode.
- Amnesia for the episode.
- Dangerous or potentially dangerous episode.
- The disturbance is not explained by any other disorder, medication, or substance use.

Associated Features

Increased sleep problems are reported in children with sleep terrors. In one study, 56 % of children with sleep terrors had frequent arousals in one night [5]. Children with parasomnia have bedtime resistance, sleep onset delay, inappropriate sleep duration, and increased night waking [37]. It is, however, unclear if this is the cause or effect of parasomnia.

Other parasomnias are common in children with sleep terror. Ninety-two percentages of children with persistent sleep terror at age 6 years had somniloquy and 41 % of children with sleepwalking had sleep terrors [5]. Increased bruxism is also seen [37]. Sleep terror progressing to sleepwalking at a later age is reported [38]. Hypnogogic hallucination and nightmares can also occur with night terror [39].

There is conflicting evidence in adults with night terror related to comorbid psychiatric conditions [40]. Psychiatric illnesses are not shown to be associated with sleep terror in preschool age children [41]. However, in a study, 85 % of the teen age children with sleepwalking or sleep terrors had a psychiatric comorbidity. These included panic disorder, overanxious disorder, alcohol or cigarette use, suicidal ideation, and simple phobia. There were also increased fatigue, dysmenorrhea, and low mood in patients [42]. In another study, persistent sleep terrors at 6 years of age were

associated with separation anxiety [5]. In a Turkish study, more behavioral disturbance, adjustment problems, and learning difficulties were seen in children with parasomnia [6].

A few cases of sudden death associated with night terrors were reported in 1988 [43]. However, the description is not suggestive of night terrors based on current diagnostic criteria. In fact, a study suggested that it is common to overreport sleep terrors [13].

Differential Diagnosis

Nocturnal frontal lobe epilepsy (NFLE) can be confused as sleep terrors or other parasomnias [44]. In a study by Provini et al. [45], 100 cases of NFLE were reviewed. Among them, 34 % of the patients had personal history and 39 % had a family history in first-degree relative, suggestive of parasomnia. Hence, differentiation of nocturnal events is important for adequate treatment. Frequently, NFLE patients may have exclusively nocturnal seizures and video EEG may not be abnormal [45]. Seizures of NFLE are typically predominant in male, brief, highly stereotyped, occur multiple times in night, tend to cluster, occur mostly out of stage N2 sleep, and are typically associated with memory of the event [2, 46–49]. A validated frontal lobe epilepsy and parasomnias (FLEP) scale can also be used for differential diagnosis. The positive and negative predictive values are reported to be 0.91–1 and 1–0.91, respectively in two studies [50, 51].

Differentiating nightmares from sleep terrors may be confusing. Nightmares occur out of REM sleep, and are not associated with intense autonomic activity. The child is less vocal and easily arousable during the event. There is complete consciousness after the event and memory of the dream [41, 52].

Nocturnal panic attacks also occur once at night, within 1–3 h of falling asleep and associated with autonomic features of tachycardia, tachypnea, and diaphoresis. Daytime panic attacks are present and resemble the nocturnal events in almost all cases. Other differentiating features are lack of complex motor movement, recall of the event, and difficulty returning to sleep [48].

A few cases of cluster headache presenting as night terrors have been reported. History of the event, family history of headache, local as opposed to generalized autonomic features may help diagnose cluster headaches [53].

Evaluation

Detailed history is of prime importance, diagnostic tests are often not required. The history of screaming associated with autonomic arousal, inconsolability, and occurrence during the first third of the night may suggest the diagnosis. Family history of parasomnia is also important. Thorough physical examination should be performed

keeping in mind, the associated and precipitating factors, as well as differential diagnoses. In cases with unclear history, injurious behavior, multiple episodes in a night, or suspicion of associated or precipitating factors, polysomnography with extended montage video EEG may be performed. Video EEG may help to rule out nocturnal seizures and polysomnography to rule out obstructive sleep apnea (OSA) or PLMD. Increased awakenings and reduced sleep efficiency can be seen on polysomnography [28]. Increased delta activity prior to sleep terror events [54] and rhythmic and synchronous delta activity during sleep terror events may also be seen [55]. Sleep deprivation before polysomnography and auditory arousal during slow-wave sleep may be attempted to precipitate events. Psychological evaluation and evaluation for excessive daytime sleepiness may also be needed based on history [24]. Brain imaging is only suggested if clinically indicated.

Treatment

Behavioral Methods

In most cases, behavioral management may be enough to control the events. The parents should be reassured that the child will not have recollection of the event, and will grow out of it. Trying to awaken children from the episode may prolong the duration and severity of the episode, so it should be avoided. Safety of the child should be ensured during the events and the child should be put back to bed at the end of it. Children with violent behavior and risk of injury should be put to sleep in a safe environment [56, 57]. This may include padding the bed, moving mattress to the floor, putting gates, removing sharp objects from reach, and putting bells or bolts on doors.

Increasing sleep time may be an effective treatment as sleep deprivation may precipitate the events. This can be achieved by earlier bedtime, increasing or reintroducing naps, or later wake-up times.

In patients with frequent chronic sleep terrors, waking them 30 min prior to typical episode has been effective. Arousal right before the child goes into slow-wave sleep may lead to change in the sleep pattern and reduce or eliminate the episodes over a period of time [58–62].

Several case reports have suggested that hypnosis may be a treatment option [57, 63–66]. Anxiolytic effects of hypnosis have been suggested to reduce the frequency of sleep terrors in patients [67]. Other treatment options are psychotherapy and relaxation therapy [68].

Medications

Drug treatment is reserved for severe cases with violent behavior, frequent events, or cases refractory to above treatments. Medications that suppress slow-wave sleep such

as benzodiazepines have been suggested as treatment. There are limited randomized studies, but case reports and case series have suggested treatment options. Benzodiazepine drugs may stabilize sleep by reducing transition into N2 or N1 and may reduce slow-wave sleep [69]. Diazepam at 5–10 mg was efficacious in 3 cases and relapses following withdrawal were noted [70, 71]. In another four cases, diazepam 5–20 mg was effective and reduced slow-wave sleep [72]. In a case series, diazepam and clorazepate were effective with significant reduction in stage 4 sleep [73]. Midazolam at 15 mg dose, following and preceding placebo was shown to be effective in eliminating or decreasing night terrors episodes in 15 children [74]. It was shown to increase sleep time, reduce arousals, and improve subjective quality of sleep. Clonazepam at low doses is commonly used [69]. In a randomized study, in subjects treated with L-5-hydroxytryptophan, 93 % showed resolution or improvement at 1 month and 84 % at 6 months. Imipramine and desipramine have (shown to be) effective [68, 71, 75]. Tricyclic antidepressants block the reuptake of nor-epinephrine and 5-hydroxytryptamine [69]. Successful treatment of night terror with melatonin alprazolam, and paroxetine has been reported [76–79].

Treatment of Associated Conditions

Treatment of comorbidity is also imperative. OSA, RLS, and PLMD should be treated adequately. This by itself may improve sleep terrors [16]. Significantly reduced sleep terrors were seen in a study following adenoidectomy and tonsillectomy [80]. This is presumably due to treatment of OSA precipitating sleep terrors. Also, anxiety related to bedtime should also be addressed.

Confusional Arousals

Confusional arousals are common in infants and children. The episodes begin with moaning and progress to movements in bed, or thrashing [26]. Child appears confused and disoriented with eyes open or closed. Typical episode may last 5–15 min, but may last up to 40 min. Attempts to awaken the child may lead to prolongation of the events. Agitation and complex motor behavior may occur. There is diminished mentation and blunted responses to questions. No or limited memory of the event is seen the next morning [4, 81–84]. Confusional arousals due to forced arousals may lead to vigorous, highly resistive, and violent behavior lasting up to hours. Behaviors may be simple to complex and even sexual in nature.

The ICSD-2 criteria are as follows [3]:

- Recurrent mental confusion or confusional behavior occurs during and arousal or awakening from nocturnal sleeps or daytime naps.
- The disturbance is not better explained by another disorder, drug or substance.

Prevalence of 17 % in 3–13-years-old children and 3–4 % in 15 years or older have been reported [3]. In a study, lifetime prevalence of 10 % was reported [85]. Derry

et al. [2] evaluated 120 nocturnal events for semiology and conferred that, based on arousal behavior and duration of the events, confusional arousals, sleepwalking, and sleep terror are a spectrum of disorder from less to more severe. Confusional arousals may coexist with other parasomnias such as sleep terror or sleepwalking. Confusional arousals are reported with sleep talking [39].

Predisposing and precipitating factors are similar to sleep terrors, as discussed in previous sections. Cases have been reported with posterior hypothalamus, midbrain reticular area, or periventricular gray area lesions. However, in most cases, no structural pathology is found [3]. Confusional arousals in adolescents are associated with shift work, hypnogogic hallucination, smoking, bipolar disorder, and adjustment disorder [39]. Fifty-six percentages of adults reported a relatively recent stressful event [39]. Diagnostic testing is similar to listed above. Scheduled awakening, increasing sleep time, and avoiding consoling patients during an event are mainstay in the treatment of confusional arousals. Treatment with tricyclic antidepressant such as imipramine and clomipramine and low-dose clonazepam is beneficial [68].

Sleep inertia occurs during transition from sleep to wakefulness in morning. Since the clinical features are indistinguishable from confusional arousals, it is considered a subtype of confusional arousal. Similarly, complex sexual behaviors associated with arousals or "sexsomnias" are also considered a subtype of confusional arousals [3]. Along with both the subtypes, confusional arousals have legal and societal implications due to complex behaviors leading to violent, injurious, and sexual behaviors.

Practical Points

- Sleep terrors and confusional arousals are common in young children and occur out of slow-wave sleep.
- Sleep terrors are associated with separation anxiety and treatment of anxiety should be considered.
- In atypical cases, differentiation from nocturnal seizures should be done.
- Avoiding sleep deprivation, good sleep hygiene, and increasing sleep time are vital for treatment.
- Precipitating factors such as OSA, PLMD, and RLS are important in treatment of sleep terrors and confusional arousals.

Case Example

A 17-months-old female was referred to sleep clinic with nighttime awakenings. The mother described that the patient was moaning and crying in sleep, multiple times a night. Mother used to try to wait few minutes, but was ultimately going into the patient's room to console the patient. When she did try to console her, the patient

was not recognizing her and continued to cry. The episodes were occurring multiple times in night, lasting 30–60 min. Mother used to give milk bottle to the patient and then the patient returned to sleep.

The patient used to go to bed at 8.30–9.30 pm. She was falling asleep within 30–40 min. She resisted going to bed and required the mother to rock her and give milk bottle. She used to wake up at 5.30–6.30 am without difficulty on her own. She took two naps, but resisted that as well. She had history of occasional quiet snoring.

She was born at 40 weeks gestation by forceps delivery. The mother had preeclampsia during pregnancy. The patient was born healthy and discharged after regular stay at the newborn nursery.

Extended family health history revealed sleep apnea in great aunt and great grandmother, snoring in father, depression and anxiety in the mother, alcoholism in great grandparents, and substance abuse in uncle. History of nocturnal events was not present in the family.

Her physical examination was normal.

She had a polysomnography study with extended EEG. Typical events were captured on the study. During the events, initially she was moaning with her eyes closed, followed by a loud cry, agitation, and thrashing around in the bed. Her eyes were open in some of the episodes. Episodes lasted around 15 min and she went back to sleep after that. Figure 8.1 show EEG patterns during one of the events. The events occurred out of N3. The EEG showed rhythmic diffuse delta activity during the events. The polysomnography study did not show obstructive sleep apnea or periodic limb movement disorder.

She was diagnosed with confusional arousals. She was sent to behavioral psychologists for behavioral therapy. She continued to have episodes, so she was started on clonazepam 0.125 mg at bedtime. The mother was instructed to use gradual extinction method for sleep onset association problems and try not to console the patient during the episodes. She was only partially following these recommendations. On the last follow-up, she had reduction in the frequency of the events.

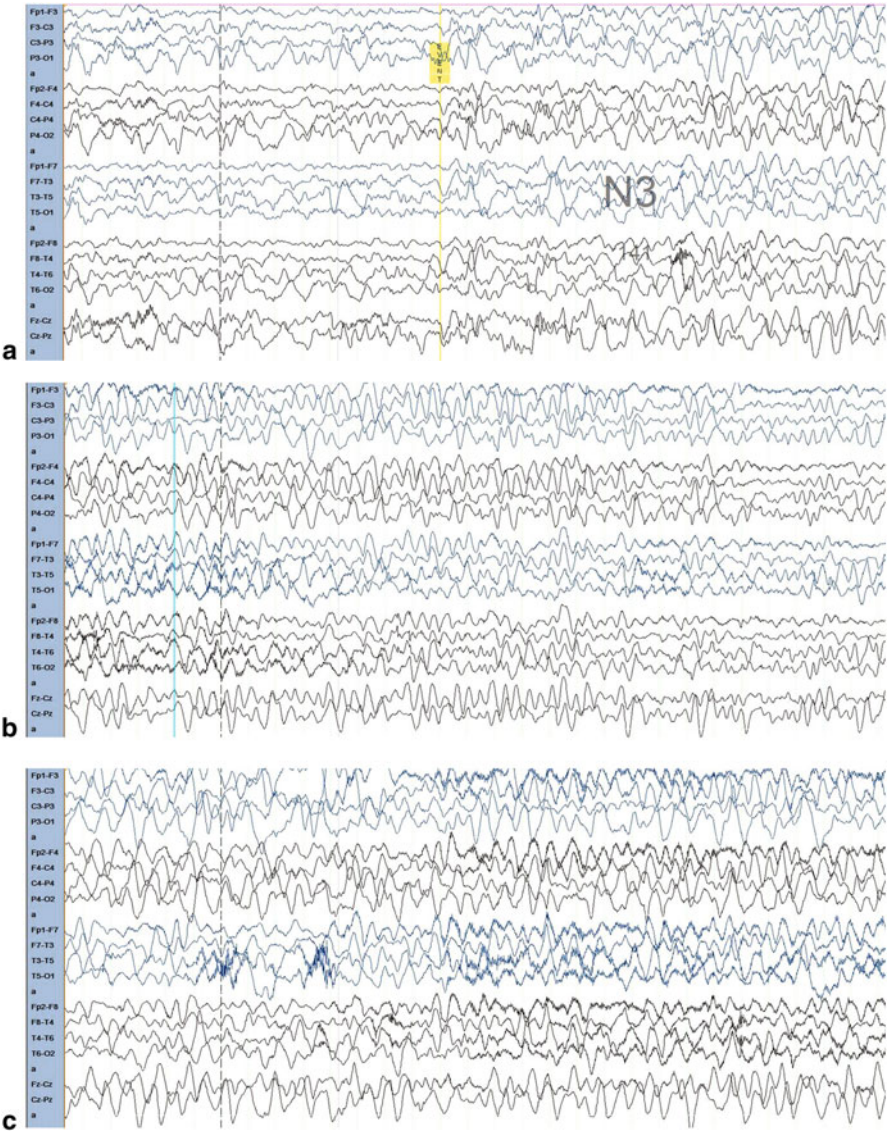


Fig. 8.1 a–c EEG showing confusional arousal in the patient. (The event onset represented by a *yellow line*.)

References

1. Laberge L, Tremblay RE, Vitaro F, Montplaisir J. Development of parasomnias from childhood to early adolescence. Pediatrics. 2000 Jul;106(1 Pt 1):67–74.
2. Derry CP, Harvey AS, Walker MC, Duncan JS, Berkovic SF. NREM arousal parasomnias and their distinction from nocturnal frontal lobe epilepsy: a video EEG analysis. Sleep. 2009;32(12):1637–44.

3. American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic & coding manual. 2nd ed. Westchester: American Academy of Sleep Medicine; 2005.
4. Mason TB 2nd, Pack AI. Pediatric parasomnias. Sleep. 2007 Feb;30(2):141–51.
5. Petit D, Touchette É, Tremblay RE, Boivin M, Montplaisir J. Dyssomnias and parasomnias in early childhood. Pediatrics. 2007;119(5):e1016–e25.
6. Agargun MY, Cilli AS, Sener S, Bilici M, Ozer OA, Selvi Y, et al. The prevalence of parasomnias in preadolescent school-aged children: a Turkish sample. Sleep. 2004 Jun 15;27(4):701–5.
7. Furet O, Goodwin JL, Quan SF. Incidence and remission of parasomnias among adolescent children in the Tucson Children's Assessment of Sleep Apnea (TuCASA) Study. Southwest J Pulm Crit Care. 2011 Jan 1;2:93–101.
8. Hällström T. Night terror in adults through three generations. Acta Psychiatr Scand. 1972;48(4):350–2.
9. Kales A, Soldatos CR, Bixler EO, Ladda RL, Charney DS, Weber G, et al. Hereditary factors in sleepwalking and night terrors. Br J Psychiatry. 1980 Aug;137:111–8.
10. Abe K, Oda N, Ikenaga K, Yamada T. Twin study on night terrors, fears and some physiological and behavioural characteristics in childhood. Psychiatr Genet. 1993;3(1):39–43.
11. Hublin C, Kaprio J. Genetic aspects and genetic epidemiology of parasomnias. Sleep Med Rev. 2003 Oct;7(5):413–21.
12. Abe K, Amatomi M, Oda N. Sleepwalking and recurrent sleeptalking in children of childhood sleepwalkers. Am J Psychiatry. 1984 Jun;141(6):800–1.
13. Hublin C, Kaprio J, Partinen M, Koskenvuo M. Limits of self-report in assessing sleep terrors in a population survey. Sleep. 1999 Feb 1;22(1):89–93.
14. Nguyen BH, Perusse D, Paquet J, Petit D, Boivin M, Tremblay RE et al. Sleep terrors in children: a prospective study of twins. Pediatrics. 2008 Dec;122(6):e1164–e7.
15. Sehgal A, Mignot E. Genetics of sleep and sleep disorders. Cell. 2011 Jul 22;146(2):194–207.
16. Guilleminault C, Palombini L, Pelayo R, Chervin RD. Sleepwalking and sleep terrors in prepubertal children: what triggers them? Pediatrics. 2003 Jan;111(1):e17–e25.
17. Kotagal S. Parasomnias in childhood. Sleep Med Rev. 2009;13(2):157–68.
18. Pilon M, Montplaisir J, Zadra A. Precipitating factors of somnambulism: impact of sleep deprivation and forced arousals. Neurology. 2008 Jun 10;70(24):2284–90.
19. Joncas S, Zadra A, Paquet J, Montplaisir J. The value of sleep deprivation as a diagnostic tool in adult sleepwalkers. Neurology. 2002 Mar 26;58(6):936–40.
20. Ghanizadeh A. Insomnia, night terror, and depression related to clonidine in attention-deficit/hyperactivity disorder. J Clin Psychopharmacol. 2008;28(6):725–6.
21. Prueter C, Luecke FG, Hoff P. Pavor nocturnus as a side effect of a single daily risperidone dose. Gen Hosp Psychiatry. 2005 Jul–Aug;27(4):300–1.
22. Pressman MR. Factors that predispose, prime and precipitate NREM parasomnias in adults: clinical and forensic implications. Sleep Med Rev. 2007 Feb;11(1):5–30; discussion 1–3.
23. Di Gennaro G, Autret A, Mascia A, Onorati P, Sebastiano F, Paolo Quarato P. Night terrors associated with thalamic lesion. Clin Neurophysiol. 2004 Nov;115(11):2489–92.
24. Zadra A, Pilon M. Non-rapid eye movement parasomnias: diagnostic methods. Sleep Med Clin. 2011;6(4):447–58.
25. Terzaghi M, Sartori I, Tassi L, Didato G, Rustioni V, LoRusso G et al. Evidence of dissociated arousal states during NREM parasomnia from an intracerebral neurophysiological study. Sleep. 2009 Mar;32(3):409–12.
26. Mahowald MW, Cramer Bornemann MA Kryger MH. Non-REM arousal parasomnias. In: Kryger M, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 5th ed. Philadelphia: Elsvier Saunders; 2011. p. 1075–82.
27. Mahowald MW, Cramer Bornemann MA, Schenck CH. State dissociation, human behavior, and consciousness. Curr Top Med Chem. 2011;11(19):2392–402.
28. Bruni O, Ferri R, Novelli L, Finotti E, Miano S, Guilleminault C. NREM sleep instability in children with sleep terrors: the role of slow wave activity interruptions. Clin Neurophysiol. 2008;119(5):985–92.

29. Halasz P, Ujszaszi J. Gadoros J. Are microarousals preceded by electroencephalographic slow wave synchronization precursors of confusional awakenings? Sleep. 1985;8(3):231–8.
30. Guilleminault C, Poyares D, Abat F, Palombini L. Sleep and wakefulness in somnambulism: a spectral analysis study. J Psychosom Res. 2001;51(2):411–6.
31. Fisher C, Kahn E, Edwards A, Davis DM, Fine J. A psychophysiological study of nightmares and night terrors. III. Mental content and recall of Stage 4 night terrors. J Nerv Ment Dis. 1974;158(3):174–88.
32. Oudiette D, Leu S, Pottier M, Buzare MA, Brion A, Arnulf I. Dreamlike mentations during sleepwalking and sleep terrors in adults. Sleep. 2009;32(12):1621–7.
33. Ohayon MM, Schenck CH. Violent behavior during sleep: prevalence, comorbidity and consequences. Sleep Med. 2010;11(9):941–6.
34. Pressman MR. Disorders of arousal from sleep and violent behavior: the role of physical contact and proximity. Sleep. 2007;30(8):1039–47.
35. Snyder DM, Goodlin-Jones BL, Pionk MJ, Stein MT. Inconsolable night-time awakening: beyond night terrors. J Dev Behav Pediatr. 2008;29(4):311.
36. Schenck CH, Pareja JA, Patterson AL, Mahowald MW. Analysis of polysomnographic events surrounding 252 slow-wave sleep arousals in thirty-eight adults with injurious sleepwalking and sleep terrors. J Clin Neurophysiol. 1998;15(2):159–66.
37. Mehlenbeck R, Spirito A, Owens J, Boergers J. The clinical presentation of childhood partial arousal parasomnias. Sleep Med. 2000 Oct 1;1(4):307–12.
38. Poblano A, Poblano-Alcalá A, Haro R. Sleep-terror in a child evolving into sleepwalking in adolescence. Case report with the patient's point of view. Rev Bras Psiquiatr. 2010;32(3):321–2.
39. Ohayon MM, Guilleminault C, Priest RG. Night terrors, sleepwalking, and confusional arousals in the general population: their frequency and relationship to other sleep and mental disorders. J Clin Psychiatry. 1999;60(4):268–76.
40. Szelenberger W, Niemcewicz S, Dabrowska AJ. Sleepwalking and night terrors: psychopathological and psychophysiological correlates. Int Rev Psychiatry. 2005;17(4):263–70.
41. Kales A, Soldatos CR, Kales JD. Sleep disorders: insomnia, sleepwalking, night terrors, nightmares, and enuresis. Ann Intern Med. 1987;106(4):582–92.
42. Gau SF, Soong WT. Psychiatric comorbidity of adolescents with sleep terrors or sleepwalking: a case-control study. Aust N Z J Psychiatry. 1999 Oct;33(5):734–9.
43. Melles RB, Katz B. Night terrors and sudden unexplained nocturnal death. Med Hypotheses. 1988;26(2):149–54.
44. Grigg-Damberger M. Neurologic disorders masquerading as pediatric sleep problems. Pediatr Clin North Am. 2004 Feb;51(1):89–115.
45. Provini F, Plazzi G, Tinuper P, Vandi S, Lugaresi E, Montagna P. Nocturnal frontal lobe epilepsy. A clinical and polygraphic overview of 100 consecutive cases. Brain. 1999 Jun;122 (Pt 6): 1017–31.
46. Tinuper P, Provini F, Bisulli F, Vignatelli L, Plazzi G, Vetrugno R, et al. Movement disorders in sleep: guidelines for differentiating epileptic from non-epileptic motor phenomena arising from sleep. Sleep Med Rev. 2007 Aug;11(4):255–67.
47. Derry C. Nocturnal frontal lobe epilepsy vs parasomnias. Curr Treat Options Neurol. 2012;14(5):451–63.
48. Derry CP, Duncan JS, Berkovic SF. Paroxysmal motor disorders of sleep: the clinical spectrum and differentiation from epilepsy. Epilepsia. 2006 Nov;47(11):1775–91.
49. Zucconi M, Ferini-Strambi L. NREM parasomnias: arousal disorders and differentiation from nocturnal frontal lobe epilepsy. Clin Neurophysiol. 2000 Sep;111(Suppl 2):S129–S35.
50. Manni R, Terzaghi M, Repetto A. The FLEP scale in diagnosing nocturnal frontal lobe epilepsy, NREM and REM parasomnias: data from a tertiary sleep and epilepsy unit. Epilepsia. 2008 Sep;49(9):1581–5.
51. Derry CP, Davey M, Johns M, Kron K, Glencross D, Marini C, et al. Distinguishing sleep disorders from seizures: diagnosing bumps in the night. Arch Neurol. 2006 May;63(5):705–9.
52. Fisher C, Kahn E, Edwards A, Davis DM. A psychophysiological study of nightmares and night terrors. I. Physiological aspects of the stage 4 night terror. J Nerv Ment Dis. 1973;157(2):75–98.

53. Isik U, D'Cruz OF. Cluster headaches simulating parasomnias. Pediatr Neurol. 2002 Sep;27(3):227–9.
54. Zadra AL, Nielsen TA. Topographical EEG mapping in a case of recurrent sleep terrors. Dreaming. 1998;8(2):67–74.
55. Zadra A, Pilon M, Joncas S, Rompré S, Montplaisir J. Analysis of postarousal EEG activity during somnambulistic episodes. J Sleep Res. 2004;13(3):279–84.
56. Gates D, Morwessel N. Night terrors: strategies for family coping. J Pediatr Nurs. 1989;4(1):48–53.
57. Wills L, Garcia J. Parasomnias: epidemiology and management. CNS Drugs. 2002;16(12): 803–10.
58. Durand VM, Mindell JA. Behavioral intervention for childhood sleep terrors. Behav Ther. 1999;30(4):705–15.
59. Lask B. Novel and non-toxic treatment for night terrors. BMJ. 1988 Sep 3;297(6648):592.
60. Lask B. Sleep disorders. "Working treatment" best for night terrors. BMJ. 1993 May 29; 306(6890):1477.
61. Tobin JD Jr. Treatment of somnambulism with anticipatory awakening. J Pediatr. 1993 Mar;122(3):426–7.
62. Frank NC, Spirito A, Stark L, Owens-Stively J. The use of scheduled awakenings to eliminate childhood sleepwalking. J Pediatr Psychol. 1997 Jun;22(3):345–53.
63. Howsam DG. Hypnosis in the treatment of insomnia, nightmares, and night terrors. Aust J Clin Exp Hypn. 1999;27(1):32–9.
64. Koe GG. Hypnotic treatment of sleep terror disorder: a case report. Am J Clin Hypn. 1989;32(1):36–40.
65. Kramer RL. The treatment of childhood night terrors through the use of hypnosis—a case study: a brief communication. Int J Clin Exp Hypn. 1989;37(4):283–4.
66. Ng BY, Lee TS. Hypnotherapy for sleep disorders. Ann Acad Med Singapore. 2008;37(8): 683–8.
67. Kennedy GA. A review of hypnosis in the treatment of parasomnias: nightmare, sleepwalking, and sleep terror disorders. Aust J Clin Exp Hypn. 2002;30(2):99–155.
68. Attarian H. Treatment options for parasomnias. Neurol Clin. 2010;28(4):1089–106.
69. Kotagal S. Treatment of dyssomnias and parasomnias in childhood. Curr Treat Options Neurol. 2012:1–20.
70. Glick BS, Schulman D, Turecki S. Diazepam (valium) treatment in childhood sleep disorders. A preliminary investigation. Dis Nerv Syst. 1971 Aug;32(8):565–6.
71. Mindell JA, Durand VM. Treatment of childhood sleep disorders: generalization across disorders and effects on family members. J Pediatr Psychol. 1993 Dec;18(6):731–50.
72. Fisher C, Kahn E, Edwards A, Davis DM. A psychophysiological study of nightmares and night terrors. The suppression of stage 4 night terrors with diazepam. Arch Gen Psychiatry. 1973;28(2):252–9.
73. Allen RM. Attenuation of drug-induced anxiety dreams and pavor nocturnus by benzodiazepines. J Clin Psychiatry. 1983;44(3):106–8.
74. Popoviciu L, Corfariu O. Efficacy and safety of midazolam in the treatment of night terrors in children. Br J Clin Pharmacol. 1983;16(Suppl 1):97S–102S.
75. Bruni O, Ferri R, Miano S, Verrillo E. L-5-Hydroxytryptophan treatment of sleep terrors in children. Eur J Pediatr. 2004 Jul;163(7):402–7.
76. Cameron OG, Thyer BA. Treatment of pavor nocturnus with alprazolam. J Clin Psychiatry. 1985 Nov;46(11):504.
77. Wilson SJ, Lillywhite AR, Potokar JP, Bell CJ, Nutt DJ. Adult night terrors and paroxetine [3]. Lancet. 1997;350(9072):185.
78. Jan JE, Freeman RD, Wasdell MB, Bomben MM. A child with severe night terrors and sleepwalking responds to melatonin therapy. Dev Med Child Neurol. 2004 Nov;46(11):789.
79. Lillywhite AR, Wilson SJ, Nutt DJ. Successful treatment of night terrors and somnambulism with paroxetine. Br J Psychiatry. 1994 Apr;164:551–4.
80. Mindell JA. Sleep disorders in children. Health Psychol. 1993 Mar;12(2):151–62.

81. Hopkins B, Glaze D. Disorders of arousal in children. Pediatr Ann. 2008;37(7):481–7.
82. Provini F, Tinuper P, Bisulli F, Lugaresi E. Arousal disorders. Sleep Med. 2011;12(Suppl 2):S22–S6.
83. Davey M. Kids that go bump in the night. Aust Fam Physician. 2009;38(5):290–4.
84. Avidan AY, Kaplish N. The parasomnias: epidemiology, clinical features, and diagnostic approach. Clin Chest Med. 2010;31(2):353–70.
85. Bjorvatn B, Gronli J, Pallesen S. Prevalence of different parasomnias in the general population. Sleep Med. 2010 Dec;11(10):1031–4.

Part III
Clinical Characteristics of Sleep-Wake Transition Disorders

Chapter 9
Sleep Starts and Sleep Talking

Shelly K. Weiss

Introduction

Sleep starts (hypnic jerks) and sleep talking (somniloquy) are both common physiologic phenomenon that occur during sleep in healthy children and adults. They are not classified as parasomnias in the most recent international classification of sleep disorders (ICSD 2) [1]. However, it is important to include a review of sleep starts and sleep talking in this textbook about parasomnias due to the possible confusion between these entities. Sleep starts and/or sleep talking may be a source of concern to parents, partners, or others who are watching or listening to a child or bed-partner during sleep. Neither of these phenomena disturb sleep; hence they should not have any daytime consequences. It is important to recognize and properly diagnose these parasomnias in healthy children, adolescents, and adults to avoid unnecessary anxiety as either sleep phenomena may be misinterpreted as being pathologic.

Sleep talking can also be disturbing to individuals sleeping in close proximity simply because it disturbs their own sleep, or the observer may misinterpret the talking as being pathologic. Sleep starts can be disturbing as they may be confused with sleep-onset seizures. Either phenomenon can coexist with other mental or physical health or other sleep disturbances. Proper diagnosis and where appropriate, reassurance can relieve parental and/or bed-partner's anxiety and avoid costly and time-consuming evaluations that are often unnecessary. Health care providers must be able to differentiate this phenomenon from other worrisome sleep disturbances, and be able to determine when other parasomnias or sleep disorders such as sleep-related breathing disorders may coexist, thus, requiring further evaluation.

S. K. Weiss (✉)
Division of Neurology, Department of Pediatrics, Hospital for Sick Children,
555 University Avenue, Toronto, ON M5G 1X8 Canada
e-mail: shelly.weiss@sickkids.ca

University of Toronto, Toronto, ON M5S 1A1 Canada

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_9,

Classification of Sleep Starts and Sleep Talking (ISCD II)

In the previous ISCD revised (2001), sleep starts and sleep talking were classified as parasomnias. In the current classification of sleep disorders, (the third ISCD is currently undergoing revisions, but is not available at the time of the publication of this textbook), there is a section entitled "Isolated Symptoms, Apparently Normal Variants and Unresolved Issues." This group is described as "sleep-related symptoms that either lie at the borderline between normal and abnormal sleep or that exist in the continuum of normal to abnormal events in sleep" [1].

The symptoms that are listed in this section are:

- Long sleeper,
- Short sleeper,
- Snoring,
- **Sleep talking,**
- **Sleep starts (hypnic jerks)**,
- Benign sleep myoclonus of infancy,
- Hypnagogic foot tremor and alternating leg muscle activation during sleep,
- Propriospinal myoclonus at sleep onset, and
- Excessive fragmentary myoclonus.

Sleep Starts

Sleep starts are also referred to as hypnic or hypnagogic jerks. Hypnagogic refers to a phenomenon that occurs at sleep onset. Another less common synonym for sleep starts is predormital myoclonus. All of these terms represent a sleep phenomenon which is a normal accompaniment of sleep that frequently occur in normal people and at any age. Although rare, "when sleep starts or hypnic jerks are frequent, intense or repetitive, they may lead to sleep-onset insomnia" [1].

Sleep starts are sudden, brief contractions of the legs, sometimes also involving the arms and head that occur at sleep onset. They are described as bilateral, sometimes asymmetric, brief body jerks lasting less than 1 s [2]. They may affect only one or two limbs or parts thereof [3], and usually the trunk and extremities are involved in the jerk simultaneously. They usually occur in isolation, in a spontaneous form, or evoked by sensory stimuli [4]. Sleep starts are considered a physiologic, rather than a pathologic sleep phenomenon that occurs during sleep–wake transition. They are an almost universal component of the sleep-onset process [2]. Sleep starts are frequently associated with a perception of falling or a sensory flash or a visual hypnagogic dream or hallucination [1]. The sleep start may result in the individual wakening with an awareness of the event, or in the case of an individual who is cosleeping, it may not waken the person with the sleep start, but disturb the bed-partner's or parent's sleep.

Sleep starts can be associated with autonomic activation with transient tachycardia, tachypnea, and sudomotor activity, and sometimes with a peculiar sensory

feeling of "shock" or "falling into the void", i.e., sensory sleep starts [5, 6]. In addition to being associated with this perception of falling, a sleep start may also be accompanied by a sensory flash or a visual hypnagogic dream or hallucination [1]. Sleep starts may also be accompanied by an auditory sound such as an utterance [8]. The sleep start does not have to have a motor component, or body jerk, but may be only a brief sensory experience [9]. There is also a related disturbance that occurs at sleep onset and is equivalent to a hypnic jerk, but may be alarming to the individual experiencing it called an "exploding head syndrome." This is an experience of a sudden fleeting dramatic sensation (e.g., loud bang or flash of light) that occurs at wake–sleep transition [10]. This has been described in adults and although it is reported that it can occur at any age, most reported cases are older than 50 years of age [11].

In the normal state, sleep starts can occur in a brief cluster, possibly due to the physiological oscillation between sleep and wakefulness during the period of falling asleep [12]. If an EEG is done at the time of a sleep start, it will be seen to either coincide with sleep onset and/or with a K-complexes or an EEG arousal which is indicated with a reappearance of alpha activity [5]. It is hypothesized by Vetrugno and Montagna [5] that the cause of a sleep start is due to descending volleys within the pyramidal tract at the transition from wakefulness to sleep.

Sleep starts can be triggered by fatigue, emotional stress, sleep deprivation, vigorous exercise, and stimulants such as caffeine and nicotine [4, 5, 13]. In pediatric populations, there may be confusion between when a child is having sleep starts versus myoclonic seizures at sleep onset, particularly in children with comorbid neurologic conditions

Case of a Child with Sleep Starts

The parents bring their 3-year-old daughter, Sara to the pediatrician as they are concerned with the sudden brief movements of her arms and legs, which they see when she is falling asleep. This does not happen every night, and Sara's parents cannot determine any particular precipitating factor that would make it more likely to occur. To her parents, it looks like she has a sudden "shock." Sometimes after the movement, she wakes up and seems startled, but usually settles back to sleep. Sara is a healthy preschooler with normal development and is on no medication. She seems well-rested during the day and takes a 1 h nap every day after lunch. She has never been a great sleeper and the only way that her parents can get her to go to sleep is if they lie down with her at bedtime. Sometimes, she wakes at night and comes into her parents' room and gets into their bed where she falls asleep quickly. Often parents are so tired, they just fall back asleep when this happens, and they do not take her back to her own bedroom. Sara's parents are concerned that these movements could be related to her poor sleep habits.

Upon completion of this chapter, it will be evident that Sara's parents are describing "sleep starts" or "hypnic jerks." This sleep phenomenon, seen during transition from wake to sleep is a normal physiologic occurrence in healthy children and adults.

It is not related to, or exacerbated by Sara's need to fall asleep with her parents at sleep onset. However, it would be more commonly reported by families who cosleep, or are together at sleep onset, or reported by older children, teenagers, and adults who will be aware and able to describe experiencing sleep starts.

Prevalence

Sleep starts are an essentially universal component of the sleep-onset process and the prevalence is around 60–70 % in the general adult population [3]. It is also highly prevalent in children, but it is more difficult to establish an accurate estimate of prevalence in pediatrics as young children may not be able to self-report and studies will have inherent bias based on the frequency of cosleeping in a population. Two studies reporting on the frequency of sleep starts in children show similar results. In a population-based study of young children in Finland, parents reported that about half (47 %) had been observed to startle or jerk part of the body while falling asleep [14]. In a second study in Singapore, of children 2–19 years, sleep starts were reported in 24–35 % of children and teenagers [15].

The following are the diagnostic criteria of sleep starts (hypnic jerks) in the ICSD 2 [1]:

1. The patient complains of sudden brief jerks at sleep onset, mainly affecting the legs or arms
2. The jerks are associated with at least one of the following:
   (a) A subjective feeling of falling,
   (b) A sensory flash, and
   (c) A hypnagogic dream
3. The disorder is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.

Differential Diagnosis

The differential diagnosis of repetitive sleep starts includes other repetitive motor manifestations during sleep [12]. This may include seizures, particularly epileptic spasms, periodic limb movements of sleep, and propriospinal myoclonus, the latter being primarily seen in individuals with spinal cord pathology. Other motor phenomena which may be confused with sleep starts are listed in Table 9.1 and described in the next subsections.

Table 9.1 Motor phenomena that may be confused with simple sleep starts

Benign sleep myoclonus
Nocturnal leg cramps
Periodic limb movements of sleep
Excessive sleep starts
Epileptic spasms and other myoclonic epilepsies
Propriospinal myoclonus
Hyperekplexia
Psychogenic myoclonus

Benign Sleep Myoclonus

The syndrome of benign sleep myoclonus is seen in infants. There are benign myoclonic syndromes and malignant neonatal and childhood-onset myoclonic epilepsies that are generally easy to distinguish from sleep starts. The benign myoclonic syndromes include benign sleep myoclonus in infancy (BSMI), benign myoclonus of early infancy (BMI), and benign neonatal sleep myoclonus (BNSM) [16]. BMI should be easy to differentiate from sleep starts as in this disorder, which starts between 3 and 15 months of age, the myoclonic jerks occur during the waking state. BNSM and BSMI are the same disorder, distinguished by the onset which is either in the neonatal or infancy period [16]. Both disorders are a nonpathologic type of myoclonus that is characterized by the occurrence of repetitive myoclonic jerks during nonrapid eye movement (NREM) sleep in the healthy neonates or infants. Infants with BNSM are usually born following an unremarkable prenatal and perinatal course and normal delivery and early neonatal course. The myoclonic jerks may start on the first day of life, or in the first few weeks. The jerks always stop with awakening. The jerks are usually synchronous and generalized, although there may be more involvement of the arms than the legs. As these myoclonic jerks occur during NREM sleep, it should be easy, by history of the description of the event, the age of the infant, the termination of the myoclonus when the child is wakened, to differentiate these benign entities from epilepsy and from simple sleep starts.

Nocturnal Leg Cramps

Nocturnal leg cramps can be a problem for children or adults. In the pediatric or adult patient, they would be unlikely to be confused with sleep starts. In pediatrics, nocturnal leg cramps (commonly called “growing pains”) occur in up to one-third of children at some time during childhood [17] and are often associated with sleep. Growing pains are severe, generally bilateral lower extremity pains. Growing pains are easily differentiated from sleep starts as the former are painful and the latter are not. In addition, leg cramps are relieved with stretching or massage, application of heat or movement, another distinct feature from sleep starts. In adults, nocturnal leg cramps which are also called “rest cramps” are “painful involuntary muscle contractions, typically in the legs or feet that occur during prolonged rest and often disrupt sleep” [18]. They are reported to be common in older adults with prevalence

from 37 to 50 % [19, 20]. Nocturnal leg cramps may be seen in adults with a number of predisposing conditions (e.g., neurologic, endocrine, metabolic, vascular, and congenital/hereditary or medications or toxins [21, 22].

Periodic Limb Movements of Sleep

Periodic limb movements are "periodic episodes of repetitive and highly stereotyped limb movements that occur during sleep" [11]. A careful history should be adequate to differentiate periodic limb movements of sleep (PLMS) from sleep starts. The muscle contractions of PLMS are easily differentiated from a hypnic jerk as they last much longer, involve mainly the lower extremities, and occur within sleep. The duration of movement is typically between 1.5 and 2.5 s and varies in intensity from slight extension of the great toe to a triple flexion response of the leg. Other tonic and myoclonic patterns are less frequently observed and arms are involved in only a minority of cases [23]. In addition, PLMS will occur throughout the night, although the intensity and frequency lessens with deeper sleep. They are more pronounced in NREM stage 1 and 2 of sleep, but may persist in a reduced manner in REM sleep. Therefore, these movements are seen throughout the night, in contrast to sleep starts seen at wake–sleep transitions. In addition, the characteristics of PLMS are markedly different from sleep starts as they "do not look like startles, are not a massive movement and are not elicited by acoustic stimulation" [12].

Excessive Sleep Starts

Excessive sleep starts have only been reported very rarely in children. It is important to differentiate video EEG recordings of a child with sleep-onset seizures from excessive sleep starts as both of these problems have been reported to occur in children with epilepsy [24]. Excessive sleep starts consist of clusters that last from a few to 15 min with the duration of each muscle contraction lasting from 500 ms to 5 s. On the simultaneous EEG, no corresponding ictal pattern is observed and often an arousal follows the jerks [12]. A case series of three children with excessive sleep starts all had a diagnosis of ongoing or previous epilepsy. The authors of this small series of children suggest that the prone position is recommended to parents to diminish this phenomenon rather than use of pharmacotherapy. It is proposed that the prone position may be of benefit to decrease the chance of the arousal caused due to the movement. When pharmacotherapy is needed, the authors recommend benzodiazepine as the first choice [12].

Epileptic Spasms and Other Myoclonic Epilepsies

Another pediatric problem that should be easily differentiated from sleep starts in children includes infantile spasms (West syndrome) and other myoclonic epilepsies. These epilepsy syndromes should be easily differentiated from those with sleep starts

or hypnic jerks by a careful history and physical examination. A child with sleep starts will have normal development, no developmental regression, and a normal neurologic examination. An EEG done during a hypnic jerk will be normal and show ictal or interictal abnormalities in a child with an epileptic myoclonus associated with sleep.

Propriospinal Myoclonus

Propriospinal myoclonus is a rare disorder characterized by axial flexion or extension myoclonic jerks, which are produced by activation of spinal segments that spread rostrally or caudally [25]. The jerking arises from an axial muscle (in the neck, chest, or abdomen) and then spreads rostrally or caudally supposedly along propriospinal pathways intrinsic to the cord [25]. It occurs at sleep onset and can lead to sleep-onset insomnia. This is different from spinal myoclonus where the jerks (myoclonus) that are experienced by the subject occur in muscles that are innervated by only a few spinal segments.

Propriospinal myoclonus propagates both proximally and distally at a rate of 3–11 m/s by means of propriospinal pathways. The underlying mechanism is thought to be hyperactivity of spinal inhibitory circuits, resulting in rhythmic spinal discharge [26]. The myoclonus is often stimulus sensitive and typically increases when the person is supine [25]. The cause can be idiopathic or it can occur after spinal cord trauma or other spinal cord pathology (e.g., malignancy, ischemia, inflammatory myelopathy, infection, and has also been reported following epidural anesthesia, toluene toxicity, and in one case report, following a single exposure to inhaled cannabis) [27]. The clinical correlates described with propriospinal myoclonus include worsening in the lying position and during wake–sleep transitions with the person feeling a premonitory sensation [28].

Another rare condition described in a letter to the editor was a 34-year-old man with a mitochondrial encephalomyopathy who had sleep-onset insomnia secondary to excessive fragmentary hypnic myoclonus [29]. If a patient is considered to have either propriospinal myoclonus or excessive fragmentary hypnic myoclonus (both rare conditions), then further detailed investigations with video-polysomnographic recordings including extensive EMG monitoring would be needed to confirm this diagnosis.

Hyperekplexia

Hyperekplexia is a rare hereditary or sporadic disorder with excessive startle responses. Children who are affected develop generalized stiffness beginning in infancy and exaggerated myoclonic startle reactions [30, 31]. One of the genetic causes of the hereditary form can be from mutations in the gene encoding the glycine receptor

(GLRA1) on chromosome 5. Children with this disorder should be easily differentiated from healthy children with simple sleep starts both by history and physical examination.

Psychogenic Myoclonus

Psychogenic myoclonus, a condition that may present in adult patients, may be similar in presentation to propriospinal myoclonus. The clinical clues that may help to separate the two include the former having a variable muscle pattern, distractibility, preexisting psychiatric history, and/or multiple somatizations [32]. This should be easily differentiated from simple sleep starts by history.

Evaluation

In most cases, the recognition and diagnosis of hypnic jerks is straightforward. The evaluation must include:

- Experienced or observed during sleep onset or transitions during sleep, but not in wakefulness.
- Frequency, duration.
- A description of the event by the patient or observer may be useful.
- If the occurrence is in a pediatric patient, there should also be a history of normal developmental milestone with absence of plateau or regression.
- Normal physical examination including normal neurologic examination.

Further Evaluation

The following algorithm outlines the evaluation of an individual with sleep starts (Fig. 9.1).

Treatment

Usually no treatment is necessary, other than reassurance for the individual and his parent (in the case of a pediatric patient) or the spouse/bed-partner (in the case of an adult patient). In the adult subject with excessive sleep starts which were refractory and caused sleep-onset insomnia, it was recommended in one study to treat with either a benzodiazepine (usually clonazapam) or short-acting hypnotic medication [2]. Prior to consideration of pharmacotherapy in a child, adolescent, or adult with

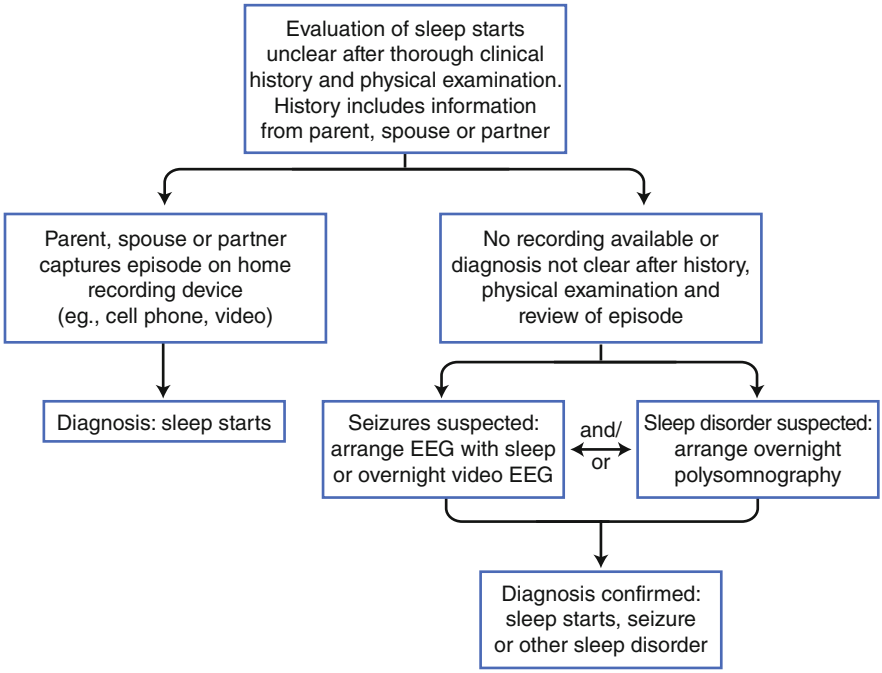


Fig. 9.1 Evaluation of sleep starts

unusual, refractory, or recurrent sleep starts causing sleep-onset insomnia, a referral to a sleep specialist would be warranted.

Table 9.2 outlines the semiological features of nocturnal simple motor phenomena.

Sleep Talking

Sleep talking or somniloquy is a very common phenomenon. It is generally felt to be frequent in children and teenagers, and can persist, but less frequently into adulthood. It is not a disorder, but a physiologic phenomenon of sleep. Other terms which are used to describe sleep talking include utterances, moans, and verbalizations. Sleep talking as defined by the ICSD 2 as follows: "Sleep talking is usually reported by the bed partner or someone sleeping in the same room or sleeping area as the affected individual. The sleep talker is rarely aware of his or her sleep talking" [1].

Sleep talking is usually brief and infrequent, but can range from a person making a few sounds during sleep that are brief and unintelligible to full phrases with understandable content or even frequent and long speeches which sound hostile or angry [13]. It can occur at various times during sleep, often at sleep–wake transitions, and can occur in either NREM or REM stages of sleep. It is only disturbing

Table 9.2 Semiological features of nocturnal simple motor phenomena. (From Tinuper et al. [2] reprinted with permission from Elsevier)

Phenomena	Features
Sleep starts	Usually a single, brief, and isolated contraction of the body or one or more body segments during drowsiness often associated with a perception of falling
Propriospinal myoclonus at sleep onset	Quasiperiodical jerks arising from an axial muscle spreading up and down during relaxed wakefulness suppressed by mental and sensory stimulation
Excessive fragmentary myoclonus	Arrhythmic, asynchronous, asymmetric twitches that do not cause gross movement across a joint space usually throughout the night
Periodic limb movements during sleep	Repetitive, highly stereotyped limb movements (typically extension of the big toe) in a sequence of four or more movements, lasting from minutes to hours, more frequent during stage 2 NREM sleep
Oromandibular myoclonus	Nocturnal myoclonic jerks involving only the muscles of the face and jaw

to others—bed partners or parents/siblings cosleeping, room sharing with a child. It may be disturbing due to the noise or the content of the utterances. There is interest among psychiatrists regarding the analysis of dreams and sleep talking; however, a review of the psychiatric literature on this topic is beyond the scope of this chapter. Usually, no evaluation or treatment is needed for an individual who talks in his/her sleep.

Case of a Child with Sleep Talking

Tom is a healthy 6-year-old boy who is brought by his parents to the pediatrician with concerns about sleep talking. The family lives with their extended relatives in a home where Tom and his two brothers share a bedroom. Tom is doing well in his grade 1 class, has no behavioral problems, and parents do not have any concerns about his health. He also seems very well-rested during the day. Since he was 3 years old, he has the habit of talking in his sleep. This can occur any time during the night. It is his older brother who is most bothered by it. His brother says that Tom usually says a few words, but they do not always make sense and sometimes are mumbled and incomprehensible. When Tom is sleep talking, he does not respond to his brother when questioned, and he does not remember the talking in the morning. His parents notice that when he has a fever with an intercurrent illness, he is more likely to talk in his sleep.

Table 9.3 Studies reporting the prevalence of sleep talking in childhood.

Country	Age (years)	Number of subjects (approximate)	Results (% of age)	Reference
Canada	3–13	1,400	55	[34]
USA	6–10	500	23	[36]
Brazil	3–10	2,000	50	[37]
Sweden	6–10	1,400	42	[36]
Finland	3–6	1,000	55	[14]
China	6–10	500	23	[35]
India	3–10	100	14.6	[33]

Upon completion of this chapter, it will be clear that children and adults sleep talk and this is a normal phenomenon and a common parasomnia. As illustrated in this case, often sleep talking persists throughout childhood and it is less common, but still frequently reported in adults. The person who is sleep talking is not disturbed by it, and does not remember this parasomnia in the morning, but it can be disturbing to others who are sleeping in close proximity.

Prevalence

The prevalence of sleep talking has been mainly reported in pediatric sleep studies. In the pediatric literature, there are studies from different countries of the prevalence or incidence of sleep talking, mainly by parent report or questionnaire surveys and collected retrospectively. A sample of the studies done reporting on the prevalence (Canada, USA, Brazil, Sweden, Finland, China and India) is outlined in Table 9.3. The prevalence in these different studies is influenced by cultural and environmental differences in homes and sleeping practices. In the research that is available evaluating the prevalence, it appears to occur at least once per year in about 50 % of children (Table 9.3) [14, 34, 37]. There are few population-based studies to estimate the prevalence of sleep talking in adults. One population-based cross-sectional study of adults older than 18 years from Norway reports lifetime and current prevalence as 66.8 and 17.7 % [38].

Persistence of Sleep Talking

In the longitudinal population-based study in Canada, where the cohort of > 1,400 children were followed to 13 years, it was reported that 52 % of the 437 children identified by parent report to have sleep talking, continued to sleep talk beyond the age of 13 years [34]. The incidence may decrease with childhood, but remains a common

occurrence in adults [39]. In both adult and pediatric populations, it is usually reported to occur once monthly or less frequently in the majority of individuals.

There is no gender difference or socioeconomic difference reported for sleep talking in children [37, 40]. It would be evident that when the incidence of sleep talking is determined by parental report, cultural and environmental practices, as well as the sleep habits of the adults will be important in how often this is reported. In countries where cosleeping is common, or there is more crowding or smaller homes, the incidence of sleep talking will be reported with increased frequency [35].

Sleep talking can occur in isolation or with other sleep-related disorders, or other physical or mental health comorbid conditions. In an adult population, sleep talking may be loud, emotional or profane, and accompany rapid eye movement behavior disorder (RBD). In children and adults, sleep talking may coexist with other parasomnias such as somnambulism, sleep terrors, or other sleep disorders such as sleep-related breathing disorders. A longitudinal study in children reported that somniloquy, sleep walking, and night terrors are often reported together [34]. Another pediatric study in Hong Kong reported that among other comorbidities, sleep talking was especially common in children with sleep bruxism [41].

Children with obstructive sleep apnea are more likely to sleep talk as well as have other sleep disturbances. A large population-based study was reported using parent questionnaire to determine the frequency of sleep talking, in addition to polysomnography to evaluate sleep disordered breathing in 480 children aged 6–11 years in the USA. In this study, school-aged children with sleep disordered breathing were more likely to have a number of sleep disturbances (enuresis, somnambolism) in addition to a statistically significant difference in sleep talking (18.3 % versus 9.0 %) [42]. Another study done in Germany with retrospective parent questionnaire also reported that children who were habitual snorers were at increased risk for sleep–wake transition disorders (e.g., rhythmic movements, hypnic jerks, sleep talking, and bruxism) [43].

When specific pediatric populations are evaluated to determine the coexistence of sleep talking with other comorbidities, e.g., headaches, the frequency of sleep talking was found to be very common. A study of the frequency of sleep talking and other sleep disorders in children with headaches aged 8–16 years was done in Poland [44]. In this study, sleep talking was more frequent (48 %) in children 8–16 years of age with headaches compared with 38 % in the control group. It was not reported if more children with headaches coslept, which would increase reporting of sleep talking in this study.

Evaluation of Sleep Talking

Sleep talking is usually a benign occurrence that requires no investigation or treatment, other than reassurance to the individual, (and in the case of a child, reassurance to the parent) that this is a frequently reported, normal sleep phenomenon. It may be precipitated by factors unrelated to sleep, e.g., febrile illness, mental health conditions such as anxiety or stress, or may be exacerbated by sleep deprivation or coexist

with other sleep disorders such as other parasomnias or sleep-related breathing disorders [13]. Even when sleep talking persists into adolescence or adulthood, if it is seen in an otherwise healthy well-rested individual, no treatment other than reassurance of the benign nature of this phenomenon is needed.

Sleep-Related Groaning (Catathrenia)

There is another phenomenon, which is similar but a different phenomenon to sleep talking called sleep groaning or catathrenia. Catathrenia may be confused with sleep talking. This is described as a chronic, unusual expiratory groaning noise that occurs during sleep, which can occur nightly [45, 46]. It has been reported to be more common in the second half of the night, mainly during REM sleep [2]. In adults reported to have groaning, it can last from 2 to 49 s and can be repeated in clusters, recurring many times per night [2]. It is a sound made during expiration and the patient does not have any respiratory distress, abnormal oxygen saturation, or motor phenomenon at the same time. The person is also not aware of this noise made during sleep. It is important to differentiate an individual with catathrenia from sounds which may occur during a nocturnal seizure.

Conclusions

Sleep starts (hypnic jerks) and sleep talking (somniloquoy) are both classified in the current ISCD II under the category of "Isolated symptoms, apparently normal variants and unresolved issues" [1]. Sleep starts and sleep talking are common, normal, physiologic experiences that occur both during childhood and throughout adult life. The true prevalence of sleep talking during childhood may be underestimated due to reporting of this phenomenon being dependant on observation during sleep by a parent or caregiver. Children and adults who experience either sleep starts and/or sleep talking may have some awareness of the occurrence of these phenomenon if an arousal occurs following the episode. However, neither phenomenon, in the normal physiologic state should disrupt sleep or lead to daytime sleepiness or other daytime consequences. Often, reassurance of the benign nature of sleep starts or sleep talking is all that is required. It is important for the physician to be able to differentiate these phenomenon from parasomnias or other diagnosis such as nocturnal seizures. It is also important to recognize pediatric and adult patients where the diagnosis is not clear, when there is unexplained daytime consequences, or when recurrent sleep starts lead to sleep-onset insomnia. In these rare cases, referral to a sleep specialist for further investigations is warranted.

Practical Points

- Sleep starts are also referred to as hypnic jerks, hypnagogic jerks, and predormital myoclonus.
- Sleep talking is also called somniloquy.
- Both sleep starts and sleep talking are common physiologic phenomenon.
- Both commonly occur during sleep in healthy children and adults.
- Both may be a source of concern—sleep starts if repetitive, may lead to sleep-onset insomnia or be misinterpreted for seizures or pathologic conditions—sleep talking may be disturbing to individual(s) sleeping in close proximity.
- The individual (child or adult) who experiences either phenomenon should not have daytime fatigue or other daytime consequences.
- Either disturbance can coexist with other mental or physical health or other sleep disorders.
- Health care providers must be able to differentiate these phenomenon from pathologic conditions that require further evaluation.

References

1. American Academy of Sleep Medicine. International classification of sleep disorders: diagnostic & coding manual. 2nd ed. Westchester: American Academy of Sleep Medicine; 2005.
2. Tinuper P, Provini F, Bisulli F, Vignatelli L, Plazzi G, Vetrugno R, et al. Movement disorders in sleep: guidelines for differentiating epileptic from non-epileptic motor phenomena arising from sleep. Sleep Med Rev. 2007;11(4):255–67.
3. Montagna P. Sleep-related non epileptic motor disorders. J Neurol. 2004;251(7):781–94.
4. Freedom T. Sleep-related movement disorders. Dis Mon. 2011;57(8):438–47.
5. Vetrugno R, Montagna P. Sleep-to-wake transition movement disorders. Sleep Med. 2011;12(Suppl 2):S11–S6.
6. Sander HW, Geisse H, Quinto C, Sachdeo R, Chokroverty S. Sensory sleep starts. J Neurol Neurosurg Psychiatry. 1998;64(5):690.
7. Shprecher D, Silberstein H, Kurlan R. Propriospinal myoclonus due to cord compression in the absence of myelopathy. Mov Disord. 2010;25(8):1100–1.
8. Oswald I. Sudden bodily jerks on falling asleep. Brain. 1959;82:92–3.
9. Sander HW, Geisse H, Quinto C, Schdeo R, Chokroverty S. Sensory sleep starts. N Neurol Neurosurg Psychiartry. 1998:64:690.
10. Stores G. Aspects of parasomnias in childhood and adolescence. Arch Dis Child. 2009;94(1):63–9.
11. Green MW. The exploding head syndrome. Curr Pain Headache Rep. 2001;5(3):279–80.
12. Fusco L, Pachatz C. Cusmai R, Vigevano F. Repetitive sleep starts in neurologically impaired children: an unusual non-epileptic manifestation in otherwise epileptic subjects. Epileptic Disord. 1999;1(1):63–7.
13. Avidan AY. Parasomnias and movement disorders of sleep. Semin Neurol. 2009;29(4):372–92.
14. Simola P, Niskakangas M, Liukkonen K, Virkkula P, Pitkäranta A, Kirjavainen T, et al. Sleep problems and daytime tiredness in Finnish preschool-aged children-a community survey. Child Care Health Dev. 2010;36(6):805–11.
15. Mahendran R, Vaingankar JA, Mythily S, Cai YM. Co-sleeping and clinical correlates in children seen at a child guidance clinic. Singapore Med J. 2006;47(11):957–9.

16. Hrastovec A, Hostnik T, Neubauer D. Benign convulsions in newborns and infants: occurrence, clinical course and prognosis. Eur J Paediatr Neurol. 2012;16(1):64–73.
17. Lowe RM, Hashkes PF. Growing pains: a noninflammatory pain syndrome of early childhood. Nat Clin Pract Rheumatol. 2008;4(10):542–9.
18. Garrison SR, Dormuth CR, Morrow RL, Carney GA, Khan KM. Nocturnal leg cramps and prescription use that preceeds them. Arch Intern Med. 2012:172(2):120–6.
19. Naylor JR, Young JB. A general population survey of rest cramps. Age Ageing. 1994;23(5):418–20.
20. Abdulla AJ, Jones PW, Pearce VR. Leg cramps in the elderly: prevalence, drug and disease associations. Int J Clin Pract. 1999;53(7):494–6.
21. Monderer RS, Wu WP, Thorpy MJ. Nocturnal leg cramps. Curr Neurol Neurosci Rep. 2010;10:53–9.
22. Freedom T. Sleep-related movement disorders. Dis Mon. 2011;57:438–47.
23. Ondo WG. Restless legs syndrome. Neuro Clin. 2009;27:739–99.
24. Fusco L, Specchio N. Non-epileptic paroxysmal manifestations during sleep in infancy and early childhood. Neurol Sci. 2005;26(Suppl 3):S205–S9.
25. Brown P, Thompson PD, Rothwell JC, Day BL, Marsden CD. Axial myoclonus of propriospinal origin. Brain. 1991;114(Pt 1A):197–214.
26. Di Lazzaro V, Restuccia D, Nardone R, Oliviero A, Profice P, Insola A, et al. Changes in spinal cord excitability in a patient with rhythmic segmental myoclonus. J Neurol Neurosur Psychiatry. 1996;61(6):641–4.
27. Lozsadi DA, Forster A, Fletcher NA. Cannabis-induced propriospinal myoclonus. Mov Disord. 2004;19(6):708–9.
28. Roze E, Bounolleau P, Ducreux D, Cochen V, Leu-Semenescu S, Beaugendre Y, et al. Propriospinal myoclonus revisited: clinical, neurophysiologic, and neuroradiologic findings. Neurology. 2009;72(15):1301–9.
29. Pincherle A, Mantoani L, Villani F, Confalonieri P, Erbetta A. Excessive fragmentary hypnic myoclonus in a patient affected by a mitochondrial encephalomyopathy. Sleep Med. 2006;7(8):663.
30. Suhren O, Bruyn GW, Tuynman A. Hyperexplexia, a hereditary startle syndrome. J Neurol Sci. 1966;3:577–605.
31. Shiang R, Ryan SG, Zhu YZ, Hahn AF, O'Connell P, Wasmuth JJ. Mutations in the alpha 1 subunit of the inhibitory glycine receptor cause the dominant neurologic disorder, hyperekplexia. Nat Genet. 1993;5(4):35–8.
32. Van derS, Koelman JHTM, Henneke S, Van RAF, Tijssen MA. Axial jerks: a clinical spectrum ranging from propriospinal to psychogenic myoclonus. J Neurol. 2010;257:1349–55.
33. Bharti B, Malhi P, Kashyap S. Patterns and problems of sleep in school going children. Indian Pediatr. 2006;43(1):35–8.
34. Laberge L, Tremblay RE, Vitaro F, Montplaisir J. Development of parasomnias from childhood to early adolescence. Pediatrics. 2000;106(1 Pt 1):67–74.
35. Liu X, Liu L, Owens JA, Kaplan DL. Sleep patterns and sleep problems among schoolchildren in the United States and China. Pediatrics. 2005;115(Suppl 1):241–9.
36. Nevéus T, Cnattingius S, Olsson U, Hetta J. Sleep habits and sleep problems among a community sample of schoolchildren. Acta Paediatr. 2001;90(12):1450–5.
37. Rubens NAA, Reimao RN, Lefevre AB. Prevalence of sleep-talking in childhood. Brain Dev. 1980;2(4):353–7.
38. Bjorvatn B, Gronli J, Pallesen S. Prevalence of different parasomnias in the general population. Sleep Med. 2010;11:1031–4.
39. Bloomfeld ER, Shatkin JP. Parasomnias and movement disorders in children and adolescents. Child Adolesc Psychiatric Clin N Am. 2009;18(4):947–65.
40. Petit D, Touchette E, Tremblay RE, Boivin M, Montplaisir J. Dyssomnias and parasomnias in early childhood. Pediatrics. 2007;119(5):e1016–e25.
41. Lam MH, Zhang J, Li AM, Wing YK. A community study of sleep bruxism in Hong Kong children: association with comorbid sleep disorders and neurobehavioral consequences. Sleep Med. 2011;12(7):641–5.

42. Goodwin JL, Kaemingk KL, Fregosi RF, Rosen GM, Morgan WJ, Smith T, et al. Parasomnias and sleep disordered breathing in Caucasian and Hispanic children—the Tucson children's assessment of sleep apnea study. BMC Med. 2004;2:14.
43. Eitner S, Urschitz MS. Guenther A, Urschitz-Duprat PM, Bohnhorst B, Schlaud M, et al. Sleep problems and daytime somnolence in a German population-based sample of snoring school-aged children. J Sleep Res. 2007;16(1):96–101.
44. Zarowski M, Mlodzikowska-Albrecht J, Steinborn B. The sleep habits and sleep disorders in children with headache. Adv Med Sci. 2007;52(Suppl 1):194–6.
45. Vetrugno R, Provini F, Piazzi G, Vignatelli L, Lugaresi E, Montagna P. Catathrenia (nocturnal groaning): a new type of parasomnia. Neurology. 2001;56(5):681–3.
46. DeRoeck J, Van Hoof E, Cluydts R. Sleep-related expiratory groaning: a case report. Sleep Res. 1983;12:237.

Part IV
Clinical Characteristics of Parasomnias Associated with REM Sleep

Chapter 10
Physiology and Content of Dreams

Ujjwal P. Ramtekkar, Anna Ivanenko and Sanjeev V. Kothare

Introduction

Dreams have aroused curiosity and fascination since the origin of the recorded history of mankind. The perceived importance of dreams as a tool to describe human experience is evidenced throughout history in arts, literature, religion, philosophy, and psychology [1–5]. However, the questions about the origins and functions of dreams continue to be elusive to modern science. This chapter provides an overview of psychological and neurophysiological research of dreaming, describes main theories of dreams, and reviews literature on dream content associated with different clinical conditions.

Definition of Dreams

Generally, the term 'dream' is used interchangeably with dream report or recollection of dream content by the dreamer upon awakening. Usually, it represents a single-witness verbal description that is subjective and dependent on the ability of

U. P. Ramtekkar (✉)
Department of Child and Adolescent Psychiatry, Boston Children's Hospital,
Harvard Medical School, 300 Longwood Avenue, Fegan 8, Boston, MA 02115, USA
e-mail: Ujjwal.Ramtekkar@childrens.harvard.edu

A. Ivanenko
Division of Child and Adolescent Psychiatry, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 East Chicago Avenue, Chicago, Illinois 60611-2605, USA
e-mail: aivanenko@sbcglobal.net

S. V. Kothare
Center for Pediatric Sleep Disorders,
Department of Neurology, Boston Children's Hospital,
Harvard Medical School, Boston, MA 02115, USA
e-mail: sanjeevkothare@hotmail.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_10, © Springer Science+Business Media New York 2013

the dreamer to recall the experience and content of dreaming. Depending on the study, the definition of dream could be overly inclusive—where any form of imaginative cognition, including recall of daytime events that occurs during transition to sleep may also be considered as dreams. Although dreams are believed to represent some form of mental activity or cognitive process that occurs during sleep [6], the methodological issues and wide variety of operational definitions in dream research have lead experts in the field to conclude that a single definition of dreams is not possible because of the wide variety of currently applied definitions [7]. Dreams can be broadly conceptualized as 'sleep mentation', which refers to any mental activity or experiences (e.g., thoughts, tactile perceptions, emotions, etc.) occurring while asleep that are remembered on awakening. Currently, there is no consensus on how to differentiate dreams from other forms of cognitive processes such as daydreaming and thinking during transition to sleep. In their review of quantitative findings of dream content, Zadra and Domhoff [8] concluded that dreams can be distinguished from other forms of mentation by the dreamer's sense of participation in some form of social activity along with other characters (person or animal) that simulates waking reality and are recalled as elaborate, story-like experiences upon awakening. However, these characteristics are influenced by various factors including sleep stage prior to awakening, time of awakening, method of awakening, etc. It is the subjective nature of dreams, dependent on the dreamer's recall after awakening that poses challenges in the direct assessment and systematic study of dreams. Despite these challenges, encouraging progress has been made in the last century in relating dreams to cognition, mental health, sleep, underlying brain activities, and physiological correlates.

Theories of Dreams

Dream research has been influenced by three major theories: psychoanalytic, physiologic, and, more recently, neurocognitive models of dreaming.

Psychoanalytic Theory of Dreams

Psychoanalytic perspective of dreaming and dream content was first proposed by Freud at the end of nineteenth century in his landmark publication, "The interpretation of dreams" [9]. Freud suggested that dreams are the product of our remote memories and they represent fulfillment of unconscious wishes related to infantile impulses. He proposed 'dream work' theory in which he stated that the actual memories undergo complex alterations like 'condensation' and 'displacement' before appearing as dreams. According to the psychoanalytic theory, dreams are considered to carry meaningful information about the dreamer that can be interpreted and therapeutically used by psychoanalysts. Although Freudian dream work theory was

popular for many decades, it was challenged by his successors [10] and later questioned due to nonconcordance with the rapidly accumulating body of research based on physiologic and neurocognitive framework.

Continuity Hypothesis of Dreaming

Another psychological approach towards dreaming called 'continuity hypothesis' was put forth by Hall and Nordby [11]. This hypothesis states that dreams simply reflect waking-life concerns and preoccupations. Schredl proposed a detailed modification of this hypothesis with a mathematical model to predict the relationship between waking-life experience and dream content [12]. The main factors included in Shredl's model are emotional involvement, type of waking-life experience, personality traits, time of the night, and time elapsed between waking-life experience and actual dream. The empirical evidence for continuity hypothesis has been elaborately discussed elsewhere [12].

Activation-Synthesis Hypothesis of Dreams

In the 1950s, the discovery of distinct stages of sleep—rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep [13] represented a paradigm shift toward the physiologic basis of dreaming. Based on the report of a correlation with dreaming [14, 15], REM sleep stage was initially considered a physiologic substrate of dream state. However, further research by Foulkes [16] suggested that dreams also occur during other stages, including NREM and wake–sleep transition. In the 1970s, Hobson presented an activation-synthesis theory [17] proposing that dreams result from the random brain activation during REM sleep. This model suggests that during REM sleep, ponto-geniculo-occipital (PGO) waves that originate from the pons arrive at the primary visual occipital cortex through the thalamic lateral geniculate nucleus (LGN) and are interpreted by the brain as visual information that is experienced as dreams. It assumes a 'bottom-up' approach where activation of certain brain areas leads to formation of sensory outputs in the form of dreams. The theory has since been revised to the activation-input-modulation (AIM) model [18] based on the findings of cholinergic transmission during REM sleep in experimental and neuroimaging data accrued over time (described later in the physiology section).

Neurocognitive Model of Dreams

In the recent years, progress in cognitive neuroscience has compounded a significant body of information to provide a neurocognitive model of dreaming. In this model, dreaming is believed to develop due to activation of the brain when disconnected

from any form of external stimuli. The specific contents are then drawn from memory schemas, episodic memory, and general themes of waking life that are later synthesized as dreams. This approach assumes 'top-down' propagation of signals in the formation of dreams where abstract information and thoughts are processed back to form the perceptual phenomenon or 'dream' [19, 20]. This model considers dreams as a byproduct of the appropriate activation of underlying neural circuits involved in neurocognitive processes, such as sleep dependent memory processing and consolidation.

Analysis and Classification of Dreams

Dream classification has been a formidable task for dream researches due to the lack of consensus on the definition of dream as well as methodological challenges in having uniform ways to operationalize the defining features of dreams.

The method of collection and quantification of different aspects of dream contents in order to systematically study and classify them is termed as 'dream content analysis'. Since dreams cannot be studied directly, researchers depend mainly on the collection of dream recall reports. These dream reports are collected by various methods, such as data from home dream journals, self-report questionnaires, sleep logs, and sleep studies for recording sleep stages prior to the report. The characteristics of dream reports are then evaluated on standardized rating scales using various systems for analyzing dream content.

Content Analysis of Dreams

Although, more than 150 dreams rating scales have been described, Hall and Van de Castle coding system for dream content analysis is the most widely used instrument [21]. The common domains for studying dream contents include emotions (range of positive and negative emotions), sensory perceptions or activity (visual, auditory, vestibular, olfactory, gustatory, vestibular, and pain), bizarreness (deviation from realistic to degrees of improbable/bizarre themes), and clarity or vividness [22]. The reports collected from individuals on self-report as well as independent rater(s) are then scored on the rating scale for each domain to be used for statistical analyses.

Despite systematic approach, there are major methodological issues of reliability and validity in using the instruments for dream content analysis. The reliability is usually ensured by using multiple dream reports for ratings, whereas validity is addressed by using multiple instruments. However, given the subjective nature of dream report and inherent issues with recollection of dreams, the content analysis remains challenging. Nonetheless, systematic dream content analysis provides a framework for classification of dreams. The comprehensive review of qualitative and quantitative methods of dream content analysis has been published by several authors. For review refer to references [8, 21, 23].

Classification of Dreams

Dreams can be broadly classified based on the sleep stages as following:

(a) *REM dreams*: These dream reports are more vivid, detailed in narrative, longer in duration, story-like in progression, and more bizarre or hallucinatory in nature. The reports often involve experiencing improbable events and usually contain unpleasant emotions in a narrative structure. These dreams also involve motor activity [18, 24, 25]. Nightmares are parasomnias occurring in REM sleep and are associated with extreme negative emotions leading to awakening in a state of distress.
(b) *NREM dreams*: These dream reports are less frequent and occur later in the night. The contents are more realistic in nature, thought-like in character, and related to memory of recent events. These dreams are less likely to be unpleasant and the settings are often familiar [25, 26]. Night terrors are NREM stage parasomnias that are characterized by sudden arousal with intense anxiety.
(c) *Sleep onset* (*Hypnagogic*) *dreams*: These include transient experiences of sounds, imagery or bodily sensations during wake–sleep transition period (N1). Usually, these are static, do not include a self-character and might be influenced by activities performed before sleep [27]. These dreams possibly represent REM intrusion during the transition and are thought to result from asymmetric deactivation of different regions of brain [28].
(d) *Lucid dreams*: Lucid dreaming is the experience of achieving conscious awareness of dreaming while still asleep. Although, lucid dreams are generally thought to arise from nonlucid dreams in REM sleep, it has been demonstrated that these occur in a distinct state with features of both REM sleep and waking [29].

Functions of Dreams

Since dreams are considered products of underlying brain activity, the question whether dreams have any biologically significant function independent of neural activity has long been debated. Although dreams have been considered the 'spandrels of sleep', representing an epiphenomenon of neurophysiologic activity during sleep stages [30], contemporary research findings suggest that dreams may serve significant psychological and biological functions.

Psychoanalytical Interpretation of Dreaming

According to Freud [9], dreams serve only one purpose: they are the "*guardians of sleep*". He proposed that dreams serve the psychological function of keeping sleep from being disturbed by overwhelming thoughts. Freud did not believe that dreams

help deal with disturbing emotional experiences; rather, he believed that dreaming dissipates the threat of overwhelming anxiety caused by the tension of repressed impulses. On the contrary, the contemporary psychoanalysts suggest that dreaming is the primary function of mind in pursuit of truth through thinking and feeling in dreams to deal with emotional problems [10]. Another analytic theory as proposed by Carl Jung, who was a follower of Freud, suggested that the function of dreams is to compensate for those parts of the psyche (total personality) that are underdeveloped in waking life.

In the modern era of analytic theory, Hartmann [31] viewed dreams in the context of trauma, suggesting that dreams are adaptive mechanisms to deal with the overwhelming emotions related to trauma by integrating the traumatic experience with the internal emotional material or dominant emotions from dreamer's waking life. In essence, dreams are ways of contextualizing the experience and adapting to it in preparation of any future trauma. In the absence of trauma, however, dreams only deal with the predominant emotions which are in response to events in waking life. The psychoanalytic model for the functions of dream has been elaborated and modified by many other contributors in the context of object relations theory, personality traits, unconscious conflicts, and attachment issues. However, these theories are subjective and are adaptations of theorist's own interpretations to suit the clinical needs at that time.

Mood Regulating Function of Dreaming

The mood regulating function of dreaming has been proposed based on the observations of postsleep mood improvement after experiencing dreams [32]. Dreams in healthy individuals were initially studied by Snyder [33] who found that unpleasant emotions, primarily fear and anxiety, were more commonly reported after REM awakenings, substantiating some function related to emotional processing. Based on further observations of self-reported home dreams, Cartwright [34, 35] proposed a model suggesting that the postsleep mood was systematically predicted by the quality of presleep mood, dream characteristics, and quality of sleep. The observations were further extended by Breger et al. [36], who investigated the effect of manipulated presleep stress in laboratory and found that dreams showed progressive down-regulation of negative mood in healthy subjects but not in depressed patients with inadequate coping skills. Thus, dreaming may play important role in sequential mood regulation by creating a narrative by integrating previous experiences and expression of affect in relation to current concerns. Studies of negative life events such as divorce and surgeries have also supported that dreams may play role in the adaption to external stressors [37, 38].

Some other models of a possible 'evolutionary significance' have also been proposed. For example, dreams are hypothesized as 'simulations' of anxiety provoking situations, thereby providing a secure platform for systematic desensitization [39]

and also preparation to face or avoid such dangerous situations [40]. Although these theories are interesting and plausible, they are largely speculative and have little scientific basis.

Reverse Learning Theory

Recent studies in cognitive neurosciences propose new models of possible dream functions. However, these are closely linked to the functions of sleep itself and may not be exclusively attributed to dreaming. One of the proposed models suggests that dreaming reflects *offline processing* of the memories related to daytime events [41]. This process includes consolidation, integration, and at times reversals of information obtained during the day. Thus, dreaming may be involved in storing the meaningful information while unlearning the unnecessary information (reverse learning theory). On the contrary, it is also suggested that dreaming is only a secondary result or byproduct of the sleep-dependent reactivation of memory networks required for critical functions such as declarative memory consolidation, visual and motor skills learning, and emotional processing. Thus, dreams are the "conscious perception of stream of images, thoughts, and feelings evoked by one of many forms of offline learning that occurs during sleep" [41].

In conclusion, the question about the primary functions of dreaming remains unresolved, but there is growing evidence that dreaming is not a random activity occurring during sleep and it may very well serve important biological functions.

Physiology and Neurobiology of Dreams

Knowledge of the brain mechanisms underlying the synthesis of dreams has advanced in the recent years. Insight into the neural basis of dreaming mainly comes from the integration of information derived from neurochemistry, electrophysiology, functional neuroimaging, and brain lesion studies.

Neurochemistry of Dreaming

Three major neurochemicals, acetylcholine (Ach), dopamine (DA), and serotonin (5-hydroxytryptamine (5-HT)) are proposed to be correlated with the process of dreaming. In Hobson's original activation-synthesis theory, dreaming was believed to be mediated by increased cholinergic activation leading to the formation of PGO waves that activated the forebrain during REM. Hobson's revised AIM model [18] suggests that consciousness is determined by three factors, Activation (A) of brain regions, Input (I) of external or internal stimuli, and Modulation (M) of aminergic and cholinergic neurons. According to the AIM model, dreams are generated during

REM sleep due to high levels of activation of the forebrain, higher levels of internal input in ascending reticular activating system of the thalamus by mesopontine cholinergic nuclei, and higher level of cholinergic modulation by inhibition of Gamma aminobutyric acid (GABA)ergic neurons in the thalamus.

Induction of REM sleep and dreams by cholinesterase inhibitors [42] support the model of cholinergic abundance during dreaming. The role of DA in dreaming was suggested based on observations that DA pathways in the ventral tegmental area (VTA) of the mesocortical brain, show increased bursts of activity during REM sleep [43]. Extrapolating these findings, Solms [44] postulated that stimulation of limbic and prefrontal reward networks by these dopaminergic projections from the midbrain to the VTA may be responsible for the initiation of dreaming.

Lastly, the role of serotonin in dreaming is based on animal studies that suggest that low or fluctuating serotonin levels may induce cortical outputs that may be conducive for hallucinations seen in dreaming [45]. In humans, cortical serotonin levels are lowest during REM sleep and fluctuations are seen during sleep transitions [18]. In addition, selective serotonin reuptake inhibitors are also known to intensify dreaming, further substantiating the role of serotonin in dream formation.

Electrophysiological Correlates of Dreaming

Monitoring of the awake–REM–NREM cycle using electroencephalography (EEG) provides information about the electrophysiological changes occurring in each stage over time. In general, REM sleep is associated with more activity of fast brain waves of gamma frequency (30–80 Hz), similar to wakefulness. These waves are postulated to correlate with REM dreaming and are thought to be associated with perceptual processing [46], memory processing, and temporal binding of dream imagery [47].

In contrast, NREM sleep is associated with more slower frequency waves representing the thalamo-cortical interactions that may interfere with mental activity, resulting in the decreased frequency of dreams [48]. Another electrophysiological measure is ‘coherence’ or phasic synchrony between different brain regions. Any decrease in coherence indicates functional disconnection between those brain regions. It has been shown that gamma frequency waves during REM sleep become desynchronized between the frontal and posterior cortical regions [49]. It is suggested that anteroposterior desynchronization during REM sleep reflects functional disconnection of executive control of frontal lobe on perception related posterior cortical areas leading to a ‘hypofrontal’ state resulting in bizarreness and enhanced perceptual vividness of REM dreams [49, 50].

Brain Lesion Studies of Dreaming

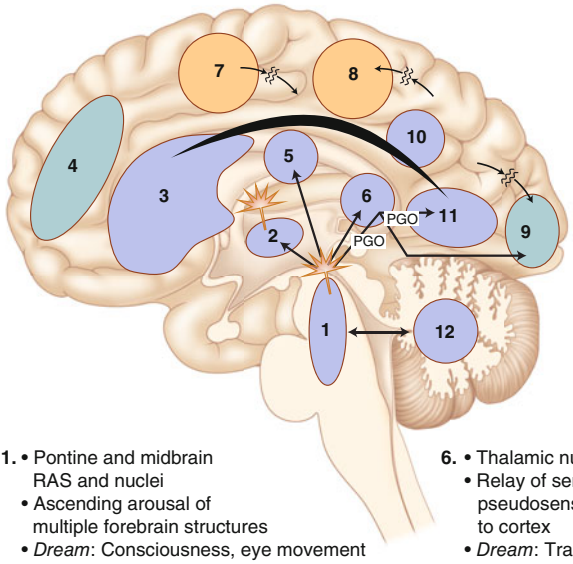
A comprehensive study of dreaming in more than 300 neurological patients was described by Solms [51]. He proposed a clinico-anatomical model based on the brain

lesions observed in his cohort, as well as from previously published data. His findings were later supported by neuroimaging and neuropsychological research. Majority of studies that used brain lesions indicated that dreaming depends on forebrain regions. Contrary to prior belief, pontine brainstem lesions do not affect dreaming, suggesting that the brainstem is less important than forebrain regions for generation of dreams. The phenomenon of global cessation of dreaming is generally seen after unilateral or bilateral damage around *Broadmann's area 40* (temporo-parieto-occipital junction). Since this region is necessary for mental imagery, it is speculated that mental imagery is the cognitive process essential for dreaming. The global cessation of dreaming also follows lesions of the *head of caudate nucleus* which includes white matter tracts surrounding the frontal horns of the lateral ventricles, the underlying *ventromedial prefrontal cortex* and *prefrontal lobotomy* (done in schizophrenic patients in the past). Loss of dopaminergic fibers in white matter tracts that originate from the limbic system is thought to be responsible for the loss of dreaming capacity in individuals with these lesions.

In contrast, lesions of some brain regions may lead to increased frequency and vividness of dreams. These areas include: *the medial prefrontal cortex, the anterior cingulate cortex, and the basal forebrain*. Nocturnal seizures, particularly complex partial seizures, may present with recurrent nocturnal nightmares, possibly reflecting the typical 'aura' producing nightmares with parallel content during sleep. These nightmares resolve after surgical or pharmacological treatment of the seizures.

Functional Neuroimaging of Dreams

Positron emission tomography (PET) and functional magnetic resolution imaging (fMRI) are the main techniques to study dreaming, mainly REM dreaming and the associated activation or deactivation of brain regions. Most of the brain lesion study findings as described above have been convergent with the neuroimaging findings [52]. Overall, dreaming is associated with the activation of limbic and paralimbic structures in the basal ganglia, activation of posterior cortical areas 19, 22, and 37, and deactivation of the dorsolateral prefrontal cortex. Based on the regional activation of brain areas and concurrent dream reports, some specific areas have been suggested to be linked to the specific dream features [53, 54]. Some of these associations include (i) activation of posterior (occipito-temporal) cortices with visual and perceptual aspects of dream, (ii) activation of amygdalar complex, the anterior cingulate gyrus, and the orbito-frontal cortex with emotionality in dreams, (iii) hypoactivation of the prefrontal cortex with illogical nature of dreams as well as episodic memory retrieval required for dreams. An integrated working model of widely distributed networks with distinct epicenters subserving critical role in dream phenomenology based on neurophysiological, neuropsychological, and neuroimaging data has been proposed by Hobson et al. as represented in Fig. 10.1 [18].



1. • Pontine and midbrain RAS and nuclei
• Ascending arousal of multiple forebrain structures
• *Dream*: Consciousness, eye movement and motor pattern information via PGO system

2. • Diencephalic structures (hypothalamus, basal forebrain)
• Autonomic and instintual function, cortical arousal
• *Dream*: Consciousness, instinctual elements

3. • Anterior limbic structures (amygdala, anterior cingulate, parahippocampal cortex, hippocampus, medial frontal areas)
• Emotional labeling of stimuli, goal-directed behavior, movement
• *Dream*: Emotionality, affective salience, movement

4. • Dorsolateral prefrontal cortex
• Executive functions, logic planning
• *Dream*: Loss of volition, logic orientation, working memory

5. • Basal gaglia
• Initiation of motor actions
• *Dream*: Initiation of fictive movement

6. • Thalamic nuclei (e.g. LGN)
• Relay of sensory and pseudosensory information to cortex
• *Dream*: Transmits PGO information to cortex

7-9. • Primary motor (7) and sensory (8, 9) cortices
• Generation of sensory percepts and motor commands
• *Dream*: Sensorimotor hallucinosis

10. • Inferior parietal cortex (BA 40)
• Spatial integration of processed heteromodal input
• *Dream*: Spatial organization

11. • Visual association cortex
• High order integration of visual percepts and images
• *Dream*: Visual hallucinosis

12. • Cerebellum
• Fine tuning of movement
• *Dream*: Fictive movement

Subcortical and neocortical areas relatively activated during dreaming

Neocortical areas relatively deactivated during dreaming

Neocortical structures preferentially contributing to circuitry active during dreaming

Ascending activation systems

Subcortical input/output blockade

Fig. 10.1 Forebrain processes in normal dreaming—an integration of neurophysiological, neuropsychological, and neuroimaging data. Regions *1* and *2*, ascending arousal systems; region *3*, subcortical and cortical limbic and paralimbic structures; region *4*, dorsolateral prefrontal executive association cortex; region *5*, motor initiation and control centers; region *6*, thalamocortical relay centers and thalamic subcortical circuitry; region *7*, primary motor cortex; region *8*, primary sensory cortex; region *9*, inferior parietal lobe; region *10*, primary visual cortex; region *11*, visual association cortex; region *12*, cerebellum. (Adapted from Hobson et al., [18] with permission from Cambridge University Press.)

Dream Content in Sleep Disorders

Sleep disorders inherently affect quality and associated physiology of sleep; therefore, it can be assumed that presence of sleep disorders may differentially affect the process of dreaming. The sleep disorders that have been studied with regard to dreaming will be reviewed in the current section.

Sleep Apnea

In spite of few studies [55, 56] reporting illustrious description of themes of choking or breathing related topics, sleep apnea does not appear to affect dream content as compared to healthy controls [57]. It is postulated that these topics are not incorporated in dreams due to the 'adaptation' to these chronic respiratory stimuli over months to years. However, patients with untreated sleep apnea experience dreams with negative emotions possibly reflecting the 'continuity' of waking-life worries secondary to daytime sleepiness.

Continuous positive airway pressure (CPAP) treatment is noted to resolve these negative emotions in dreams as well as reduce dream recall and increase dream length [58]. It may be assumed that the changes with CPAP treatment are indicative of correction of sleep fragmentation and longer duration of undisturbed REM sleep necessary for dreaming. Although systematic research is lacking about the effect of cognitive impairment and frequent arousals related to sleep apnea, studies suggest that dream recall frequency is not correlated with the intensity of sleep apnea parameters such as oxygen saturation nadir and respiratory disturbance index [56, 59].

Restless Leg Syndrome

There are no published studies of dream content in patients with restless leg syndrome (RLS). Although, studies demonstrating correlation between limb activity and electromyography (EMG) recordings exist, there has not been any attempt to study relationship between dream content and associated limb movements in patients with RLS. In a study of dream recall frequency in 131 patients with RLS, Schredl [60] reported negative correlation between dream recall frequency and periodic limb movement index. Interestingly, the self-reported frequency of nocturnal awakening was higher in the same group indicating that increased sleep fragmentation may interfere with the process of dream synthesis.

Nightmares and Night Terrors

Nightmares, by definition, include repeated awakenings from the major sleep period or naps with detailed recall [61]. Nightmares consist of extended and extremely

frightening dreams, usually involving threats to survival, security, or self-esteem. On awakening, the dreamer usually describes a detailed, associated, bizarre dream plot. The contents of nightmares are specifically related to the areas of internal strain that may be a troubling impulse, concern or feeling that is not modulated effectively [62, 63]. Usually, intense sense of anxiety and other negative emotions are reported upon awakening. Nightmares are associated with a variety of psychopathology and the nature of underlying diagnosis affects the content of nightmares (described later).

Night terrors, on the other hand, may be associated with dream recall in less than 50 % of time. Typically, night terrors constitute a single frightening visual imagery or thought that appears instantaneously and lacks a vivid or story-like nature. Wide variety of themes may occur in night terrors and commonly include imagery of things closing in, entrapment in small area, choking, drowning, getting crushed, falling, and fear of aggression from a person [63].

REM Behavior Disorder

REM behavior disorder (RBD) is associated with 'acting out' of dreams due to failure of muscle paralysis during REM sleep [64, 65]. Dreams in RBD are vivid, active, and aggressive in nature and often involve sense of defending against attack by other people or animals. Dream content in RBD has inverse correlation with the personality traits and waking life behavior of the dreamer, for example, increased aggression in RBD dreams are reported by the dreamers who are mild mannered and less aggressive in nature [64, 66]. The dreams usually normalize with treatment of RBD.

Narcolepsy

Narcolepsy is a REM sleep disorder that is associated with abnormal dreaming. The night time dreams in narcolepsy are generally negatively toned and bizarre in nature [57]. The dreams occur immediately as sleep onset REM, and also persist on awakening have predominance of frightening and unpleasant content such as themes of being under attack or scary figures of animals or humans and may be repetitive in nature [67, 68]. During daytime, dreamer is partially aware of dreaming and dreams may be similar to hypnagogic hallucinations that incorporate surrounding environment [67, 68].

Dream Content in Psychiatric Disorders

Sleep difficulties and primary sleep disorders are often comorbid in a variety of psychiatric disorders. Given the biological differences in each of psychiatric illness, the nature of sleep problems also differs. Similarly, it is commonly observed that the

dream content change with the change in the status of dreamer. As described earlier, there exists a mutual relationship between the dream content and mood regulation that may be influenced by the underlying psychopathology.

Schizophrenia

The dream reports of schizophrenics are usually related to changes in the waking experiences as well as the nature of fantasies or delusions related to underlying psychopathology. The specific features of dream contents in schizophrenia include emotional tone of anxiety and apprehension, presence of encounters with more strangers, and bizarreness that is congruent with the bizarre fantasies or delusions of waking life [69]. Other common themes in dreams of schizophrenia also include anxieties related to death and self-mutilation, ambivalent hostility, and aggression towards the dreamer by strangers [70].

A recent textual analysis study of dream reports in schizophrenia showed significant differences in linguistic domains as compared to controls, including increased use of indirect speech, unusual consistency in presence tense, lack of emotional expressions, and reduced frequency of hearing and differentiating the similar sounding words [71], all consistent with deficits due to psychopathology in the waking life. The effects of waking activities and themes on dream features of schizophrenics, therefore, support the 'continuity hypothesis' as described earlier [12]. However, it is unclear if the content of dreams also affects mood and thought disorder during waking life.

Affective Disorders

Mood regulating functions of dreams has been proposed by dream investigators based on the dream contents in individuals with mood disorders [35–38]. Dream content is generally congruent with the mood state, for example, negative tone of dreams is more frequent during depressed mood. Some of the most prominent emotions in depression include hostility, failure, and anxiety and the positive shift in these emotions is noted with improvement in mood [72]. The dream recall frequency is lower and the dreams are less detailed in depressed patients. The antidepressant treatment in depressed individuals suppresses the dream recall frequency but increases intensity as well as content of dreams [73, 74] however, the same effect of antidepressants has also been demonstrated in normal individuals [75]. The repetitive nightmares with persistent themes of dreams can be reflective of suicidal tendency [76, 77].

Similar to depression, the dream recall frequency reduces during mania. However, the contents of dreams are significantly different and often include themes of death of self or others, bodily injuries, and bizarre and unrealistic events. A change in dream content from neutral or negative to improbable themes may indicate impending mania [78, 79].

Posttraumatic Stress Disorder

Recurrently occurring dreams or nightmares related to the trauma is considered as an integral criterion for posttraumatic stress disorder (PTSD) [61]. In general, the dream recall frequency in individuals with PTSD is higher than controls, although, it decreases as the individuals are well adjusted over time [80]. Depending on the context, the dreams in PTSD may be unaltered replication of memories related to traumatic event as seen in combat veterans or acute disasters like fire and hurricanes [81–85]. In children, the dreams after trauma are mostly thematically related and include themes of persecution, aggression, threat, hostility, and sexual contents [86, 87].

The dreams in PTSD are usually recurring, more negatively toned, and activated by any form of stressful life events. These dreams are vivid, descriptive, and oriented to past events even with or without presence of content related to trauma. The well adjusted individuals with chronic PTSD may continue to experience nightmares related to trauma in the form of reference to the stressful situations without direct representation of trauma that is hypothesized to be helpful in emotional adaptation to stress.

In conclusion, the trauma related content and repetitive nature of dreams can predict the development of PTSD after traumatic event and change of content from direct replication of trauma to only thematic representation predicts the outcome and stage of PTSD.

Eating Disorders

Dreams in individuals with eating disorders often include themes about food, more in bulimia than anorexia [69]. The dream contents are usually less aggressive and are thought to reflect a passive avoidant approach of these individuals. Dream recall is often low but the reported dreams are often useful in psychotherapy for these individuals [88].

Substance Use

In an observational study, dreaming about alcohol was found to be a positive predictor of abstinence and better compliance with treatment [89]. Although this finding has not been replicated, it may have significance in terms of dream function in adaptive processing. Similar observations have been described for outcome of drug addiction, specifically crack cocaine abuse and smoking cessation [90, 91]. The exploration of content and progression of dreams can therefore be a useful tool in the treatment of substance use disorders.

Clinical Implications

With advancement of neuroscience and development of experimental and neuroimaging tools, biological and neuropsychological basis of dreams is becoming clear. Dreams may serve as the first indicators of progression of underlying psychiatric or sleep disorder and potential need for intervention in an individual. The bidirectional relationship between characteristics of dreams and underlying sleep or psychiatric disorders as well as their response to treatment interventions (such as selective serotonin reuptake inhibitors (SSRIs), CPAP, etc.) can be used prognostically during effective treatment planning. Although the biological and psychological functions of dreams remain unclear, assessment of dreams may yield meaningful information that could be best understood as a reflection of clinical changes in underlying pathology. The treatment interventions including medication management may warrant careful assessment and alterations based on their effect of dreams or progression of dream content.

Conclusion

Further examination and characterization of dreams in variety of disorders such as Tourette's syndrome, attention deficit-hyperactivity disorder (ADHD), obsessive compulsive disorder, and prodromal psychosis may yield clinically relevant information for diagnostic and prognostic purpose. Research on effects of psychotropic and neuroleptic medications on dreams may be customary to advance the understanding of underlying mechanisms of disorders and appropriate selection of agents.

Case Example

A 12-year-old male with recent diagnosis of major depression without any psychotic features was initiated on Fluoxetine 20 mg daily to address depressive symptoms. About 3 weeks after initiation of the medication, parents reported child being lethargic and observing fast eye movements while falling asleep. The child himself was unaware of the movements and reported 'no memory' of these events. However, he reported waking up with nightmares and new onset of vivid dreams. EEG revealed prominent, sustained, and high voltage eye movements during wake–sleep transition. There was no evidence of seizures and the child was awake for the most part during the observed eye movements. The eye movements resolved after 4 weeks of discontinuation of Fluoxetine. Although the nightmares and intensity of dreams reduced, the child continued to have negatively toned dreams that correlated with his daytime depressive symptoms and themes.

SSRIs are known to produce REMs, commonly termed as 'Prozac eyes' usually observed during wake–sleep transition and sometimes during stage one NREM sleep.

These movements are thought to be due to increased serotonin and may sustain for few weeks even after discontinuation of SSRIs. In addition, SSRIs are correlated with increase in vivid dreams and nightmares. These are independent of the dreams seen in depression that are usually characterized by negative tone with themes of anxiety, failure, and hostility in congruence with the mood state. The questions about dreams should therefore be asked in patients treated with SSRIs.

Practical Points

- Dream is a form of 'sleep mentation'—any mental activity or experiences occurring while asleep that is remembered on awakening.
- Dreams are thought to be a result of appropriate activation of underlying neural circuits involved in neurocognitive processes and may have a role in sleep dependent memory processing and consolidation.
- REM and NREM sleep stages have different dream characteristics including duration, content, and recall.
- Changes in dream content over time can potentially reflect on the clinical progression of underlying psychiatric and sleep disorders.
- Medications have differential effects on dream characteristics independent of underlying disorder.

References

1. Hughes J. Dream interpretation in ancient civilizations. Dreaming. 2000;10(1):7–18.
2. Rosselli D. Brief history of dreams. Rev Neurol. 2000;30(2):195–8. (Breve historia de los suenos).
3. Palagini L, Rosenlicht N. Sleep, dreaming, and mental health: a review of historical and neurobiological perspectives. Sleep Med Rev. 2011; 15(3):179–86.
4. Dreisbach C. Dreams in the history of philosophy. Dreaming. 2000;10:31–41.
5. Stoll RT. Sleep and dreams in pictures. Praxis (Bern 1994). 1995;84(15):432–9. (Schlaf und Traum im Bild).
6. Schredl M, Wittmann L. Dreaming: a psychological view. Schweiz Arch Neurol Psychiatr. 2005;156:484–92.
7. Pagel J, Blagrove M, Levin B, Stickgold B, et al. Definitions of dream: A paradigm for comparing field descriptive specific studies of dream. Dreaming. 2001;11:195–202.
8. Zadra A. Domhoff G. The content of dreams: methods and findings. 5th ed. In: Kryger M, Roth T, Dement W, editors. Principles and practices of sleep medicine. Philadelphia: Elsevier; 2011. pp. 585–94.
9. Freud S. The interpretation of dreams. New York: Random House; 1900.
10. Shneider J. From Freud's dreamwork to Bion's work of dreaming—changing conception of dreaming in psychoanalytic theory. Int J Psychoanal. 2010;91(3):521–40.
11. Hall C, Nordby V. The individual and his dreams. New York: New American Library; 1972.
12. Schredl M, Hofmann F. Continuity between waking activities and dream activities. Conscious Cogn. 2003;12(2):298–308.
13. Aserinsky E, Kleitman N. Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. Science. 1953;118(3062):273–4.

14. Dement W, Kleitman N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. Electroencephalogr Clin Neurophysiol. 1957;9(4):673–90.
15. Dement W, Kleitman N. The relation of eye movements during sleep to dream activity: an objective method for the study of dreaming. J Exp Psychol. 1957;53(5):339–46.
16. Foulkes WD. Dream reports from different stages of sleep. J Abnorm Soc Psychol. 1962;65:14–25.
17. Hobson JA, McCarley RW. The brain as a dream state generator: an activation-synthesis hypothesis of the dream process. Am J Psychiatry. 1977;134(12):1335–48.
18. Hobson JA, Pace-Schott EF, Stickgold R. Dreaming and the brain: toward a cognitive neuroscience of conscious states. Behav Brain Sci. 2000;23(6):904–1121. (discussion)
19. Domhoff G. The scientific study of dreams: neural networks, cognitive development, and content analysis. American Psychological Association; 2003.
20. Foulkes D. Dreaming: a cognitive-psychological analysis. Lawrence Erlbaum Associates; 1985.
21. Winget CN, Kramer M. Dimensions of dream. Gainsville: University presses of Florida; 1979.
22. Cohen D. Sleep and dreaming. New York: Pergamon press; 1979.
23. Hall CS, van de Castle R. The content analysis of dreams. New York: Appleton-Century-Crofts; 1966.
24. Stickgold R, Pace-Schott E, Hobson JA. A new paradigm for dream research: mentation reports following spontaneous arousal from REM and NREM sleep recorded in a home setting. Consious Cogn. 1994;3:16–29.
25. McNamara P, Johnson P, McLaren D, Harris E, Beauharnais C, Auerbach S. REM and NREM sleep mentation. Int Rev Neurobiol. 2010;92:69–86.
26. Baylor GW, Cavallero C. Memory sources associated with REM and NREM dream reports throughout the night: a new look at the data. Sleep. 2001;24(2):165–70.
27. Hobson JA, Pace-Schott EF. The cognitive neuroscience of sleep: neuronal systems, consciousness and learning. Nat Rev Neurosci. 2002;3(9):679–93.
28. Magnin M, Rey M, Bastuji H, Guillemant P, Mauguiere F, Garcia-Larrea L. Thalamic deactivation at sleep onset precedes that of the cerebral cortex in humans. Proc Natl Acad Sci U S A. 2010;107(8):3829–33.
29. Voss U, Holzmann R, Tuin I, Hobson JA. Lucid dreaming: a state of consciousness with features of both waking and non-lucid dreaming. Sleep. 2009;32(9):1191–200.
30. Flanagan O. Deconstructing dreams: The spandrels of sleep. Towards science of consiousness: Complex adaptive systems. In: Hameroff SR, Kaszniak A, Scott AC, editors. Cambridge: MIT press; 1996. pp. 67–88.
31. Hartmann E. Nightmare after trauma as paradigm for all dreams: a new approach to the nature and functions of dreaming. Psychiatry. 1998;61(3):223–38.
32. Kramer M. The dream experience: a systematic exploration. New York: Routledge; 2007.
33. Snyder F. The Phenomenology of dreaming. In: Madow L, Snow L, editors. The psychodynamic implications of the physiological studies on dreams. Springfield: Thomas; 1970. pp. 124–51
34. Cartwright RD. The nature and function of repetitive dreams: a survey and speculation. Psychiatry. 1979;42(2):131–7.
35. Cartwright R, Luten A, Young M, Mercer P, Bears M. Role of REM sleep and dream affect in overnight mood regulation: a study of normal volunteers. Psychiatry Res. 1998;81(1):1–8.
36. Breger L, Hunter I, Lane RW. The effect of stress on dreams. Psychol Issues. 1971;7(3):1–213.
37. Cartwright RD, Kravitz HM, Eastman CI, Wood E. REM latency and the recovery from depression: getting over divorce. Am J Psychiatry. 1991;148(11):1530–5.
38. Cartwright R, Baehr E, Kirkby J, Pandi-Perumal SR, Kabat J. REM sleep reduction, mood regulation and remission in untreated depression. Psychiatry Res. 2003;121(2):159–67.
39. Valli K, Revonsuo A, Palkas O, Ismail KH, Ali KJ, Punamaki RL. The threat simulation theory of the evolutionary function of dreaming: Evidence from dreams of traumatized children. Conscious Cogn. 2005;14(1):188–218.

40. Revonsuo A. The reinterpretation of dreams: an evolutionary hypothesis of the function of dreaming. Behav Brain Sci. 2000;23(6):877–901; discussion 4–1121.
41. Stickgold R. EW. Why we dream. 5th ed. Principles and practice of sleep medicine. In: Kryger T, WD, editors. Philadelphia: Elsevier; 2011. p. 635.
42. Kitabayashi Y, Ueda H, Tsuchida H, Yamashita T, Narumoto J, Fukui K. Donepezil-induced nightmares in mild cognitive impairment. Psychiatry Clin Neurosci. 2006;60(1):123–4.
43. Miller JD, Farber J, Gatz P, Roffwarg H, German DC. Activity of mesencephalic dopamine and non-dopamine neurons across stages of sleep and walking in the rat. Brain Res. 1983;273(1):133–41.
44. Solms M. The neurochemistry of dreaming: cholinergic and dopaminergic hypotheses. Neurochemistry of consiousness: Advances in Consiousness research. In: Perry E, Ashton H, Young A, editors. Amsterdam: Benjamin's publishing; 2002. p. 123–31.
45. Aghajanian GK, Marek GJ. Serotonin and hallucinogens. Neuropsychopharmacol. 1999;21 (2 Suppl):16–23.
46. Cantero JL, Atienza M, Madsen JR, Stickgold R. Gamma EEG dynamics in neocortex and hippocampus during human wakefulness and sleep. Neuroimage. 2004;22(3):1271–80.
47. Kahn D, Pace-Schott EF, Hobson JA. Consciousness in waking and dreaming: the roles of neuronal oscillation and neuromodulation in determining similarities and differences. Neuroscience. 1997;78(1):13–38.
48. Steriade M. Corticothalamic resonance, states of vigilance and mentation. Neuroscience. 2000;101(2):243–76.
49. Corsi-Cabrera M, Miro E, del-Rio-Portilla Y, Perez-Garci E, Villanueva Y, Guevara MA. Rapid eye movement sleep dreaming is characterized by uncoupled EEG activity between frontal and perceptual cortical regions. Brain Cogn. 2003;51(3):337–45.
50. Perez-Garci E, del-Rio-Portilla Y, Guevara MA, Arce C, Corsi-Cabrera M. Paradoxical sleep is characterized by uncoupled gamma activity between frontal and perceptual cortical regions. Sleep. 2001;24(1):118–26.
51. Solms M. The neurpsychology of dreaming: a clinico anatomical study. Lawrence Erlbaum Associates; 1997.
52. Pace-Schott EF, Hobson JA. The neuropsychology of dreams: a clinico-anatomical study. Trends Cogn Sci. 1998;2(5):199–200.
53. Schwartz S, Maquet P. Sleep imaging and the neuro-psychological assessment of dreams. Trends Cogn Sci. 2002;6(1):23–30.
54. Dang-Vu TT, Desseilles M, Petit D, Mazza S, Montplaisir J, Maquet P. Neuroimaging in sleep medicine. Sleep Med. 2007;8(4):349–72.
55. Hobson JA, Goldfrank F, Snyder F. Respiration and mental activity in sleep. J Psychiatr Res. 1965;3(2):79–90.
56. Schredl M, Schmitt J, Hein G, Schmoll T, Eller S, Haaf J. Nightmares and oxygen desaturations: is sleep apnea related to heightened nightmare frequency? Sleep Breath. 2006;10(4):203–9.
57. Schredl M. Dreams in patients with sleep disorders. Sleep Med Rev. 2009;13(3):215–21.
58. Carrasco E, Santamaria J, Iranzo A, Pintor L, De Pablo J, Solanas A et al. Changes in dreaming induced by CPAP in severe obstructive sleep apnea syndrome patients. J Sleep Res. 2006;15(4):430–6.
59. Schredl M. Snoring, breathing pauses, and nightmares. Percept Mot Skills. 2008;106(3):690–2.
60. Schredl M. Dream recall frequency and sleep quality of patients with restless legs syndrome. Eur J Neurol. 2001;8(2):185–9.
61. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: text revision. 4th ed. Washington: American Psychiatric Pub; 2000.
62. Fisher C, Byrne J, Edwards A, Kahn E. A psychophysiological study of nightmares. J Am Psychoanal Assoc. 1970;18(4):747–82.
63. Fisher C, Kahn E, Edwards A, Davis DM, Fine J. A psychophysiological study of nightmares and night terrors. 3. Mental content and recall of stage 4 night terrors. J Nerv Ment Dis. 1974;158(3):174–88.

64. Ferini-Strambi L, Fantini ML, Zucconi M, Castronovo V, Marelli S, Oldani A, et al. REM sleep behaviour disorder. Neurol Sci. 2005;26;Suppl 3:186–92.
65. Schenck CH, Mahowald MW. REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in SLEEP. Sleep. 2002;25(2):120–38.
66. Fantini ML, Corona A, Clerici S, Ferini-Strambi L. Aggressive dream content without daytime aggressiveness in REM sleep behavior disorder. Neurology. 2005;65(7):1010–5.
67. Fosse R. REM mentation in narcoleptics and normals: an empirical test of two neurocognitive theories. Conscious Cogn. 2000;9(4):488–509.
68. Vogel G. Studies in psychophysiology of dreams III. The dream of narcolepsy. Arch Gen Psychiatry. 1960;3:421–8.
69. Kramer M, Nuhic Z. A review of dreaming by psychiatric patients. Sleep and psychosomatic medicine. In: Pandi-Perumal SR, Routi R, Kramer M, editors. Boca Raton: Taylor and Francis; 2007. pp. 137–55.
70. Stompe T, Ritter K, Ortwein-Swoboda G, Schmid-Siegel B, Zitterl W, Strobl R et al. Anxiety and hostility in the manifest dreams of schizophrenic patients. J Nerv Ment Dis. 2003;191(12):806–12.
71. Zanasi M, Calisti F, Di Lorenzo G, Valerio G, Siracusano A. Oneiric activity in schizophrenia: textual analysis of dream reports. Conscious Cogn. 2011;20(2):337–48.
72. Barrett D, Loeffler M. Comparison of dream content of depressed vs. nondepressed dreamers. Psychol Rep. 1992;70(2):403–6.
73. Armitage R, Trivedi M, Rush AJ. Fluoxetine and oculomotor activity during sleep in depressed patients. Neuropsychopharmacology. 1995;12(2):159–65.
74. Armitage R, Emslie G, Rintelmann J. The effect of fluoxetine on sleep EEG in childhood depression: a preliminary report. Neuropsychopharmacology. 1997;17(4):241–5.
75. Pace-Schott EF, Gersh T, Silvestri R, Stickgold R, Salzman C, Hobson JA. SSRI treatment suppresses dream recall frequency but increases subjective dream intensity in normal subjects. J Sleep Res. 2001;10(2):129–42.
76. Agargun MY, Cartwright R. REM sleep, dream variables and suicidality in depressed patients. Psychiatry Res. 2003;119(1–2):33–9.
77. Agargun MY, Cilli AS, Kara H, Tarhan N, Kincir F, Oz H. Repetitive and frightening dreams and suicidal behavior in patients with major depression. Compr Psychiatry. 1998;39(4):198–202.
78. Beauchemin KM, Hays P. Prevailing mood, mood changes and dreams in bipolar disorder. J Affect Disord. 1995;35(1–2):41–9.
79. Beauchemin KM, Hays P. Dreaming away depression: the role of REM sleep and dreaming in affective disorders. J Affect Disord. 1996;41(2):125–33.
80. Wittmann L, Schredl M, Kramer M. Dreaming in posttraumatic stress disorder: A critical review of phenomenology, psychophysiology and treatment. Psychother Psychosom. 2007;76(1):25–39.
81. Esposito K, Benitez A, Barza L, Mellman T. Evaluation of dream content in combat-related PTSD. J Trauma Stress. 1999;12(4):681–7.
82. Mellman TA, Kulick-Bell R, Ashlock LE, Nolan B. Sleep events among veterans with combat-related posttraumatic stress disorder. Am J Psychiatry. 1995;152(1):110–5.
83. van der Kolk B, Blitz R, Burr W, Sherry S, Hartmann E. Nightmares and trauma: a comparison of nightmares after combat with lifelong nightmares in veterans. Am J Psychiatry. 1984;141(2):187–90.
84. Pagel J, Vann B, Altomare C. Reported association of stress and dreaming: community background levels and changes with disaster (hurricane Iniki). Dreaming. 1995;5:43–50.
85. Siegel A. Dreams of firestorm survivors. Trauma and dreams. In: Barrett D, editor. Cambridge: Harvard university press; 1996.
86. Terr LC. Childhood traumas: an outline and overview. Am J Psychiatry. 1991;148(1):10–20.
87. Nader K, Pynoos R, Fairbanks L, Frederick C. Children's PTSD reactions one year after a sniper attack at their school. Am J Psychiatry. 1990;147(11):1526–30.

88. Kramer M. Dream differences in psychiatric patients. In: Perumal SRP, Kramer M, editors. Cambridge University Press; 2010.
89. Choi SY. Dreams as a prognostic factor in alcoholism. Am J Psychiatry. 1973;130(6):699–702.
90. Christo G, Franey C. Addicts' drug-related dreams: their frequency and relationship to six-month outcomes. Subst Use Misuse. 1996;31(1):1–15.
91. Reid SD, Simeon DT. Progression of dreams of crack cocaine abusers as a predictor of treatment outcome: a preliminary report. J Nerv Ment Dis. 2001;189(12):854–7.

Chapter 11
Nightmare Disorders in Adults

Antonio Zadra and Barry Krakow

Introduction

Considerable progress has been made in the clinical conceptualization and treatment of nightmares, yet many clinicians remain unaware of the suffering caused by chronic nightmares and of their negative consequences on patients' sleep quality and mental health. Moreover, this lack of awareness extends to the existence of therapeutic interventions that effectively and quickly reduce or eliminate the problem in a majority of cases. In the early nineteenth century, Waller [1] had remarked that there were few afflictions more universal among all classes of society than the nightmare. In fact, idiopathic nightmares are the most commonly experienced parasomnias in the general population, while dream-related disorders are among the most frequently reported and most persistent symptoms exhibited by trauma victims [2–5]. Nightmares are also one of the ways an individual may reexperience a traumatic event and as such are considered a core symptom of posttraumatic stress disorder (PTSD) (Cluster B) in the Diagnostic and Statistical Manual of Mental Disorders-fourth edition (DSM-IV) [6]. Finally, irrespective of populations, increased frequency of nightmares is correlated with severe sleep disturbances, including higher rates of sleep-onset and sleep-maintenance insomnia, increased severity of psychological and psychiatric distress, and poor physical health [7–13].

A. Zadra (✉)
Department of Psychology, Université de Montréal, C.P. 6128,
succ. Centre-ville, Montréal,
Quebec, Canada
e-mail: antonio.zadra@umontreal.ca

Center for Advanced Research in Sleep Medicine,
Hôpital du Sacré-Cœur de Montréal,
Montréal, Quebec, Canada

B. Krakow
Maimonides Sleep Arts & Sciences, Ltd., Sleep & Human Health Institute,
6739 Academy Road NE, Ste. 380,
Albuquerque, NM 87109, USA
e-mail: bkrakow@sleeptreatment.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_11, © Springer Science+Business Media New York 2013

Diagnostic Criteria for Nightmare Disorder

In standard diagnostic texts such as the DSM-IV [6] and the International Classification of Diseases (ICD-10) [14] (see Table 11.1), nightmares are characterized by repeated awakenings, usually from late-night rapid eye movement (REM) sleep, with clear recall of frightening dream content. Upon awakening from the disturbing dream, the person is quickly alert with little to no confusion or disorientation. The use of the waking criterion is based on the idea that sleepers awaken from a nightmare because of the extreme intensity of the emotions experienced. However, empirical and clinical findings indicate that this may not always be the case [15–17]. Consequently, disturbing dreams that do not awaken the sleeper ("bad dreams") can also be considered clinically significant. It should also be noted that although nightmares are typically defined as *frightening dreams*, patients' nightmares may involve intensification of many different unpleasant emotions (e.g., extreme sadness, confusion, and anger) even though fear remains the most frequently reported [16, 18, 19]. An excellent and thorough discussion of how nightmares can be defined for clinical practice (*diagnostic definitions*) as well as in research settings (*operational definitions*) is presented in Levin and Nielsen [12].

Nightmare Prevalence and Association to Other Conditions

Studies of undergraduate students indicate that 8–30 % of students report having one or more nightmares per month [20–24], while surveys of students and general adult populations in different countries find that 2–6 % of people report experiencing one or more nightmares per week [18, 22, 25]. Irrespective of actual indices of nightmare frequency, 5–8 % of the general population reports having a current problem with nightmares [26, 27].

A high prevalence of nightmares has been documented in various clinical populations including patients seen in psychiatric emergency services [28], alcohol and drug users [29], patients with borderline personality [30, 31] or dissociative disorders [32], and individuals suffering from schizophrenia-spectrum disorders [33]. Frequent nightmares can also occur in individuals exposed to a wide range of traumatic experiences [34–36], are experienced by a significant majority of PTSD patients [37–39], and have been related to elevated risk for suicide in both adolescents and adults [40–42]. That being said, clinicians need to bear in mind that frequent nightmares can be experienced by relatively well-functioning individuals, who do not show clinical signs of psychopathology.

Variations in nightmare frequency and severity may be viewed as reflecting the influence of two underlying factors: *affect load*, or day-to-day variations in emotional stress and *affect distress*, or a disposition to experience heightened distress and negative affect and to react with extreme behavioral expressions [12]. Genetic factors may also contribute to nightmares' aetiology [43].

Different classes of drugs may induce nightmares and bizarre dreams. These include catecholaminergic agents, some antidepressants (e.g., bupropion), barbiturates,

Table 11.1 Clinical criteria for nightmare disorder. (Source: Nielsen T, Zadra A. Ideopathic nightmares and dream disturbances associated with sleep-wake transitions. In: Kryger M, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 5th ed. New York: Elsevier; 2011. pp. 1106–15, with permission from Elsevier)

	DSM-IV diagnostic criteria for nightmare disorder (307.47)	ICSD-II diagnostic criteria for nightmares (307.47-0)
Nature of recalled dream	A. Repeated awakenings from the major sleep period or naps with detailed recall of extended and extremely frightening dreams, usually involving threats to survival, security, or self-esteem	A. Recurrent episodes of awakenings from sleep with recall of intensely disturbing dream mentation, usually involving fear or anxiety but also anger, sadness, disgust and other dysphoric emotions B. Recall of sleep mentation is immediate and clear
Nature of awakening	B. On awakening from the frightening dreams, the person rapidly becomes oriented and alert (in contrast to the confusion and disorientation seen in sleep terror disorder and some forms of epilepsy)	C. Alertness is full immediately on awakening, with little confusion or disorientation
Nature of distress	C. The dream experience, or the sleep disturbance resulting from the awakening, causes clinically significant distress or impairment in social, occupational, or other important areas of function	D. Associated features include at least one of the following: return to sleep after the episodes is typically delayed and not rapid
Timing	A. The awakenings generally occur during the second half of the sleep period	D. Associated features include at least one of the following: the episodes typically occur in the later half of the habitual sleep period
Differential diagnosis	D. The nightmares do not occur exclusively during the course of another mental disorder (e.g., a delirium, posttraumatic stress disorder) and are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition	*Nightmares are distinguished from several other disorders in a differential diagnosis section*: seizure disorder, arousal disorders (sleep terrors, confusional arousal), REM sleep behavior disorder, isolated sleep paralysis, nocturnal panic, posttraumatic stress disorder, acute stress disorder

DSM-IV Diagnostic and Statistical Manual of Mental Disorders-fourth edition, *ICSD-II* International Classification of Sleep Disorders-second edition, *REM* rapid eye movement

alcohol, and beta-blockers. The neuropharmacological basis of drug-induced or withdrawal-associated disturbed dreaming remains unclear but several reviews have detailed nightmare inducing classes of drugs and their suspected modes of action [44, 45].

Vivid and disturbing nightmares can also be associated with REM sleep behavior disorder (RBD). The main features of this disorder are an excessive muscle tone and undesirable and often violent behavioral manifestations (i.e., attempted dream-enactment) during REM sleep. For a detailed account of RBD, see Vaughn's chapter on REM sleep behavior disorder in adults in the present volume. Finally, as reviewed elsewhere [5], nightmares and other forms of disturbing dreams can occur in association with other sleep disorders, including dream-interruption insomnia, sleep–wake transition disturbances, sleep starts, hypnagogic hallucinations, and sleep paralysis.

Treatment

Numerous nonpharmacological techniques have been proposed to treat PTSD-related or idiopathic nightmares [46] and clinical support is provided for many such interventions including desensitization [47–49], lucid dreaming [50, 51], and hypnosis [52]. However, no intervention for nightmares has been the subject of more clinical and empirical investigation than imagery rehearsal therapy (IRT), also known as imagery rescripting and rehearsal.

IRT for nightmares is comprised of two general elements, each of which targets a distinct, yet overlapping problem in the nightmare sufferer. The first component is an educational/cognitive restructuring element, focused on helping the nightmare suffer to consider their disturbing dreams as a learned sleep disorder. The second component is an imagery education/training element, which teaches nightmare patients how to implement a specific set of imagery steps to decrease nightmares. IRT can be delivered individually or in groups and the complete teaching and acquisition of this technique typically requires one to four treatment sessions. A peer-reviewed session by session guide for clinicians is available [53]. IRT is effective in reducing nightmare frequency, including maintenance of changes at long-term follow-up [54–58], and effectively relieves idiopathic, recurrent, and PTSD-related forms of nightmares [8, 15, 54, 56, 58–60], although not all studies have found significant ameliorations [61].

For those patients where IRT may be impractical or counterproductive, pharmacotherapy (e.g., Prazosin, a central alpha-1 adrenoreceptor blocker) may be a useful alternative therapeutic option for PTSD-related nightmares [62–64].

Case Example

A 38-year-old single woman reports insomnia and nightmares for the past 20 years, which started after a teenage sexual assault. She never sought psychotherapy for these problems, but received sleeping pills and antidepressants. She's worked as

an administrative assistant since completing high school and has maintained steady employment. She has a boyfriend of several years, but sees no reason to get married, although they are reconsidering as they want children. She has no drug, alcohol or tobacco usage, but occasionally obtains a few prescription stimulants from her sister with attention deficit-hyperactivity disorder (ADHD), because she feels exhausted after bouts of nightmares.

She was diagnosed with PTSD at age 33 after insomnia disrupted her work to the point where she was required to seek counseling. She completed a group therapy program, which helped her PTSD, but her nightmares and insomnia persisted. In the PTSD program, there was no mention of nightmare treatment other than hearing "nightmares will recede when your PTSD improves." Current medications include nightly zolpidem and daily citalopram at low doses, but she was not convinced these drugs help her sleep or mood, yet she saw no reason to stop taking them. When she learned of a nightmare treatment program, she wanted to hear more despite being skeptical about the possibility of a "nightmare treatment."

At the first session, the patient was asked to briefly describe her PTSD symptoms, and past PTSD treatments, including any benefits or lack thereof from her medications. She also recounted several of her more severe nightmares, often punctuating each graphic scenario with a rhetorical "I wonder what that means?" When asked how often she experienced nightmares, she stated virtually every night and sometimes more than once per night.

She was informed that nightmare treatment usually did not require addressing the presumed cause of the disturbing dreams and also did not require detailing their specific content. Moreover, she was instructed that the IRT approach did not attempt to interpret possible meanings of bad dreams, and therefore time would not be devoted to how the nightmares and PTSD might be related. Instead, she was educated on a model that implied that nightmares function like an independent sleep disorder because it disrupts sleep and exacerbates mental health distress.

The patient thought it odd that nightmares could be treated without working on PTSD issues or addressing the cause of the nightmares. She indicated that since her initial diagnosis of PTSD 5 years ago, several physicians and therapists had explained nightmares were best understood as a symptom of PTSD, "so you really could not expect to see them disappear unless you worked on the PTSD." Regardless, the patient resonated with the idea that nightmares were impacting her sleep, and with further probing she came to the realization that she had been delaying her bed time out of a fear of suffering bad dreams. *The seemingly obvious nightmare-insomnia connection is rarely considered by nightmare sufferers until probed on the topic*. Once she comprehended that nightmares were disrupting her sleep, it was easier for her to see how nightmares might be an independent source of distress, if for no other reason than making her tired and sleepy during the day and unable to cope as well.

In the final part of the session, she was asked to evaluate her mental imagery system by first responding to the instruction: "Please give me directions from your house to your favorite restaurant?". Then, she was asked to describe what occurred in her mind's eye in providing directions, and she reported seeing various streets,

landmarks, turns, and so forth, which indicated that she had a relatively normal-functioning imagery system up to this point. Next, she was instructed to close her eyes and imagine spending time at her most recent and enjoyable vacation. With the instruction to spend about 5–10 min on this imagery practice, she was left alone in the clinic room to ease any potential anxieties. Next, in discussing her efforts she was asked if any unpleasant images arose in her mind's eye during the self-practice. She reported at one point while picturing herself on the beach, she saw a strange man in a distance, which made her tense, but then she saw seagulls flying over the water.

At the end of the first session, she was instructed to practice pleasant imagery sessions for a few minutes each day just like she had done. If she noticed anything distressing in the images, she was instructed to "see if you can change the scene like you mentioned with the seagulls entering the picture and maybe that will be enough to move you away from the disturbing images." If it did not, she was informed she could open her eyes and stop the imagery session temporarily or completely, then start over again later.

At the second session, the patient reported imagery practice was relaxing, and she only experienced a couple of distressing images at which point changing the scene solved the issue. Next, we discussed again how nightmares take on a life of their own, how evidence-based research shows that anxiety symptoms consistently decrease when nightmares decrease, and how nightmares may be triggered by trauma but sustained by learned behavior. She did not reject the latter idea, but it was difficult for her to comprehend how "a nightmaring process" could somehow settle into one's dream world like "a broken record." She wanted more time to consider these ideas, but remained comfortable proceeding with the final steps of IRT.

In this final part, the patient was asked to select a dream in her mind's eye, then change it any way she wished; *see Joseph Neidhardt's original model* [54, 56]. She was then asked to briefly describe the nightmare she selected (patients are strongly encouraged to not select their most intense bad dreams when first learning IRT) and then spend more time describing the manner in which she changed it into a "new dream." She was directed to spend 5–10 min rehearsing this new dream. Further instructions included the idea that the new dream might change further once she began the imagery session and that such changes were perfectly normal. Also, she was to apply the idea of "changing the scene" if distressing images emerged in the process. (Some patients may need to learn IRT steps by going through this first attempt by writing out the original bad dream and the changed version.) She was instructed to repeat the same exercise on just one or two different nightmares per week and told there was no need to work on each and every nightmare. However, she was encouraged to rehearse one of her new dreams a few minutes each day. Also, it was explained that she was taking control of her waking imagery system, which would likely influence her sleeping imagery system, such that the IRT approach tended to have a ripple effect on overall nightmare frequency.

The patient returned for a booster session 2 months later where she reported a 50 % decrease in her disturbing dreams. She also reported a decrease in the frequency and intensity of her insomnia, and according to her therapist her PTSD symptoms had also improved. At one-year follow-up, her nightmares decreased from her initial

report of virtually every night to once or twice per month, insomnia was markedly reduced, and she was only using zolpidem a couple times per month.

Typically, most IRT patients will report their most dramatic drop-off in nightmare frequency in the initial 2 weeks to 2-month period upon initiating the program. Most patients also report improvements in sleep and PTSD symptoms during that same interval.

Practical Points

- Nightmares can be associated with important sleep disturbances as well as considerable psychological and psychiatric distress.
- Chronic nightmares may represent a primary sleep disorder rather than a symptom of a psychiatric disorder, and direct targeting of nightmares is a feasible clinical approach to the problem.
- Cognitive-behavioral techniques can alleviate nightmares rather rapidly with gains being maintained over time.

References

1. Waller J. A treatise on the incubus or nightmare. London: E. Cox and Son.; 1816.
2. Hefez A, Metz L, Lavie P. Long-term effects of extreme situational stress on sleep and dreaming. Am J Psychiatry. 1987;144(3):344–7.
3. Kramer M, Kinney L. Sleep patterns in trauma victims with disturbed dreaming. Psychiatr J Univ Ott. 1988;13:12–6.
4. Van der Kolk B. The dream experience in dream-disturbed Vietnam veterans. In: Van der Kolk B, editor. Post-traumatic stress disorder: psychological and biological sequelae. Washington, DC: American Psychiatric Press; 1984.
5. Nielsen T, Zadra A. Idiopathic nightmares and dream disturbances associated with sleep-wake transitions. In: Kryger M, Roth T, Dement W, editors. Principles and practice of sleep medicine. 5th ed. Philadelphia: Saunders; 2011. pp. 1106–15.
6. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. 4th ed. Washington, DC: American Psychiatric Association; 2000.
7. Miro E, Martinez M. Affective and personality characteristics in function of nightmare prevalence, nightmare distress, and interference due to nightmares. Dreaming. 2005;15(2):89–105.
8. Krakow B, Tandberg D, Scriggins L, Barey M. A controlled comparison of self-rated sleep complaints in acute and chronic nightmare sufferers. J Nerv Ment Dis. 1995;183(10):623–7.
9. Madrid S, Marquez H, Nguyen TT, Hicks RA. Nightmare distress and stress-related health problems. Percept Mot Skills. 1999;89(1):114–5.
10. Nguyen TT. Type A-B behavior, nightmare frequency, nightmare distress. Sleep & Breathing. 2003;23:A326–7.
11. Cukrowicz KC, Otamendi A, Pinto JV, Bernert RA, Krakow B, Joiner TE Jr. The Impact of Insomnia and Sleep Disturbances on Depression and Suicidality. Dreaming. 2006;16;1–10.
12. Levin R, Nielsen TA. Disturbed dreaming, posttraumatic stress disorder, and affect distress: a review and neurocognitive model. Psychol Bull. 2007;133(3):482–528.
13. Cellucci A, Lawrence P. Individual differences in self-reported sleep variable correlations among nightmare sufferers. J Clin Psychol. 1978;34(3):721–5.

14. WHO. International Statistical Classification of Diseases and Related Health Problems. Tenth Revision. ed. Geneva: WHO; 1994.
15. Krakow B, Kellner R, Pathak D, Lambert L. Imagery rehearsal treatment for chronic nightmares. Behav Res Ther. 1995;33(7):837–43.
16. Zadra A, Pilon M, Donderi DC. Variety and intensity of emotions in nightmares and bad dreams. J Nerv Ment Dis. 2006;194(4):249–54.
17. Levitan HL. The significance of certain dreams reported by psychosomatic patients. Psychother Psychosom. 1978;30(2):137–49.
18. Belicki K, Cuddy MA. Nightmares: facts, fictions and future directions. In: Gackenbach J, Sheikh AA, editors. Dream images: a call to mental arms. Amityville: Baywood; 1991. pp. 99–113.
19. Dunn KK, Barrett D. Characteristics of nightmare subjects and their nightmares. Psychiatr J Univ Ott. 1988;13(2):91–3.
20. Haynes SN, Mooney DK. Nightmares: etiological, theoretical, and behavioral treatment considerations. Psychol Rec. 1975;25(2):225–36.
21. Belicki K, Belicki D. Predisposition for nightmares: a study of hypnotic ability, vividness of imagery, and absorption. J Clin Psychol. 1986;42(5):714–8.
22. Feldman MJ, Hersen M. Attitudes toward death in nightmare subjects. J Abnorm Psychol. 1967;72(5):421–5.
23. Wood JM, Bootzin RR. The prevalence of nightmares and their independence from anxiety. J Abnorm Psychol. 1990;99(1):64–8.
24. Zadra A, Donderi DC. Nightmares and bad dreams: their prevalence and relationship to well-being. J Abnorm Psychol. 2000;109(2):273–81.
25. Janson C, Gislason T, De Backer W, Plaschke P, Bjornsson E, Hetta J, et al. Prevalence of sleep disturbances among young adults in three European countries. Sleep. 1995;18(7):589–97.
26. Bixler EO, et al. Prevalence of sleep disorders in the Los Angeles metropolitan area. Am J Psychiatry. 1979;136(10):1257–62.
27. Klink M, Quan SF. Prevalence of reported sleep disturbances in a general adult population and their relationship to obstructive airways diseases. Chest. 1987;91(4):540–6.
28. Brylowski A. Nightmares in crisis: clinical applications of lucid dreaming techniques. Psychiatr J Univ Ott. 1990;15(2):79–84.
29. Cernovsky ZZ. MMPI and nightmares in male alcoholics. Percept Mot Skills. 1985;61:841–2.
30. Claridge G, Davis C, Bellhouse M, Kaptein S. Borderline personality, nightmares, and adverse life events in the risk for eating disorders. Pers Indiv Differ. 1998;25(2):339–51.
31. Semiz UB, Basoglu C, Ebrinc S, Cetin M. Nightmare disorder, dream anxiety, subjective sleep quality in patients with borderline personality disorder. Psychiatry Clin Neurosci. 2008;62(1):48–55.
32. Agargun MY, Kara H, Ozer OA, Selvi Y, Kiran U, Ozer B. Clinical importance of nightmare disorder in patients with dissociative disorders. Psychiatry Clin Neurosci. 2003;57(6):575–9.
33. Hartmann E. The nightmare: the psychology and biology of terrifying dreams. New York: Basic Books; 1984.
34. Lifton JR, Olsen E. The human meaning of total disaster: The Buffalo Creek experience. Psychiatry. 1976;39:1–18.
35. Hefez A, Allodi F, Moldofsky H. Nightmares, sleep and symptoms in survivors of torture. Sleep Research. 1985;14:129.
36. Duval M, Zadra A. Frequency and content of dreams associated with trauma. Sleep Med Clin. 2010;5(2):249–60.
37. Krakow B, Schrader R, Tandberg D, Hollifield M, Koss MP, Yau CL, et al. Nightmare frequency in sexual assault survivors with PTSD. J Anxiety Disord. 2002;16(2):175–90.
38. Phelps AJ, Forbes D, Creamer M, Phelps AJ, Forbes D, Creamer M. Understanding posttraumatic nightmares: an empirical and conceptual review. Clin Psychol Rev. 2008;28(2):338–55.
39. Wittmann L, Schredl M, Kramer M. Dreaming in posttraumatic stress disorder: a critical review of phenomenology, psychophysiology and treatment. Psychother Psychosom. 2006;76(1): 25–39.

40. Tanskanen A, Tuomilehto J, Viinamaeki H, Vartiainen E, Lehtonen J, Puska P. Nightmares as predictors of suicide. Sleep. 2001;24(7):844–7.
41. Sjostrom N, Waern M, Hetta J. Nightmares and sleep disturbances in relation to suicidality in suicide attempters. Sleep. 2007;30(1):91–5.
42. Liu X. Sleep and adolescent suicidal behavior. Sleep. 2004;27(7):1351–8.
43. Hublin C, Kaprio J, Partinen M, Koskenvuo M. Nightmares: familial aggregation and association with psychiatric disorders in a nationwide twin cohort. Am J Med Genet. 1999;88(4):329–36.
44. Pagel J, Helfter P. Drug induced nightmares—an etiology based review. Hum Psychopharm. 2003;18(1):59–67.
45. Pagel J. Drugs, dreams and nightmares. Sleep Med Clin. 2010;5(2):277–88.
46. Halliday G. Direct psychological therapies for nightmares: a review. Clin Psychol Rev. 1987;7(5):501–23.
47. Miller WR, DiPilato M. Treatment of nightmares via relaxation and desensitization: a controlled evaluation. J Consult Clin Psychol. 1983;51(6):870–7.
48. Eccles A, Wilde A, Marshall W. In vivo desensitization in the treatment of recurrent nightmares. J Behav Ther Exp Psychiatry. 1988;19(4):285–8.
49. Cellucci AJ, Lawrence P. The efficacy of systematic desensitization in reducing nightmares. J Behav Ther Exp Psychiatry. 1978;9(2):109–14.
50. Spoormaker VI, van den Bout J, Meijer EJG. Lucid dreaming treatment for nightmares: a series of cases. Dreaming. 2003;13(3):181–6.
51. Zadra A, Pihl RO. Lucid dreaming as a treatment for recurrent nightmares. Psychother Psychosom. 1997;66(1):50–5.
52. Kingsbury SJ. Brief hypnotic treatment of repetitive nightmares. Am J Clin Hypn. 1993;35(3):161–9.
53. Krakow B, Zadra A. Clinical management of chronic nightmares: imagery rehearsal therapy. Behav Sleep Med. 2006;4(1):45–70.
54. Kellner R, Neidhardt J, Krakow B, Pathak D. Changes in chronic nightmares after one session of desensitization or rehearsal instructions. Am J Psychiatry. 1992;149(5):659–63.
55. Krakow B, Kellner R, Neidhardt J, Pathak D, et al. Imagery rehearsal treatment of chronic nightmares: with a thirty month follow-up. J Behav Ther Exp Psychiatry. 1993;24(4):325–30.
56. Neidhardt EJ, Krakow B, Kellner R, Pathak D. The beneficial effects of one treatment session and recording of nightmares on chronic nightmare sufferers. Sleep. 1992;15(5):470–3.
57. Krakow B, Kellner R, Pathak D, Lambert L. Long term reduction of nightmares with imagery rehearsal treatment. Behav Cog Psychother. 1996;24(2):135–48.
58. Lancee J, Spoormaker VI, van den Bout J. Long-term effectiveness of cognitive-behavioural self-help intervention for nightmares. J Sleep Res. 2011;20(3):454–9.
59. Long ME, Hammons ME, Davis JL, Frueh BC, Khan MM, Elhai JD, et al. Imagery rescripting and exposure group treatment of posttraumatic nightmares in Veterans with PTSD. J Anxiety Disord. 2011;25(4):531–5.
60. Berlin KL, Means MK, Edinger JD. Nightmare reduction in a Vietnam veteran using imagery rehearsal therapy. J Clin Sleep Med. 2010;6(5):487–8.
61. Cook JM, Harb GC, Gehrman PR, Cary MS, Gamble GM, Forbes D, et al. Imagery rehearsal for posttraumatic nightmares: a randomized controlled trial. J Trauma Stress. 2010;23(5):553–63.
62. Raskind MA, Peskind ER, Kanter ED, Petrie EC, Radant A, Thompson CE, et al. Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: a placebo-controlled study. Am J Psychiatry. 2003;160(2):371–3.
63. Thompson CE, Taylor FB, McFall ME, Barnes RF, Raskind MA, Thompson CE, et al. Non-nightmare distressed awakenings in veterans with posttraumatic stress disorder: response to prazosin. J Trauma Stress. 2008;21(4):417–20.
64. van Liempt S, Vermetten E, Geuze E, Westenberg HG. Pharmacotherapy for disordered sleep in post-traumatic stress disorder: a systematic review. Int Clin Psychopharm. 2006;21(4); 193–202.

Chapter 12
Nightmare Disorders in Children

Sriram Ramgopal, Marcin Zarowski and Sanjeev V. Kothare

Introduction

Nightmares have long intrigued thinkers and philosophers. Ancient civilizations associated nightmares with the presence of spirits or shamanistic powers [1]. Despite this fascination, however, nightmares remain an exceptionally common human experience, more so among young people. Nearly half of all children are reported to experience a nightmare [2]. In most children, nightmares are not severe enough to impair daytime functioning. In a minority of children, severe or persistent nightmares may lead to disturbances in mood and poor sleep quality. Sleep specialists should be able to determine if nightmares are interfering with daily life and if these dreams are secondary to another condition. Treatments for nightmares are largely limited to lifestyle changes, though psychiatric intervention may be beneficial for severe and persistent nightmares.

S. Ramgopal (✉) · M. Zarowski
Department of Neurology,
Boston Children's Hospital, Boston, MA, USA
e-mail: Sriram.Ramgopal@childrens.harvard.edu

8 Garfield Lane East, Andover, MA 01810, USA

M. Zarowski
Polysomnography and Sleep Research Unit,
Department of Developmental Neurology,
Poznan University of Medical Sciences, Poznan, Poland
e-mail: marcin.zarowski@gmail.com, zarowski@ump.edu.pl

S. V. Kothare
Center for Pediatric Sleep Disorders,
Department of Neurology, Boston Children's Hospital,
Harvard Medical School, Boston, MA 02115, USA
e-mail: sanjeevkothare@hotmail.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_12, © Springer Science+Business Media New York 2013

Case Example

A 14-year-old girl, evaluated by multiple computed tomography (CT) scans after suffering a fall from a height, was found to have a thyroid nodule, which was thought to be malignant in nature. A few weeks later, the patient developed episodes of behavioral arrest and nocturnal awakenings. These events were thought to be seizures, and she was started on levetiracetam. Escalating doses of the same did not reduce the frequency of these events. The patient was evaluated in the epilepsy monitoring unit, where it was found that these events did not have an electrographic correlate. The patient was subsequently diagnosed to have pseudoseizures and nightmares. Levetiracetam was discontinued and the patient was treated with counseling and reassurance. Following biopsy, the thyroid lesion was found to be benign. The patient had a gradual reduction of nightmares over 6 weeks to 3 months.

Definition

Nightmares are defined by both the American Academy of Sleep Medicine and the American Psychiatric Association. The *International Classification of Sleep Disorders, 2nd edition* defines nightmares as "recurrent episodes of awakening from sleep with recall of intensely disturbing dream mentation, usually involving fear or anxiety, but also anger, sadness, disgust, and other dysphoric emotions" [3]. Some investigators have questioned the importance of waking after sleep in the definition of nightmares, as secondary consequences of nightmares can occur in individuals who are not woken out of their sleep. A distinction may be justified on the finding that psychological morbidities may be greater in those with dreams that wake them out of sleep [4]. This has led to the introduction of the term *disturbed dreaming* to describe such dreams which have the emotional component of nightmares but which do not necessarily lead to complete awakening of the subject [5–7].

Nightmares are also defined in the *Diagnostic and Statistical Manual IV (DSM-IV)* as "repeated awakenings from the major sleep period or naps with detailed recall of extended and extremely frightening dreams, usually involving threats to survival, security, or self-esteem." Further attributes of nightmares specified by the DSM-IV are the occurrence of these events during the second half of the sleep period, a rapid awakening of the affected individuals following the dream, the presence of significant distress in daytime function, and the absence of other psychiatric disorders [8].

Epidemiology

Incidence and Prevalence

It is difficult to ascertain the prevalence of nightmares due to differences in definitions and cultural norms. Sporadic nightmares are best regarded as a normal human experience. Children may be unable to verbalize the content of their dreams, and thus

the presence of bad dreams must be ascertained by the caregiver. Approximately 50 % of 3–6-year-old children and 20 % of 6–12-year-olds experience nightmares [2]. Nightmares are present in approximately one third of children who present to a sleep specialist [9].

Age

Age is likely to be an important factor in the onset of nightmares. Nightmares are more common among younger children [10]. An epidemiological survey targeted to parents found that the prevalence of nightmares among 6–12-year-old children was 22 %. The incidence was noted to be higher amongst younger children [11], and decreased progressively as children aged. According to a study on normal school children aged 4–12 years, the incidence of scary dreams peaked among slightly older children, but this may be a reflection of the differential ability to remember and report such events [12]. The decreasing incidence of nightmares with age may reflect the attenuation of rapid eye movement (REM) sleep with pubertal growth [13].

Sex Differences

Nightmares occur with equal frequency among young boys and girls. From early adolescence, nightmares occur more frequently among females [14]. A study of 13–16-year-old individuals found that the recall of disturbing dreams rose as girls got older during this period, while it decreased in boys [15]. A study of college-aged students found that females were 50 % more likely to report having frequent nightmare attacks compare to males [16]. This finding however may suggest that females are simply more likely to recall bad dreams compared to males [17].

Pathophysiology

The exact mechanisms underlying dreams and nightmares elude any interdisciplinary study. Theories of nightmares and dreams in general, arise from a variety of disciplines, including neurocognitive research, psychoanalysis, psychology, evolutionary biology, and neurobiology. Sigmund Freud attributed nightmares to "masochistic wish fulfillment" and "maladaptive reactions" [18]. Later, personality theories, initially promoted by Hartmann, linked nightmares to impaired "ego boundaries" that fail to protect dreamers from sleep and waking state [19, 20]. Supportive evidence for these theories comes from research findings of increased frequency of nightmares in individuals with personality disorders [15, 21].

Nightmares typically occur during REM sleep, more often in the second half of the night to early morning hours (Fig. 12.1). Activation of the visual cortex during REM sleep via ponto-geniculo-occipital waves may lead to vivid visualizations

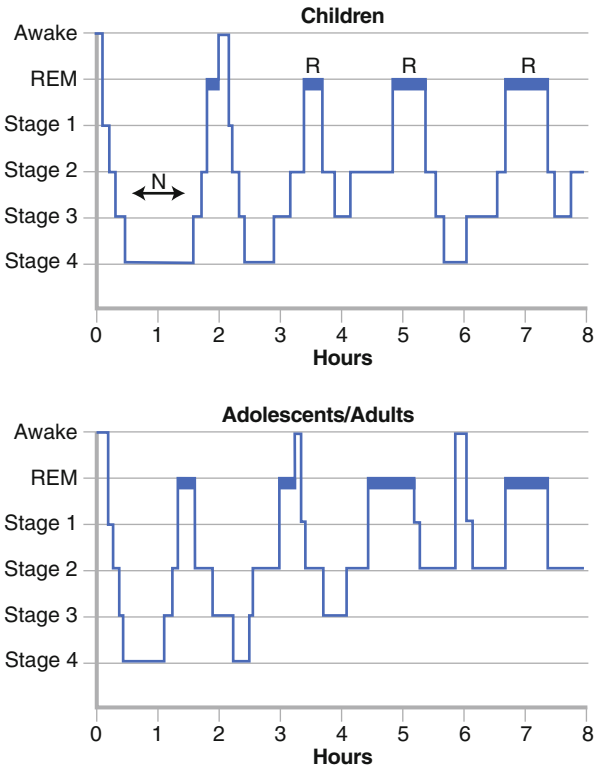


Fig. 12.1 Sleep cycles in children (*top* graph) and adolescents/adults (*bottom* graph). (**a**) Children tend to have progressively prolonged periods of rapid eye movement (REM) sleep ® during the latter part of the sleep cycle, thereby predisposing them to nightmares during the early hours of the morning. (**b**) The first non-REM phase in children is much longer in children compared to adolescents (N) and can last up to 2 h. This period of sleep, the majority of which is spent in N3 sleep, is when night terrors are most likely to occur.

characteristic of dreaming. The activation of the amygdala during REM sleep, as demonstrated by functional magnetic resonance imaging (fMRI) is postulated to be particularly important in the pathogenesis of nightmares [22]. Nightmares may thus occur following the activation of fear and emotional responses from the central nucleus of the amygdala. This hypothesis is also supported by the associations between posttraumatic stress disorder (PTSD) and hyperactivation of the amygdala [1, 23].

Complications

Psychiatric Sequelae of Nightmares

Nightmares are associated with emotional distress, though it is difficult to differentiate causes from effects. Disturbing dreams were found to correlate with anxiety, depression, neuroticism, and acute stress [7]. In older individuals, nightmares may additionally correlate with a higher risk of suicide [24]. Frequent nightmares may additionally be associated with a greater risk of psychosis [25].

Nightmares and Neurological Function

Nightmares can lead to disturbances in sleep quality, which in turn can affect daytime functioning. An adult study comparing 17 individuals with frequent nightmares with a control group found that patients with frequent nightmares had reduced sleep efficiency, increased wakefulness, reduced slow-wave sleep, and increased nocturnal awakenings [26]. Patients with frequent nightmares may also suffer from poorer functioning. A controlled adult trial found that individuals with frequent nightmares suffered from poorer executive function on objective tests. This was especially apparent on tests evaluating negative motor function. These findings could not be wholly accounted for on the basis of anxiety or sleep disturbance and are thus suggestive of alterations in frontal or prefrontal executive functioning in those with frequent bad dreams [27].

Risk Factors

Circadian Sleep Disorder

Few studies have identified risk factors for nightmares in children. A study of 218 children investigated an association between sleep problems and organization of wake/sleep cycle. The results of this study indicated that nightmares were twice as common in children with irregular sleep/wake patterns in the first year of life (46 %) compared to children with normal sleep routines (29 %), though this difference did not achieve a statistical significance [9].

Population-Based Correlates

Larger population studies have provided more information regarding risk factors for nightmares in children. A Canadian longitudinal study using a representative sample of 987 children found that a past history of nightmares was highly predictive of the persistence of nightmares through early childhood. Around 82 % of children who had nightmares at 29 months still had them at 41 months, and of these, 88 % still had nightmares at 50 months, 87 % had persistent nightmares at 5 years, and 90 % had persistent nightmares at 6 years [28]. The presence of nightmares in early childhood is thus predictive of the continued risk of nightmares in later years. High family income, absence of siblings at 29 months of age, and a nonimmigrant mother all correlated with the presence of bad dreams. Bad dreams at 50 months were more common among children in single-parent homes, in those with shorter sleep latencies, and in children who were given food or drink after awakening at night [29]. Child anxiety in earlier life, parent-reported difficulties in falling asleep at 17 months, and shorter sleep onset latencies corresponded with bad dreams at 5 years of age [29].

Psychological Factors

Emotional and psychological factors in both the child and his/her parents have long been postulated to play an important role in the development of nightmare disorders in children. The direction of causality is unclear. In a prospective study on elementary school students using parent-based surveys, children who experienced nightmares were significantly more likely to be rated as anxious by their parents [21]. In adolescents, anxiety was found to correlate strongly with the presence of disturbing dreams, a trend that was particularly more apparent in adolescent girls [15]. Other correlates for nightmares include generalized anxiety disorder, separation anxiety, and overanxious disorder [15].

Presenting Symptoms

Nightmares are common events in children, though they are usually sporadic. Children may awake from nightmares and be anxious and frightened, and may also wake up their parents during the night. Children often can recall their nightmares, and this may lead to increased anxiety during waking hours. The content of nightmares varies depending on the age of the child. Younger children may have more abstract nightmares involving ghosts or monsters. As children age, the content of these nightmares may instead involve fears to bodily injury and physical danger [30]. Concerns about behavioral competence and social approval may predominate in older children [31]. The content of dreams is similar in girls and boys in younger children. In older children, dreams classified by as "worrisome thoughts" involving harm to self or to loved ones, were more common in girls [12].

Nightmares are not associated with any specific findings on examination. On polysomnography conducted in the sleep laboratory, nightmares were shown to be associated with periodic limb movements [32], though it is not known if these findings extend to nightmares in the natural setting.

Nightmares Secondary to Other Conditions

Psychiatric Conditions

Patients with PTSD often suffer from distressing dreams. Nightmares in PTSD are often associated with longer nocturnal awakenings [32]. Most nightmares in these patients are related to the traumatizing event, though in up to half of patients, nightmares may be idiopathic in nature. Nightmares may lead to a poorer sleep in these patients and can thereby worsen the emotional symptoms of PTSD [33].

Nightmares may occur in the context of other psychiatric diseases and cause additional distress. In such situations, treatment should primarily be aimed at managing the primary psychiatric condition. Disturbing dreams may occur in delirious patients and are often recalled by patients following their recovery [34]. Patients with borderline personality disorder [35] and depression [25] have been documented to have frequent bad dreams and poor sleep quality. Patients with schizophrenia have also been reported to have greater numbers of nightmares compared to controls and which may persist despite treatment [36]. In one study, 44 % of patients with Tourette's syndrome reported frequent bad dreams and/or night terrors [37].

Medications

Bad dreams may occur as a consequence of drug toxicity. Drugs which alter the normal synaptic activity of serotonin, norepinephrine, and dopamine may lead to nightmares. Opioids [38], beta-blockers [39–41], levodopa [42], and ketamine [43] have been associated with nightmares. Statin drugs have also been reported to cause bad dreams [39–41]. Sleep physicians should particularly be aware that chronic amphetamine use and withdrawal have been implicated in the genesis of nightmares [44]. Nightmares have also been documented following withdrawal from selective serotonin reuptake inhibitors and tricyclic antidepressants [44, 45]. Other drugs associated with nightmares include benzodiazepines, anticholinergics, clonidine, and barbiturates [39–41, 44].

Drugs of Abuse

Drugs of abuse are frequently associated with bad dreams. Cannabis and cocaine withdrawal have been documented to cause unpleasant dreams [46]. Alcohol intoxication and withdrawal are noted to increase the frequency of nightmares [47, 48].

Diagnosis

Nightmares are usually reported by the patient and/or the parent. Clinicians should be aware of other conditions that may lead to frequent nightmares that require attention. Issues such as physical or sexual abuse or drug use require a high index of suspicion to identify as patients do not typically volunteer this information.

Nightmares, which occur in the latter half of the night, may be confused with night terrors. Night terrors occur during non-REM sleep in the first half of the night, and cannot be remembered upon awakening. Symptoms of night terrors include vocalizations, hyperagitation, and autonomic signs. Children with night terrors do

not awake spontaneously, are often difficult to console after waking up, and have poor to no recall of the event.

Instrumental investigations are not indicated to diagnose nightmares. However, with unusual presentations, one may consider ordering a 24-h electroencephalography (EEG) to rule out seizures. Similarly, if the suspicion for obstructive sleep apnea or periodic limb movements of sleep is high, one may order a sleep study to rule out these conditions, because treatment of these conditions can reduce sleep-fragmentation, and thereby reduce nightmares.

Treatment

Sporadic nightmares typically do not require treatment. Lifestyle measures should be tried in nightmares that occur more than once a week, persist for several weeks to months, or which are particularly severe. Parents should be advised to limit the exposure to television and/or graphic content for a few hours prior to going to sleep. Other daytime stressors should be identified and appropriately managed. Maintenance of a regular sleep schedule may be an important means to improve the quality of sleep and possibly reduce the frequency of bad dreams [9]. Treatment of the underlying anxiety may also be considered with psychological or pharmacological intervention.

Nightmares which occur more frequently and which disturb daily functioning may benefit by a comprehensive behavioral evaluation. Cognitive behavioral therapies (CBTs), including systematic desensitization [49, 50], imagery rehearsal [50–52], relaxation techniques, extinction [53], and eye movement desensitization [54] have been reported as beneficial in treating nightmares. However, these techniques have not been validated in larger prospective studies [55]. Nightmare-focused CBT may be more effective than simpler relaxation techniques [56]. In adults, the American Academy of Sleep Medicine recommends image rehearsal therapy, systematic desensitization, and relaxation training for the treatment of nightmares [57]. The feasibility and efficacy of these strategies in the pediatric age group are not fully established.

Systematic Desensitization

Systematic desensitization is a CBT which aims to reduce fears and anxieties induced by certain phobias. A procedure described by Palace et al. involves the replacement of the anxiety in addition to dream reorganization strategies. This practice was highly effective on a case report of a 10-year-old boy with recurring nightmares [50]. Another report of systematic desensitization in adults utilized manuals intended to train subjects on relaxation techniques [58]. In the study conducted by Miller et al. [59], 10 subjects underwent therapy with relaxation and systemic desensitization techniques and were compared with 11 controls. The results of the study demonstrated that behavioral therapies were more effective than in controls at 25 weeks follow-up.

Image Rehearsal Therapy

Image rehearsal therapies attempt to change the storyline of dreams towards more pleasant outcomes. Several studies [51, 52, 60] have investigated image rehearsal as a means of treating nightmares. Wile [51] evaluated three types of treatments on a group of 25 children with frequent nightmares: (a) in the first group, subjects used techniques to promote positive dreams in place of negative dreams ($n = 11$), (b) in the second group, subjects used a positive affirmation prior to going to sleep ($n = 11$), and (c) in the third group, subjects used dream-relevant coping tasks, such as exposure objects of their nightmares in a controlled daytime settings ($n = 3$). The study found that dreams disappeared in the first group at a median of 3 months, at 5 months for the second group, and at 2 months for the third group. The other study, reported by Krakow et al. [52], evaluated a three-step process for the elimination of nightmares in a series of nine adolescent girls aged 13–18 years with frequent nightmares. This treatment consisted of (a) selecting the nightmare, (b) modifying the nightmare according to the subject's desires, and (c) rehearing the new version of the dream for 5–20 min each day. When comparing the series to a control group, there was a significant decrease in reported nightmares per month in the study group. A more recent study by Lancee et al. [60] evaluated image rehearsal therapy on a larger scale on a sample of 399 patients with frequent (> 1/week) nightmares. Over a 6-week period, subjects were instructed to use cognitive restructuring techniques to visualize changed nightmares for 10–15 min per day. The study found that patients who underwent image rehearsal therapy underwent a more rapid decrease in nightmare frequency compared to controls. Additionally, subjects reported improved sleep quality, and decreased depression and anxiety. Although this large study specifically excluded children, it overall suggested that image rehearsal treatments may be an effective form of therapy in patients with frequent nightmares.

Lucid Dreaming

Lucid dreaming is a variant of image rehearsal therapy whereby patients are made aware that they are dreaming, thereby enabling them to alter a dream storyline. A study performed on a sample of 16 subjects who underwent 2 h of lucid dreaming counseling either individually or as a group found a significant fall in the frequency of events, though the decline among those who underwent individual treatment was more significant [61]. The therapy was also found to improve dream-frequency reduction in a sample of 5 patients who had PTSD or idiopathic nightmares, previously been treated with progressive deep muscle relaxation and image rehearsal therapy [62].

Progressive Deep Muscle Relaxation

Progressive deep muscle relaxations are procedures in which muscles are tightened and relaxed. The therapy can be combined with breathing exercises, word cues, and imagery. In his study on nightmare therapies, Miller found that the 11 women who underwent the deep muscle relaxation had a larger and more consistent reduction in nightmares compared to controls [59].

Hypnosis

Hypnosis may be beneficial in some children with recurrent nightmares. A prospective analysis was performed on 36 patients (four children) with frequent parasomnias who were treated with hypnosis therapy. Ten patients in the trial suffered from nightmares. All patients were treated with up to two hypnosis sessions. A sustained benefit from the therapy was observed in 40.5 % of patients who responded to the trial over a 5-year period. Unfortunately, the authors concluded that a significant fraction of patients may not respond to hypnosis. This study has not been attempted in an exclusive pediatric cohort.

Pharmacological Interventions

Pharmacological treatments are not warranted for idiopathic nightmare disorders in children, nor have they been tested. Nightmares in PTSD may respond to clonazepam, prazosin, or clonidine [57]. However, clonidine itself can provoke nightmares, because of its short half-life, with subsequent REM rebound.

Conclusion

Despite their high frequency in otherwise normal children, and a benign and self-limiting course, nightmares are distressing events for young people and can be a cause of worry among caregivers. Clinicians should be sensitive to the needs and emotional difficulties experienced by patients who complain of nightmares. Although sporadic nightmares may only require reassurance, patients with frequent nightmares may need further evaluation to identify if these events are secondary to other conditions, especially anxiety disorders. Specialists should especially be capable of differentiating frequent nightmares from those secondary to PTSD, as well as from nocturnal seizures and nocturnal panic attacks. Nightmares should also prompt the treating physician to look for an associated daytime anxiety disorder, which would need to be treated before the nightmares can be controlled.

Lifestyle measures are the mainstay of therapy for idiopathic nightmares. Options may be particularly limited in younger children with persistent nightmares.

Treatments for individuals with persistent nightmares suffer are inadequately tested and few of these strategies have been evaluated for use in children. In older children and adolescents, CBTs, such as desensitization, image rehearsal therapy and deep muscle relaxation may be helpful in controlling these events. In view of their distressing nature and their ramifications on psychiatric health and impaired sleep, better treatments are needed for children with persistent or severe nightmares.

Practical Points

- Nightmares are defined as episodes of awakening following "intensely disturbing" dream mentation involving fear, anger, disgust or other negative emotions.
- Nightmares are experienced by approximately half of 3–6-year-old children.
- Nightmares occur during rapid eye movement sleep and are most common in the early hours of the morning.
- The incidence of nightmares in childhood is roughly equal between boys and girls. Females may experience more nightmares during adolescence.
- Nightmares are more common in posttraumatic stress disorder, anxiety disorders, affective disorders, and Tourette's syndrome. They also occur more commonly in patients taking prescription or recreational drugs.
- Treatment of sporadic nightmares is limited to reassurance and lifestyle measures, including limiting exposure to television and video games before bedtime.
- Persistent nightmares may require psychological counseling and cognitive behavioral therapy.

References

1. McNamara P. Nightmares: the science and solution of those frightening visions during sleep. Westport:Greenwood Publishing Group; 2008.
2. Wittmann L, Schredl M, Kramer M. Dreaming in posttraumatic stress disorder: a critical review of phenomenology, psychophysiology and treatment. Psychother Psychosom. 2007;76(1):25–39.
3. American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic and coding manual. American Academy of Sleep Medicine; 2005.
4. Blagrove M. Haywood S. Evaluating the awakening criterion in the definition of nightmares: how certain are people in judging whether a nightmare woke them up? J Sleep Res. 2006;15(2):117–24.
5. Levin R, Fireman G, Spendlove S, Pope A. The relative contribution of affect load and affect distress as predictors of disturbed dreaming. Behav Sleep Med. 2011;9(3):173–83.
6. Levin R, Nielsen TA. Disturbed dreaming, posttraumatic stress disorder, and affect distress: a review and neurocognitive model. Psychol Bull. 2007;133(3):482–528.
7. Blagrove M, Farmer L, Williams E. The relationship of nightmare frequency and nightmare distress to well-being. J Sleep Res. 2004;13(2):129–36.
8. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. DSM-IV-TR®. Washington: American Psychiatric Association; 2000.
9. Salzarulo P, Chevalier A. Sleep problems in children and their relationship with early disturbances of the waking-sleeping rhythms. Sleep. 1983;6(1):47–51.

10. Simonds JF, Parraga H. Prevalence of sleep disorders and sleep behaviors in children and adolescents. J Am Acad Child Psychiatry. 1982;21(4):383–8.
11. Vela-Bueno A, Bixler E, Dobladez-Blanco B, Rubio M, Mattison R, Kales A. Prevalence of night terrors and nightmares in elementary school children: a pilot study. Res Commun Psychol Psychiatry. 1985;10(3):177–88.
12. Muris P, Merckelbach H, Gadet B, Moulaert V. Fears, worries, and scary dreams in 4- to 12-year-old children: their content, developmental pattern, and origins. J Clin Child Psychol. 2000;29(1):43–52.
13. Chellappa SL, Munch M, Blatter K, Knoblauch V, Cajochen C. Does the circadian modulation of dream recall modify with age? Sleep. 2009;32(9):1201–9.
14. Schredl M, Reinhard I. Gender differences in nightmare frequency: a meta-analysis. Sleep Med Rev. 2011;15(2):115–21.
15. Nielsen TA, Laberge L, Paquet J, Tremblay RE, Vitaro F, Montplaisir J. Development of disturbing dreams during adolescence and their relation to anxiety symptoms. Sleep. 2000;23(6):727–36.
16. Ross L. Sleep and dreaming characteristics of frequent nightmare subjects in a university population. Dreaming. 1994;4(2):127–37.
17. Brand S, Beck J, Kalak N, Gerber M, Kirov R, Puhse U, et al. Dream recall and its relationship to sleep, perceived stress, and creativity among adolescents. J Adolesc Health. 2011;49(5):525–31.
18. Freud S. The interpretation of dreams. Plain Label Books; 1950.
19. Ross L. Ego boundary impairment and thought disorder in frequent nightmare sufferers. Psychoanalytic Psychology. 1990;7(4):529–43.
20. Hartmann E. The nightmare: the psychology and biology of terrifying dreams. New York: Basic Books; 1984.
21. Mindell JA, Barrett KM. Nightmares and anxiety in elementary-aged children: is there a relationship. Child Care Health Dev. 2002;28(4):317–22.
22. Miyauchi S, Misaki M, Kan S, Fukunaga T, Koike T. Human brain activity time-locked to rapid eye movements during REM sleep. Exp Brain Res. 2009;192(4):657–67.
23. Rauch SL, Shin LM, Phelps EA. Neurocircuitry models of posttraumatic stress disorder and extinction: human neuroimaging research—past, present, and future. Biol Psychiatry. 2006;60(4):376–82.
24. Susanszky E, Hajnal A, Kopp M. Sleep disturbances and nightmares as risk factors for suicidal behavior among men and women. Psychiatr Hung. 2011;26(4):250–7.
25. Levin R, Fireman G. Nightmare prevalence, nightmare distress, and self-reported psychological disturbance. Sleep. 2002;25(2):205–12.
26. Simor P, Horvath K, Gombos F, Takacs KP, Bodizs R. Disturbed dreaming and sleep quality: altered sleep architecture in subjects with frequent nightmares. Eur Arch Psychiatry Clin Neurosci. 2012;262(8):687–96.
27. Simor P, Pajkossy P, Horvath K, Bodizs R. Impaired executive functions in subjects with frequent nightmares as reflected by performance in different neuropsychological tasks. Brain Cogn. 2012;78(3):274–83.
28. Simard V, Nielsen TA, Tremblay RE, Boivin M, Montplaisir JY. Longitudinal study of bad dreams in preschool-aged children: prevalence, demographic correlates, risk and protective factors. Sleep. 2008;31(1):62–70.
29. Simard V, Nielsen TA, Tremblay RE, Boivin M, Montplaisir JY. Longitudinal study of preschool sleep disturbance: the predictive role of maladaptive parental behaviors, early sleep problems, and child/mother psychological factors. Arch Pediatr Adolesc Med. 2008;162(4):360–7.
30. Bauer DH. An exploratory study of developmental changes in children's fears. J Child Psychol Psychiatry. 1976;17(1):69–74.
31. Vasey MW, Daleiden EL. Worry in children. In: Davey GCL, Tallis F, editors. Worrying: perspectives on theory, assessment and treatment. Chichester: Wiley; 1994. pp. 185–207.
32. Germain A, Nielsen TA. Sleep pathophysiology in posttraumatic stress disorder and idiopathic nightmare sufferers. Biol Psychiatry. 2003;54(10):1092–8.

33. Spoormaker VI. Montgomery P. Disturbed sleep in post-traumatic stress disorder: secondary symptom or core feature? Sleep Med Rev. 2008;12(3):169–84.
34. Roberts BL, Rickard CM, Rajbhandari D, Reynolds P. Patients' dreams in ICU: recall at two years post discharge and comparison to delirium status during ICU admission. A multicentre cohort study. Intensive Crit Care Nurs. 2006;22(5):264–73.
35. Semiz UB, Basoglu C, Ebrinc S, Cetin M. Nightmaredisorder, dream anxiety, subjective sleep quality in patients with borderline personality disorder. Psychiatry Clin Neurosci. 2008;62(1):48–55.
36. Lusignan FA, Zadra A, Dubuc MJ, Daoust AM, Mottard JP, Godbout R. Dream content in chronically-treated persons with schizophrenia. Schizophr Res. 2009;112(1–3):164–73.
37. Champion LM, Fulton WA, Shady GA. Tourette syndrome and social functioning in a Canadian population. Neurosci Biobehav Rev. 1988;12(3–4):255–7.
38. Vella-Brincat J, Macleod AD. Adverse effects of opioids on the central nervous systems of palliative care patients. J Pain Palliat Care Pharmacother. 2007;21(1):15–25.
39. Ali S, Khan SA, Iram S. Hypocholesterolemia secondary to atrovastatin therapy. J Ayub Med Coll Abbottabad. 2010;22(3):225–7.
40. Boriani G, Biffi M, Strocchi E, Branzi A. Nightmares and sleep disturbances with simvastatin and metoprolol. Ann Pharmacother. 2001;35(10):1292.
41. Gregoor PJ. Atorvastatin may cause nightmares. BMJ. 2006;332(7547):950.
42. Growdon JH, Kieburtz K, McDermott MP, Panisset M, Friedman JH. Levodopa improves motor function without impairing cognition in mild non-demented Parkinson's disease patients. Parkinson Study Group. Neurology. 1998;50(5):1327–31.
43. Blagrove M, Morgan CJ, Curran HV, Bromley L, Brandner B. The incidence of unpleasant dreams after sub-anaesthetic ketamine. Psychopharmacology (Berl). 2009;203(1):109–20.
44. Pagel JF, Helfter P. Drug induced nightmares—an etiology based review. Hum Psychopharmacol. 2003;18(1):59–67.
45. Pace-Schott EF, Gersh T, Silvestri R, Stickgold R, Salzman C, Hobson JA. SSRI treatment suppresses dream recall frequency but increases subjective dream intensity in normal subjects. J Sleep Res. 2001;10(2):129–42.
46. Schierenbeck T, Riemann D, Berger M, Hornyak M. Effect of illicit recreational drugs upon sleep: cocaine, ecstasy and marijuana. Sleep Med Rev. 2008;12(5):381–9.
47. Cernovsky ZZ. MMPI and nightmares in male alcoholics. Percept Mot Skills. 1985;61 (3 Pt 1):841–2.
48. Steinig J, Foraita R, Happe S, Heinze M. Perception of sleep and dreams in alcohol-dependent patients during detoxication and abstinence. Alcohol Alcohol. 2011;46(2):143–7.
49. Cavior N, Deutsch AM. Systematic desensitization to reduce dream-induced anxiety. J Nerv Ment Dis. 1975;161(6):433–5.
50. Palace EM, Johnston C. Treatment of recurrent nightmares by the dream reorganization approach. J Behav Ther Exp Psychiatry. 1989;20(3):219–26.
51. Wile I. Auto-suggested dreams as factor in therapy. Am J Orthopsychiatry. 1934;4:449–63.
52. Krakow B, Sandoval D, Schrader R, Keuhne B, McBride L, Yau CL et al. Treatment of chronic nightmares in adjudicated adolescent girls in a residential facility. J Adolesc Health. 2001;29(2):94–100.
53. Robertsa RN, Gordon SB. Reducing childhood nightmares subsequent to a burn trauma. Child Behav Ther. 1980;1(4):373–81.
54. Pellicer X. Eye movement desensitization treatment of a child's nightmares: a case report. J Behav Ther Exp Psychiatry. 1993;24(1):73–5.
55. Sadeh A. Cognitive-behavioral treatment for childhood sleep disorders. Clin Psychol Rev. 2005;25(5):612–28.
56. Lancee J, Spoormaker VI, Krakow B, van den Bout J. A systematic review of cognitive-behavioral treatment for nightmares: toward a well-established treatment. J Clin Sleep Med. 2008;4(5):475–80.
57. Aurora RN, Zak RS, Auerbach SH, Casey KR, Chowdhuri S, Karippot A et al. Best practice guide for the treatment of nightmare disorder in adults. J Clin Sleep Med. 2010;6(4):389–401.

58. Burgess M, Gill M, Marks I. Postal self-exposure treatment of recurrent nightmares. Randomised controlled trial. Br J Psychiatry. 1998;172:257–62.
59. Miller WR, DiPilato M. Treatment of nightmares via relaxation and desensitization: a controlled evaluation. J Consult Clin Psychol. 1983;51(6):870–7.
60. Lancee J, Spoormaker VI, van den Bout J. Cognitive-behavioral self-help treatment for nightmares: a randomized controlled trial. Psychother Psychosom. 2010;79(6):371–7.
61. Spoormaker VI, van den Bout J. Lucid dreaming treatment for nightmares: a pilot study. Psychother Psychosom. 2006;75(6):389–94.
62. Zadra AL, Pihl RO. Lucid dreaming as a treatment for recurrent nightmares. Psychother Psychosom. 1997;66(1):50–5.

Chapter 13
Recurrent Isolated Sleep Paralysis (RISP)

Sricharan Moturi and Poojitha Matta

Prevalence and Etiology

Multiple studies have looked into the prevalence of isolated sleep paralysis (ISP) episodes in various populations. Some of the earlier studies that focused on African–American populations have found prevalence ranging from 25–41 % [1, 2]. One study that looked into episodes of ISP in Nigerian workers pits the prevalence at 35.5 % [3], while studies in Asian populations described prevalence ranging from 18–40 % [4, 5]. Other studies that focused on Caucasian populations note the prevalence to be ranging from 5–23 % [6, 7, 8]. One web-based survey notes that ISP occurs at least once in a lifetime in 40–50 % of normal subjects, while as a chronic complaint it was noted to be uncommon [9]. Spanos et al. [10] note that only 4 % of the interviewed subjects reported five or more sleep paralysis episodes during their lifetime, further strengthening the notion that RISP is in fact an uncommon parasomnia. Finally, a recent systematic review that looked into prevalence studies from 1950–present concludes that 7.6 % of the general population, 28.3 % of students, and 31.9 % of psychiatric patients experienced at least one episode of sleep paralysis. The prevalence increases to 34.6 % in psychiatric patients diagnosed with panic disorder; also note that minorities tend to experience ISP more frequently than Caucasians [11]. Gender differences in prevalence have not been shown in these studies.

Many studies have documented the association between anxiety disorders and ISP episodes. One such study notes the higher incidence of ISP in individuals presenting with panic disorder and social anxiety disorder to an outpatient clinic, but

S. Moturi (✉)
Adolescent Psychiatry, Rolling Hills Hospital, 2014 Quail Hollow Circle,
Franklin, TN 37067, USA
e-mail: charanmd@gmail.com

P. Matta
Emory University, Atlanta, GA, USA
e-mail: poojitha.matta@emory.edu

8189 Londonberry Road, Nashville, TN 37221, USA
e-mail: poojithamatta@gmail.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_13, © Springer Science+Business Media New York 2013

this link appears to be inconclusive in individuals with depressive disorders [12]. One review showed higher incidence of ISP in African–Americans diagnosed with panic disorder [13]. Some other studies looked into the association of trauma and posttraumatic stress disorders with comorbid ISP [14, 15]. One case report noted the association between insufficient sleep duration and fearful RISP episodes [16]. Isolated sleep paralysis episodes were elicited in a group of individuals by forced nocturnal sleep interruption and most of these episodes occurred during sleep-onset REM periods (SOREMP) [17]. Sleep paralysis episodes with hallucinations also tend to occur more frequently in supine position, although the exact mechanism of this finding remains unknown [18]. Other potential causes that were hypothesized behind the occurrence of ISP were disrupted sleep associated with shift-work, use of anxiolytics to treat underlying anxiety states, and history of current ongoing stress. Periods of low geomagnetic activity within the earth's magnetic field has also been associated with increased incidence of ISP and intensity of bizarreness associated with dreams, but this is yet to be replicated in larger study samples [19, 20].

Pathophysiology

Neural mechanisms appear to be involved in the pathophysiology of sleep paralysis. Hishikawa and Shimizu proposed that sleep paralysis is caused by the marked dissociation between the level of alertness and muscle atonia that is often seen in SOREM sleep episodes. They also proposed that monoaminergic (Serotonin/noradrenaline) neurons tend to have an inhibiting influence on cholinergic neurons thereby causing generalized muscle atonia and REM sleep [21]. One case report suggested that sleep paralysis possibly encompasses dissociated state of mind together with the dissociative motor component and that an intermediate state of mind exists between wake and REM during the paralysis episode [22]. A non-HLA linked genetic factor along with environmental factors has also been proposed behind the occurrence of ISP episodes [23]. Psychoanalytic explanations of sleep paralysis episodes have been explored and one such explanation sees it as a manifestation of an inhibition that serves to ward off forbidden impulses.

Clinical Signs and Symptoms

ISP is characterized by a generalized transient inability to move the head, body, and extremities, but respiratory and ocular muscles are spared. These episodes can occur at either sleep onset (hypnagogic) or sleep offset (hypnapompic). Patients cannot speak during these episodes and there is atonia and areflexia. Auditory, visual, or tactile hallucinations can accompany these episodes often leading to confusion and anxiety. These episodes were often described by patients as "electricity shooting through the body" or "aliens standing next to my bed". Patients with sleep paralysis episodes also tend to attach personal and cultural narratives to explain these rather

perplexing phenomena. It appears that these narratives have significant cultural influences [24]. A specific example of this is in patients who experience breathing difficulties and sleep paralysis. These events have been described by patients as a person sitting on their chests (vivid hallucination). The specific description of who is "sitting" on the patient's chest within the narrative may vary from culture to culture (e.g., an old hag or witch may be described by a patient in Newfoundland or the USA while "kanashibari," a term related to supernatural powers, may be described by a patient in Japan) [25]. Patients who experience hallucinations with sleep paralysis may attach significance to these hallucinations leading to delusional explanations of such experiences [26]. Patients with ISP can typically become fearful about bedtime and tend to "fight off" nocturnal sleep leading to sleep deprivation and excessive daytime sleepiness further causing a vicious cycle of more frequent episodes.

Familial forms of ISP have been reported in the literature [23]. In a personal communication with a sleep clinician at a university, a familial form of ISP was recently discussed. A 10-year-old Hispanic child was referred to a university sleep clinic for evaluation of terrifying experiences at sleep onset. The child described sleep paralysis episodes associated with dissociative phenomena such as watching his entire body flying around the room along with auditory hallucinations of ringing sounds. Upon further questioning, it was ascertained that his mother and grandmother experienced similar episodes intermittently over their lifetime, but were never evaluated or received treatment [27]. Onset of ISP usually occurs in adolescence with no gender differences noted. Typically, these episodes resolve spontaneously after few seconds to minutes; or can be resolved by light, touch, or sound. Differential diagnosis of ISP episodes include nocturnal seizures, periodic paralysis associated with hyperkalemia/hypokalemia, sleep related hallucinations, primary psychosis, severe anxiety disorders including nocturnal panic attacks, conversion disorders, and cataplexy attacks. Polysomnogram (PSG) recordings during ISP were characterized by a REM-Wake stage dissociated state with predominant alpha electroencephalograph activity and persistence of muscle atonia as shown by the tonic electromyogram [17]. A study of 31 African–American patients with elevated blood pressure revealed that 41.9 % had isolated sleep paralysis, 35.5 % had panic attacks, and 9.7 % had panic disorder. These hyperadrenergic phenomena may be related to the development of hypertension in certain individuals [28]. Another study explored the effects of ISP on quality of life in obstructive sleep apnea patients and concluded that ISP was independently associated with excessive daytime sleepiness, worse sleep quality, and impaired mental health-related quality of life [29]. Therefore, it is important to screen for such comorbidities in patients with ISP and appropriately address them.

Management

It is important to identify precipitants to sleep paralysis episodes and to avoid them completely including sleep deprivation. Improving sleep hygiene with strict bedtime and wake time is equally important. Initiating a sleep diary with recordings of event

type and frequency can be helpful for discussions with clinicians during regular follow-up visits. Serotonergic agents like Fluoxetine have been shown to be helpful in reducing the frequency of ISP episodes [30]. In the personal communication noted above about familial RISP, it was also noted that the child had complete resolution of sleep paralysis episodes with a mixture of low-dose melatonin and sleep hygiene measures [27]. Patients should also be screened for underlying anxiety disorders and appropriate referrals and treatments should be initiated.

Practical Points

- ISP is a relatively rare parasomnia in its recurrent form, but common in its isolated form.
- RISP is often associated with auditory, visual, or tactile hallucinations mostly hypnapompic in nature.
- Familial forms of illness have been reported and may pave the way for genetic studies and gene mapping.
- Patients often attach cultural significance to these episodes and are associated with intense fright and fear during the episodes.
- Daytime sequelae of these episodes could be sleepiness, anxious preoccupations, and delusional explanations.
- RISP can be precipitated by stress, irregular sleep patterns, sleep disruption, and reduced total sleep duration, and therefore improving sleep hygiene and sleep duration is paramount to reduce the frequency of these episodes. Screening for underlying sleep disorders, medical disorders, and psychiatric disorders should be undertaken in patients with RISP.

Case Example

A 10-year-old child presents to a sleep clinic brought by his parents for evaluation of frightening nocturnal experiences at bedtime. The child describes them as of gradual onset, and often experiencing intense dissociative symptoms. He would often describe himself as flying above his head, hovering around his bed, but also cannot move his body during the experiences. He also experiences auditory hallucinations of "someone" calling his name in the midst of these episodes. These episodes tend to occur mostly surrounding his bedtime or during random nocturnal awakenings but the child describes himself as being fully wake during the actual episodes. These episodes seem to have intensified in their frequency from once a month to twice a week. As a result of these episodes, the child had been showing intense bedtime resistance with nocturnal anxiety often refusing to go into his bedroom at night. He had been feeling sleepier during the day thus affecting his attention span and grades at school. The child had no symptoms suggestive of cataplexy, sleep apnea, or

restless legs syndrome. Upon further questioning, both his mother and grandmother have been experiencing similar episodes over their lifetime and describe them as "terrifying". It is important to note that both individuals have written these episodes off as something to do with "god and culture", and have never received treatment for the same.

Examination revealed the child in no apparent distress. Blood pressure was 106/72 mm Hg; pulse was 80 beats/min and regular; height was 4 ft 9 in.; and weight was 79 pounds. Upper airway exam revealed an upper airway that is not crowded with any evidence of tonsillar hypertrophy. Neck circumference was 11.5 in. with no thyromegaly or lymphadenopathy. Cardiopulmonary exam and abdominal exam revealed no abnormalities. He was alert and fully oriented, and his thought process/content was linear, logical, and goal directed. Affect was slightly anxious but was largely appropriate.

Initial blood investigations including complete blood count (CBC) with differential/platelets and comprehensive metabolic panel including thyroid stimulating hormone were within normal limits.

References

1. Bell CC, Shakoor B, Thompson B, Dew D, Hughley E, Mays R, Shorter-Gooden K. Prevalence of isolated sleep paralysis in black subjects. J Natl Med Assoc. 1984 May;76(5):501–8.
2. Bell CC, Dixie-Bell DD, Thompson B. Further studies on the prevalence of isolated sleep paralysis in black subjects. J Natl Med Assoc. 1986 Jul;78(7):649–59.
3. Ohaeri JU. The prevalence of isolated sleep paralysis among a sample of Nigerian civil servants and undergraduates. Afr J Med Med Sci. 1997 Mar-Jun;26(1–2):43–5.
4. Fukuda K, Miyasita A, Inugami M, Ishihara K. High prevalence of isolated sleep paralysis: kanashibari phenomenon in Japan. Sleep. 1987 Jun;10(3):279–86.
5. Wing YK, Chiu H, Leung T, Ng J. Sleep paralysis in the elderly. J Sleep Res. 1999 Jun;8(2): 151–5.
6. Goode GB. Sleep paralysis. Arch Neurol. 1962;6:228–234
7. Everett HC. Sleep paralysis in medical students. J Nerv Ment Dis. 1963;136:283–287
8. Hufford D. The terror that comes in the night. Pennsylvania: University of Pennsylvania Press. 1982, p. 23
9. Buzzi G, Cirignotta F. Isolated sleep paralysis: a web survey. Sleep Res Online. 2000;3(2):61–6.
10. Spanos NP, DuBreuil C, McNulta SA et al. The frequency and correlates of sleep paralysis in a university sample. J Res Pers. 1995;29:285–305.
11. Sharpless BA, Barber JP. Lifetime prevalence rates of sleep paralysis: a systematic review. Sleep Med Rev. 2011 Oct;15(5):311–5.
12. Otto MW, Simon NM, Powers M, Hinton D, Zalta AK, Pollack MH. Rates of isolated sleep paralysis in outpatients with anxiety disorders. J Anxiety Disord. 2006;20(5):687–93.
13. Friedman S, Paradis C. Panic disorder in African–Americans: symptomatology and isolated sleep paralysis. Cult Med Psychiatry. 2002 Jun;26(2):179–98.
14. Ramsawh HJ, Raffa SD, White KS, Barlow DH. Risk factors for isolated sleep paralysis in an African–American sample: a preliminary study. Behav Ther. 2008 Dec;39(4):386–97.
15. Mellman TA, Aigbogun N, Graves RE, Lawson WB, Alim TN. Sleep paralysis and trauma, psychiatric symptoms and disorders in an adult African–American population attending primary medical care. Depress Anxiety. 2008;25(5):435–40.

16. McCarty DE, Chesson AL Jr. A case of sleep paralysis with hypnopompic hallucinations. Recurrent isolated sleep paralysis associated with hypnopompic hallucinations, precipitated by behaviorally induced insufficient sleep syndrome. J Clin Sleep Med. 2009 Feb 15;5(1):83–4.
17. Takeuchi T, Miyasita A, Sasaki Y, Inugami M, Fukuda K. Isolated sleep paralysis elicited by sleep interruption. Sleep. 1992 Jun;15(3):217–25.
18. Dahmen N, Kasten M. REM-associated hallucinations and sleep paralysis are dependent on body posture. J Neurol. 2001 May;248(5):423–4.
19. Lipnicki DM. An association between geomagnetic activity and dream bizarreness. Med Hypotheses. 2009 Jul;73(1):115–7.
20. Conesa J. Relationship between isolated sleep paralysis and geomagnetic influences: a case study. Percept Mot Skills. 1995 Jun;80(3 Pt 2):1263–73.
21. Hishikawa Y, Shimizu T. Physiology of REM sleep, cataplexy, and sleep paralysis. Adv Neurol. 1995;67:245–71.
22. Terzaghi M, Ratti PL. Manni F, Manni R. Sleep paralysis in narcolepsy: more than just a motor dissociative phenomenon? Neurol Sci. 2012 Feb;33(1):169–72.
23. Dahlitz M, Parkes JD. Sleep paralysis. Lancet. 1993 Feb 13;341(8842):406–7.
24. Douglass AB, Hays P, Pazderka F, Russell JM. Florid refractory schizophrenias that turn out to be treatable variants of HLA-associated narcolepsy. J Nerv Ment Dis. 1991 Jan;179(1):12–7.
25. Douglass AB, Shipley JE, Haines RF, Scholten RC, Dudley E, Tapp A. Schizophrenia, narcolepsy, and HLA-DR15, DQ6. Biol Psychiatry. 1993 Dec 1;34(11):773–80.
26. Moturi S, Ivanenko A. Complex diagnostic and treatment issues in psychotic symptoms associated with narcolepsy. Psychiatry (Edgmont). 2009 Jun;6(6):38–44.
27. Personal communication with Dr. David Lozano MD, University of Alabama at Birmingham. June 2010.
28. Bell CC, Hildreth CJ, Jenkins EJ, Carter C. The relationship of isolated sleep paralysis and panic disorder to hypertension. J Natl Med Assoc. 1988 Mar;80(3):289–94.
29. Hsieh SW, Lai CL, Liu CK, Lan SH, Hsu CY. Isolated sleep paralysis linked to impaired nocturnal sleep quality and health-related quality of life in Chinese-Taiwanese patients with obstructive sleep apnea. Qual Life Res. 2010 Nov;19(9):1265–72.
30. Koran LM, Raghavan S. Fluoxetine for isolated sleep paralysis. Psychosomatics. 1993 Mar-Apr;34(2):184–7.

Chapter 14
Sleep-Related Hallucinations

Anna Ivanenko and Sachin Relia

Introduction

Hallucinations are perceptual disturbances in the absence of a stimulus that can occur in the normal healthy individuals, but are most commonly associated with psychiatric and neurological conditions. Hallucinations can occur in any sensory modality—visual, auditory, olfactory, gustatory, tactile, proprioceptive, equilibrioceptive, nociceptive, thermoceptive, and chronoceptive. They occur in a conscious and awake state and are different from illusions, which involve distorted or misinterpreted real perception, and from dreams which involve recollection of mental activity during sleep. In the majority of clinical cases, several types of hallucinations occur simultaneously and are associated with some degree of emotional distress.

Sleep-related hallucinations are a type of perceptual experience that occurs during transition to sleep or at awakening. The exact pathophysiology of sleep-related hallucination remains unknown. However, it has been suggested that they may represent a state of dissociation with intrusion of dreams into wakefulness [1].

This chapter provides a comprehensive review of clinical characteristics, prevalence, differential diagnosis, and treatment of sleep-related hallucinations.

A. Ivanenko (✉)
Division of Child and Adolescent Psychiatry, Feinberg School of Medicine,
Northwestern University, Ann & Robert H. Lurie Children's Hospital of Chicago,
Chicago, IL, USA
e-mail: aivanenko@sbcglobal.net

Ann & Robert H. Lurie Children's Hospital of Chicago,
225 East Chicago Avenue, Chicago, Illinois 60611–2605, USA

S. Relia
Division of Child and Adolescent Psychiatry,
Medical College of Wisconsin, Milwaukee, WI 53326, USA
e-mail: sachinrelia@gmail.com

6492 Bantry Bay St., Dublin, CA 94568, USA

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_14, © Springer Science+Business Media New York 2013

Historical Perspective

DSM-IV defines a hallucination as "a sensory perception that has a compelling sense of reality of a true perception but that occurs without external stimulation of the relevant sensory organ" [2]. The word hallucination has its roots in the Latin word "hallucinare" or "allucinere" which means to "wander in mind". The earliest use of the word "hallucination" dates back to 1572 when Lavater used it to describe "ghostes and spirites walking the night". It was first used in the English language by Sir Thomas Browne in 1642. An outstanding French psychiatrist Jean-Etienne Esquirol coined the term "hallucination" into a modern field of clinical psychiatry in his famous textbook *Des maladies mentales, considérées sous les rapports médical, hygiénique, et médico-légal* (1838).

Hallucinations occur in various psychiatric, neurological, and medical conditions. Among subjects who met diagnostic criteria for major depressive disorder 6.8 % reported having episodes of hallucinations [3]. In patients with bipolar disorder, psychotic symptoms with hallucinations are present in 20–50 % of patients [4, 5]. Disturbing visual, auditory, and tactile hallucinations are commonly seen in patients with Parkinson's disease (PD) [6] and among patients with Alzheimer's disease (AD) ranging from 13 to 16 % [7]. Most notably, hallucinations are associated with schizophrenia. It is reported that approximately 74 % of patients with schizophrenia will experience auditory hallucinations (AH) during the course of their illness [8]. Hallucinations in patients with schizophrenia are characterized by poor reality testing, intrusiveness, and are associated with greater subjective distress.

Prevalence of Hallucinations in the General Population

Literature suggests that hallucinations may also occur in the "normal" general population. An NIMH study by Tien et al., revealed the lifetime prevalence of hallucinations as 10 % for men and 15 % for women [9]. In the same study, 2 % of men and 1.3 % of women also reported visual hallucinations (VH). Several studies have looked into a prevalence of hallucinations among college students. In a sample of 375 college students, 71 % reported occasional, brief hallucinatory voices during periods of wakefulness [10]. These findings were replicated by other studies where a considerable proportion of students reported hearing a voice speaking their thoughts aloud [11–13].

In the most recent survey of 134 medical students, 74 respondents answered affirmatively to one or more screening questions about having hallucinations: 22.2 % of those described visual and 64.8 %, auditory hallucinations [14]. The majority reported sleep-related experiences and AH such as hearing the telephone or the doorbell ring (38.8 %). All subjects had good insight and none had psychotic symptoms. Only two cases were associated with substance abuse.

Differences in characteristics of hallucinations in clinical and nonclinical populations have been examined in several studies. Most differences were found

in the content, emotional quality, and locus of control of the AH. Patient groups would frequently describe their voices as negative, frightening, and disturbing and had delusional explanations for them. Nonclinical subjects were able to keep their hallucinations under control and described them as more positive and less threatening [15, 16]

Definition of Sleep-Related Hallucinations

A hypnagogic hallucination is a vivid, dream-like sensation that is heard, seen, or felt, and that occurs near the onset of sleep. Hypnopompic hallucinations are similar experiences that occur at awakening. The term hypnagogic was coined by Maury from "hypno" meaning sleep and "agogos" meaning induced [17]. "Pompe" meaning the act of sending was first used by Myers in 1903 and he coined the term "hypnopompic" to describe imagery and pictures due to "persistence of some dream-image into first moments of waking" [18].

Prevalence and Clinical Characteristics of Sleep-Related Hallucination in the General Population

Hypnopompic and hypnagogic phenomenon is highly prevalent in the general population. In a study by Ohayon (2000) of approximately 6,000 men and women, 38.7 % reported hallucinatory experiences [19]. In another study of 400 subjects, 37 % of the sample reported at least one type of hypnagogic hallucinations (HH) and 12.5 % reported hypnopompic hallucinations occurring at least twice a week in the last year [20]. Women and individuals of younger age are more likely to report sleep-related hallucinations. Hypnagogic and hypnopompic hallucinations are usually visual but can be auditory, tactile, and kinetic. They can last from a few seconds to more than 15 min, depending on the stage of drowsiness. The main difference between dreams and HH phenomenon is that in a case of HH the individual experiences himself being on the outside observing the action. To the contrary, in a dream an individual is actively involved and there is usually a plot.

Auditory hypnagogic and hypnopompic hallucinations can include crashing noises, ones' name being called, a doorbell ringing, neologisms, irrelevant sentences, pompous nonsense, quotations, references to spoken conversations, remarks directed to oneself, and meaningful responses to ones' thought of the moment [21].

Visual component of HH can range from simple spots of light to geometric patterns to complex images [22]. Human figures or faces (torsos without heads or vice versa), animals (real or bizarre), miniature images, or scenery of outstanding beauty have been described.

The most common type of HH is an experience of falling down an abyss, and perception of something or someone being in the room. Women and younger individuals are more likely to report these phenomena. The main difference between HH and actual visual and auditory hallucinations is the significance ascribed by an individual to the perceptual phenomenon [19].

Case Example 1

An 8-year-old boy presented with his mother after he experienced several episodes of hypnopompic hallucinations. All episodes were described as similar and consistent of him waking up from sleep usually within 1–2 h from sleep onset and seeing objects in the rooms moving away from him "getting farther and farther". Each episode would last for several minutes and was accompanied by severe fear, panic, and emotional agitation. Patient would run into his parents' bedroom feeling terrified, shaking, and would refuse to go back to his bedroom. He had full recollection of the episodes and good insight into these experiences being not real. The patient started avoiding going to bed due to the fear of having hallucinations during sleep. First episode occurred during the course of acute respiratory illness when he had fever, and parents attributed it to the infection. However, the next several episodes did not seem be associated with any physical illness, although emotional triggers were identified like starting a new school or transitioning to a new house. His medical, developmental, and psychiatric history was unremarkable, except for a tendency to worry a lot and to get easily frustrated. He was not taking any medication at the time of evaluation. Nocturnal polysomnography (PSG) was conducted to rule out other intrinsic sleep disorders that showed normal results. Positive bedtime routine with relaxation at bedtime was recommended as part of therapeutic intervention. The patient was reassured about these episodes being "not dangerous" and that he can learn how to control his feelings once they happen again. Formal psychotherapy was recommended to address symptoms of anxiety and stress management.

Complex Nocturnal Visual Hallucinations

A less common variant of HH is the phenomenon of complex nocturnal visual hallucinations (CNVH). CNVH are described as prolonged episodes of complex, vivid VH, which occur after waking during the night. CNVH differ from HH as these occur after an individual awakes in the middle of the night. Silber et al. described a series of 12 patients reporting these symptoms. Mean age of the patients in this series was 40 years, and they reported having an average of 4.4 events per week. Symptoms of CNVH were described by patients as vivid, detailed, and relatively immobile images of people and animals. For example, one patient described "a witch-like, short, baggy woman, clowns, rats, and a brightly colored butterfly" [23]. The images were often distorted, e.g., woman with hair on only half of her head. The events usually lasted

for less than 5 min but in one patient it persisted for up to an hour. Several patients left the bed to investigate and one sustained an injury. Of the 12 patients, only one patient had three recordable events that occurred after arousal from stage 2 and stage 3 of non-rapid eye movement (NREM) sleep on the PSG. Electroencephalography (EEG) during the hallucinations showed alpha rhythm without any epileptic activity. Interestingly, most of the patients had associated conditions including dementia with Lewy bodies (DLB), macular degeneration, and anxiety disorder. Despite clinically significant associated conditions, CNVH were described as a separate entity from hallucinatory phenomenon in DLB and PD as patients only had CNVH on waking up from sleep. To the contrary, patients with DLB, PD, and peduncular hallucinosis (PH) tend to have hallucinations both during the day and at night.

A case of a girl with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) was recently reported who experienced a 3-h episode of nocturnal complex bizarre visual hallucinations when treated with 18 mg Osmotic release oral system (OROS) methylphenidate (MPH). Later, this child was found to have episodes of confusional arousal on nocturnal PSG and the authors speculated that her preexisting physiological vulnerability toward parasomnias increased the risk of MPH induced sleep side effects [24].

Sleep-Related Hallucinations in Patients with Narcolepsy

Narcolepsy is the central nervous system disorder characterized by excessive daytime sleepiness, fragmented sleep, and cataplexy. In addition, patients may experience sleep paralysis and hypnagogic and hypnopompic hallucinations. HHs in patients with narcolepsy can be very pervasive, vivid, and disturbing. Literature analysis indicates high prevalence of HHs across different studies. Visual, auditory, tactile, olfactory, somatic, and vestibular hallucinations were reported by 79.4 % of patients with narcolepsy when clinical characteristics were studied in 129 patients [25]. Similar rate of HHs (79.7 %) was found among patients with narcolepsy when using the Stanford Center for Narcolepsy Sleep Inventory [26]. Additional analysis of HHs demonstrated VH in 83 % of cases, kinetic in 71 %, and auditory in 45 % of patients.

A cross-sectional study was performed by Fortuyn et al. [27] to compare psychotic symptoms among three samples of subjects: 60 patients with narcolepsy-cataplexy, 102 patients with schizophrenia, and 120 normal controls. A total of 83 % of patients with narcolepsy experienced hallucinations "ever in life" compared to 70 % of patients with schizophrenia. However, only 4 % of patients with schizophrenia reported having HHs compared to 65 % of those with narcolepsy. Patients with narcolepsy reported HHs when going to sleep at night and waking up in the morning as well as during daytime sleep episodes. AH in patients with narcolepsy were often of nonverbal quality such as footsteps, animal noises, door openings, door bell rings, etc. VH associated with narcolepsy were more fragmentary and often reported in combination with auditory and tactile modality. Kinetic hallucinations like flying were reported as a frequent hypnagogic phenomena with some cases of out-of-body experiences being described. Occasionally, patients reported olfactory HHs of bad

odors. Narcolepsy patients compared to patients with schizophrenia have more insight about their perceptual experiences and understanding that they are not real.

In a more recent study, clinical characteristics of hallucinations and their risk factors were compared in 100 patients of narcolepsy with and without cataplexy and 100 patients with PD [28]. Hallucinations occurred more frequently and with more motor and multimodal aspects in narcolepsy with cataplexy (59 %) than in narcolepsy without cataplexy (28 %). Compared to PD, the hallucinations in narcolepsy were more frequently auditory and more often associated with sleep. Interestingly, patients with cataplexy had reduced immediate insight into the unreality of their hallucinations compared to other patients in the study, which is possibly due to multimodal nature and dream-like characteristics of their hallucinations. The risk factors for hallucinations in cases of narcolepsy included sleep paralysis and rapid eye movement (REM) behavior disorder. The authors suggested that high frequency of hallucinations in patients with narcolepsy with cataplexy may indicate that hypocretin-1 deficiency promotes hallucinations.

Modafinil is one of only few drugs approved by the Federal Drug Administration (FDA) for the treatment of narcolepsy. Armodafinil is a R-isomer of modafinil which became available in 2007 for the treatment of excessive daytime sleepiness associated with narcolepsy and has a longer half-life of 10–15 h than that of the S-enantiomer. Both compounds are well tolerated with the most frequent side effects reported as headache and nausea. Modafinil and armodafinil has been widely used for the treatment of excessive daytime sleepiness in patients with various sleep disorders and other neurological conditions. However, there have been cases of hallucinations and other psychotic symptoms caused by modafinil described in patients with narcolepsy, Kleine-Levin syndrome, and DLB [29–31]. Hallucinations induced by the administration of modafinil should be not be mistaken for HH associated with the natural course of narcolepsy as they remit with the discontinuation of modafinil. Reduction in the dose of modafinil may also help to alleviate undesirable side effects. Since there are limited research data available on the risks factors associated with modafinil-induced agitation and hallucinations, it should be used with caution, especially at higher therapeutic doses.

Sleep-Related Hallucination Associated with Medication Use

Use of sedative hypnotics has been associated with sleep-related behaviors, including reports of sleep-related hallucinations. Zolpidem, an imidazopyridine derivative is a widely prescribed and highly effective pharmacological agent for the treatment of insomnia. It is a relatively short-acting, with a terminal elimination half-life of 1.5–3.2 h. Zolpidem was shown to be associated with the rare episodes of complex sleep-related behaviors like VH, delirium, sleepwalking, amnesia, and nocturnal eating.

A number of cases have been described of patients who developed hallucinations shortly after taking zolpidem prior to initiating sleep. A post-marketing study of zolpidem reported 0.3 % of patients experiencing hallucinations [32]. The authors of the study proposed several factors to be considered when prescribing zolpidem: gender

because women have been found to have a higher serum levels of zolpidem than men by 40 % dose; hallucinations occurred with doses above 5 mg per day and were dose-dependent; protein-binding affinity; and since high proportion of zolpidem is protein bound, patients with low levels of free albumin may have higher concentration of free zolpidem. Also, medications that are highly protein bound may displace zolpidem from its carrier protein, therefore creating elevated serum levels of free zolpidem, so are the drugs causing. CYP3A4 isoenzyme inhibition; zolpidem metabolized via the CYP3A4 isoenzyme. Medication, especially antidepressants, may decrease zolpidem metabolism leading to toxicity [33]. The majority of patients who experienced hallucinations from zolpidem were taking antidepressants like paroxetine and fluvoxamine at the same time. Possible interactions between serotonin reuptake inhibitors (SSRIs) and zolpidem should be considered when drugs are prescribed concomitantly [34].

Case Example 2

A 10-year-old Caucasian female with a long history of ADHD and OCD who has also been suffering from the sleep onset and maintenance insomnia took 6.25 mg of zolpidem-CR at bedtime for the first time. At the time of zolpidem administration, she was taking sertraline and adderall XR. Prior to being prescribed zolpidem, she was treated with behavioral sleep interventions and several medications with sedative properties including melatonin, trazadone, and clonidine. None of them were effective in reducing sleep onset latency and in improving sleep continuity. Shortly after taking zolpidem-CR she began to experience visual and auditory hallucinations. The patient reported seeing pictures on the walls moving and angels flying in the room. She also heard voices coming from pictures talking to her and angels singing songs and became frightened and agitated by these perceptual experiences. Her mother took her to the Emergency Room at the University Medical Center where she remained until hallucinations subsided. According to the patient's mother, these episodes lasted for several hours, the patient appeared confused, and was responding to internal stimuli by talking back to the "voices" and running after "angels" in the room. She subsequently fell asleep. All her symptoms cleared without treatment and she had full recollection of the entire episode on the next day.

Sleep-Related Hallucinations Associated with Charles Bonnet Syndrome

Nocturnal VH of variable etiologies have been described in the literature going back to 1760 when Charles Bonnet first published a case of complex VH in his grandfather who developed visual impairments from cataracts [35]. Subsequently,

Menon et al. [36] conducted a study of complex VH in the visually impaired individuals. They described characteristics of complex VH as being associated with intact mental functioning, absence of any neurological/psychiatric disease, intact insight, and hallucinations present only in the visual domain.

Charles Bonnet Syndrome (CBS) can be understood as a deafferentation syndrome similar to phantom limb pain. It has been proposed that symptoms arise when cortical structures are disconnected from subcortical afferents. Absence of an appropriate input can lead to these deafferentation syndromes in different modalities. Neuroimaginig studies have supported a hypothesis that CBS is a cortical release phenomenon. Normally, external stimuli is perceived in the retina and transmitted to the primary visual cortex (BA 17) and then to secondary areas and association cortices (BA 18, 19, 37). In general, perception of external visual stimuli has an inhibitory effect on endogenous activation of the visual cortex. Visual impairment releases visual cortex from the regulation by external stimuli resulting in VH [37].

In a study of 505 patients with visual impairments, 60 met the criteria for CBS. VH caused distress in about 28 % of the patients [38]. Most commonly, hallucinations were reported in the evening (35 %) and at night (23 %). Clinical characteristics of hallucinations ranged from simple images of objects to a bizarre visual experience of "two miniature policemen guiding a midget villain to a tiny prison van". Approximately 65 % of the patients reported poor lighting as a favorable circumstance for the hallucinations [38]. There is no specific treatment for VH associated with CBS except for reassurance and education.

Sleep-Related Hallucinations Associated with Parkinson's Disease and Lewy Body Dementia

PD and DLB are neurodegenerative conditions classified as alpha-synucleinopathies. Hallucinations may occur either spontaneously or as a side effect of dopaminergic medications. In PD, the prevalence of complex VH ranges from 22 to 38 % [39]. Risk factors for VH include older age, longer duration of symptoms, cognitive impairment, severity of PD, presence of sleep disorder, and visual impairments. Hallucinations can range from benign phenomenon, such as presence of sensation, passing lights, visions at the periphery of visual field to elaborate hallucinations, such as wild animals and fantastic human creatures. The hallucinations are either experienced during the day or in the form of CNVH.

One potential pathophysiological mechanism suggests the deposition of Lewy body in the brainstem causing dysfunction of this key brain structure responsible for the state transitions between wakefulness, NREM, and REM sleep. This may lead to intrusion of REM phenomenon into wakefulness causing hallucinations. The other putative mechanism is a Lewy body deposition in the neocortical areas of the visual cortex, which gives rise to hallucinations as a cortical release phenomenon.

Sleep-Related Hallucinations in Patients with Peduncular Hallucinosis (PH)

PH is a syndrome that involves hallucinations caused by lesions in the brainstem including pons, midbrain, or subcortical structures including thalamus. This syndrome was originally described by Lhermitte in association with a rostral brainstem lesion in a patient with visual and tactile hallucinations [40]. The etiology of this syndrome is usually vascular, however, there have been cases of brain tumors and postoperative complications of brain stem surgery reported in the cases of PH [22, 41, 42]. The hallucinations consist of visual images similar to HH. They may last from minutes to several hours and may persist into waking. Interestingly, hallucinations seem to follow a diurnal pattern; they disappear during the day and reoccur in the evening [22].

Sleep-Related Hallucinations in Patients with Epilepsy

Hallucinations commonly occur in patients with epilepsy. Frontal lobe seizures frequently manifest during sleep compared to other types of partial seizures. VH associated with epilepsy are usually described as brief, stereotyped, and fragmentary. Hallucinations may be associated with other seizure manifestations, such as altered consciousness, motor activity, and behavioral automatisms. Visual images are unlikely to be identified by the patient, and may appear in color or in black and white. Complex VH have also been described in epilepsy but they occur rarely. Proposed pathophysiological mechanism of hallucinations in patients with epilepsy includes possible activation of primary sensory areas of cortex causing simple visual or auditory phenomena. Another possible etiology suggests that seizures originating in the visual or auditory association cortex can cause more complex hallucinations and memory flashbacks [43]. Differential diagnosis of this perceptual phenomenon includes epileptic illusions, déjà vu, jamais vu, macropsia, micropsia, depersonalization, derealization, and other perceptual abnormalities seen in patients with various forms of epilepsy [44].

Sleep-Related Hallucinations Associated with Migraine

VH can be a part of classical aura in migraine or a part of manifestation of migraine coma or familial hemiplegic migraine. The prevalence of migraines in the general population has been estimated to be between 15 and 29 % [45]. As many as one third of patients with migraines have an aura and about 99 % of them have some type of visual symptoms [46]. The classic visual aura starts as a flickering, uncolored, unilateral zigzag line in the center of the visual field that gradually progresses toward the periphery, often leaving a scotoma that lasts less than 30 min. These auras (or

simple VH) can occur at the time of sleep onset. Rare cases of complex VH described in the literature can be seen in patients with hemiplegic migraine or other complex forms of the disorder [22]. Functional imaging studies have revealed that migraine auras are due to spreading cortical hypoperfusion suggesting that HH associated with migraines are of a primary neurological origin rather than vascular.

Nocturnal Hallucinations in Alzheimer's Disease (AD)

Sleep disturbances are common in patients with AD, which is the most common cause of dementia. According to the recent multicenter study, approximately 4.9 % of patients with AD report having hallucinations and frequent REM-sleep related symptoms [47]. In another study, clinical characteristics of hallucinations were studied in 218 patients with AD in relation to sleep-wake cycle [48]. A total of 12 % of patients acknowledged having hallucinations. The majority of reported hallucinations were visual and occurred during wakefulness and in a small number of patients. VH occurred close to sleep onset or a specific sleep phase. Vivid dreams (11 %) and violent sleep-related behaviors (10 %) were reported by many patients with AD and were more frequently associated with hallucinations in AD. The authors suggested that disordered REM sleep has a potential role in the pathophysiology of hallucinations in AD.

Evaluation

A comprehensive clinical evaluation is recommended for cases presenting with sleep-related hallucinations. The clinical evaluation should include physical and neurological examination and a psychiatric evaluation. Past medical, psychiatric, and neurological history should be obtained including history of prescription medication and illicit substance use/abuse. Use of certain medications like zolpidem or dopaminergic drugs may cause sleep-related hallucinations that usually clears on its own once medication has been discontinued. Special attention should be given to precipitating events, such as the occurrence of hallucinations during periods of heightened stress like grief or severe emotional trauma.

Sleep-related hallucinations are primarily diagnosed by clinical history and do not require additional instrumental assessment. However, in cases of excessive daytime sleepiness being associated with sleep-related hallucinations, additional PSG followed by multiple sleep latency test (MSLT) would be recommended for evaluation of suspected narcolepsy. If sleep-related seizures are suspected, a routine wake and sleep EEG, sleep-deprived EEG, or video-EEG may be needed to help with differential diagnosis. Neuroimaging studies may be an important part of the clinical evaluation in cases when sleep-related hallucination is associated with neurological disease.

Urine toxicology screening is very helpful when substance abuse is being suspected.

Treatment

Although, there are no specific interventions for sleep-related hallucinations, it has been reported that simple hypnagogic and hypnopompic hallucinations and CNVH in normal healthy individuals usually resolve spontaneously or with reassurance. Patients with medication-induced CNVH may benefit from withdrawal of the offending agent (e.g., beta adrenergic agonists or zolpidem). Treatment of the underlying neurological disorder like migraine, epilepsy, and narcolepsy is an essential part of the management in patients with hallucinations secondary to these conditions. In patients with hallucinations associated with PD, AD, and DLB, acetylcholinesterase inhibitors and antipsychotics have been tried but potential risks should be considered while prescribing this class of medication. There have been some studies suggesting the use of tricyclic antidepressants for treatment of sleep-related hallucinations [23]. Most medications that improve cataplexy in patients with narcolepsy have a potential to reduce HH and sleep paralysis. Tricyclic antidepressants have been most commonly used for the indication of cataplexy. Other classes of antidepressants like SSRIs and norepinephrine reuptake inhibitors have been successfully implicated in the treatment of cataplexy and other REM sleep dissociation phenomena associated with narcolepsy with significantly less side effects and better tolerability [49]. In a recent case series of children with narcolepsy, venlafaxine at a low dose (37.5 mg once daily) was shown to be effective in treating cataplexy attacks and HH [50].

Sodium oxybate has been approved by the FDA for the treatment of narcolepsy and had shown conflicting results in terms of controlling HH based on the few available clinical trials. In one study, 76 % of patients with narcolepsy reported reduced frequency in CNVH with doses up to 9 g [51]. Another study failed to demonstrate improvements in HH among patients with narcolepsy when treated with sodium oxybate [52].

Conclusion

Sleep-related hallucinations represent a diverse range of perceptual experiences that occur either on falling asleep or at awakening. They are being reported in healthy individuals and in patients with various clinical conditions. CNVH represent a distinct form of sleep-related experience that occurs when the individual wakes in the middle of the night and implies detailed vivid images of people or animals with reduced insight during the episode. Hypnagogic and hypnopompic hallucinations are frequently associated with narcolepsy syndrome and tend to respond to medications with REM-suppressing effects. The exact pathophysiology of sleep-related hallucinations remains unknown, although two hypotheses have been proposed: dissociation of sleep states and cortical release phenomenon. Comprehensive clinical evaluation is warranted for patients who present symptoms of sleep-related hallucinations. Instrumental assessment of sleep and neurophysiological functions of the brain may be indicated when intrinsic sleep disorders or neurological disorders

are being suspected. Treatment of underlying/comorbid clinical conditions helps to alleviate sleep-related hallucinations in patients with associated medical, neurological, and psychiatric disorders. In cases of uncomplicated nocturnal hallucinations, psychological reassurance is usually sufficient to relieve clinical symptoms.

Practical Points

- Sleep-related hallucination is a type of perceptual experience that occurs during transition to sleep (hypnagogic) or at awakening (hypnopompic) and can be of any sensory modality.
- Nocturnal hallucinations are frequently reported in general population and are usually self-limited.
- Sleep-related hallucinations are often associated with narcolepsy, neurological, and psychiatric disorders.
- Complex nocturnal visual hallucinations (CNVH) are a form of sleep-related phenomena that occur upon awakening in the middle of the night.
- CNVH either represent a benign idiopathic condition or are associated with neurological disorder like dementia of Lewy body or use of medications like beta adrenergic blockers.
- Evaluation of sleep-related hallucinations involves comprehensive clinical assessment with additional instrumental testing such as video-EEG, PSG, MSLT, and neuroimaging if neurological or other intrinsic sleep disorder is suspected.
- Uncomplicated benign sleep-related hallucinations usually resolve spontaneously or with reassurance.
- Treatment of the underlying clinical condition such as narcolepsy, epilepsy, migraine, Parkinson's disease, dementia of Lewy body, and others was shown to be effective in reducing occurrence of sleep-related hallucinations.

References

1. Mahowald MW, Woods SR, Schenck CH. Sleeping dreams, waking hallucinations, and the central nervous system. Dreaming. 1998;8:89–102.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC: American Psychiatric Association; 2000.
3. Ohanyon MM, Schatzberg AF. Prevalence of depressive episodes with psychotic features in the general population. Am J Psychiatry. 2002;159:1855–61.
4. Pope HG, Lipinski JF. Diagnosis of schizophrenia and manic-depressive illness. A reassessment of the specificity of "schizophrenic" symptoms in the light of current research. Arch Gen Psychiatry.1978;35:811–28.
5. Keck PE, McElroy SL, Havens JR, et al. Psychosis in bipolar disorder: phenomenology and impact on morbidity and course of illness. Compr Psychiatry. 2003;44:263–69.
6. Thanvi BR, Lo TC, Harsh DP. Psychosis in Parkinson's disease. Postgrad Med J. 2005;81:644–46.

7. Lyketsos CG, Steinberg M, Tschanz JT, et al. Mental and behavioral disturbances in dementia: findings from the Cache County study on memory in aging. Am J Psychiatry. 2000;157:708–14.
8. Sartorius N, Shapiro R, Jablensky A. The international pilot study of Sch. Sch Bulletin. 1974;11:21–34.
9. Tien AY. Distributions of hallucinations in the population. Soc Psychiatry Psychiatr Epidemiol. 1991;26:287–92.
10. Posey TB, Losch ME. Auditory hallucinations of hearing voices in 375 normal subjects. Imag Cogn Pers. 1984;3:99–113.
11. Bentall RP, Slade PD. Reality testing and auditory hallucinations: a signal detection analysis. Br J Clin Psychol. 1985;24:159–69.
12. Young HF, Bentall RP, Slade PD, et al. Disposition towards hallucinations, gender and IQ scores. Pers Invivid Dif. 1986;7:247–49.
13. Millham A, Easton S. Prevalence of auditory hallucinations in nurses in mental health. J Psychiatr Ment Health Nurs. 1998;5:95–9.
14. García-Ptacek S, García Azorín D, Sanchez Salmador R, Cuadrado ML, Porta-Etessam J. Hallucinations and aberrant perceptions are prevalent among the young healthy adult population. Neurologia. 2013 Jan-Feb;28(1):19–23.
15. Honig A, Romme MA, Ensink BJ, et al. Auditory hallucinations: a comparison between patients and nonpatients. J Nerv Ment Dis. 1998;186:646–51.
16. Johns L, Hemsley D, Kuipers E. A comparison of auditory hallucinations in a psychiatric and non-psychiatric group. Br J Clin Psychol. 2002;41:81–6.
17. Maury LF. Des hallucinations hypnagogiques (in French). Ann Med Psychol (Paris). 1848;11:26–40.
18. Myers FW. Sleep, human personality and its survival of bodily death. New York: NY Longman; 1903. p. 125.
19. Ohayon MM. Prevalence of hallucinations and their pathological associations in the general population. Psychiatry Res. 2000;97:153–64.
20. Ohayon MM, Priest RG, Caulet M, Guilleminault C. Hypnagogic and hypnopompic hallucinations: pathological phenomenon? Br J Psychiatry. 1996;169:459–67.
21. Mavormatis A. Hypnagogia—the unique state of consciousness between wakefulness and sleep:. London: Routledge & Kegan Paul; 1987.
22. Manford M, Andermann F. Complex visual hallucinations. Clinical and neurobiological insights. Brain. 1998;121 (Pt 10):1819–40.
23. Silber MH, Hansen MR, Girish M. Complex nocturnal visual hallucinations. Sleep Med. 2005;6(4):363–6
24. Goetz M, Prihodova I, Hrdlicka M. Long lasting complex nocturnal hallucinations during Osmotic Release Oral System (OROS) methylphenidate treatment in a 7-year old girl. Neuro Endocrinol Lett. 2011;32(5):619–22.
25. Goswami M. The influence of clinical symptoms on quality of life in patients with narcolepsy. Neurology. 1998;50(2 Suppl 1):31–36.
26. Dahmen N, Kasten M, Mittag K, Muller MJ. Narcoleptic and schizophrenic hallucinations. Implications for differential diagnosis and pathophysiology. Eur J Health Econ. 2002; 3(suppl 2):94–98.
27. Fortuyn HAD, Lappenschaar GA, Nienhuis FJ, Furer JW, et al. Psychotic symptoms in narcolepsy: phenomenology and comparison with schizophrenia. Gen Hosp Psychiatry. 2009;31:146–54.
28. Leu-Semenescu S, De Cock VC, Le Masson VD, Debs R, Lavault S, Roze E, Vidailhet M, Arnulf I. Hallucinations in narcolepsy with and without cataplexy: contrasts with Parkinson's disease. Sleep Med. 2011;12(5):497–504.
29. Yasui-Furukori N, Kusunoki M, Kaneko S. Hallucinations associated with modafinil treatment for narcolepsy. J Clin Psychopharmacol. 2009;29(4):408.
30. Hsieh CF, Lai CL, Lan SH, Liu CK, Hsu CY. Modafinil-associated vivid visual hallucination in a patient with Kleine-Levin syndrome: case report. J Clin Psychopharmacol. 2010;30(3):347–50.

31. Prado E, Paholpak P, Ngo M, Porter V, Apostolova LG, Marrocos R, Ringman JM. Agitation and psychosis associated with dementia with Lewy bodies exacerbated by modafinil use. Am J Alzheimers Dis Other Demen. 2012;27(7):468–73.
32. Toner LC, Tsambiras BM, Catalano G et al. Central nervous system side effects associated with zolpidem treatment. Clin Neuropharmacol. 2000;23(1):54–8.
33. Inagaki T, Miyaoka T, Tsuji S, et al. Adverse reactions to zolpidem: a case reports and a review of the literature. Prim Care Companion J Clin Psychiatry. 2010;12(6):PCC.09r00849.
34. Elko CJ, Burgess JL, Robertson WO. Zolpidem-associated hallucinations and serotonin reuptake inhibition: a possible interaction. J Toxicol Clin Toxicol. 1998;36(3):195–203.
35. Bonnet C. Essai analytique sur les facultes d l'ame. Copenhagen:Philibert;1760.
36. Menon GJ, Rahman I, Menon SJ, Dutton GN. Complex visual hallucination in the visually impaired: the Charles Bonnet syndrome. Surv Opthalmol. 2003;48(1):58–72.
37. Kazui H, Ishii R, Yoshida T, Ikezawa K, Takaya M, Tokunaga H, Tanaka T, Takeda M. Neuroimaging studies in patients with Charles Bonnet Syndrome. Psychogeriatrics. 2009;9(2):77–84.
38. Teunisse RJ, Cruysberg JR, Hoefnagels WH, Verbeek AL, Zitman FG. Visual hallucinations in psychologically normal people: Charles Bonnet's syndrome. Lancet. 1996 Mar 23;347(9004):794–7
39. Fénelon G, Alves G. Epidemiology of psychosis in Parkinson's disease. J Neurol Sci. 2010;289(1–2):12–7.
40. Lhermitte J. Syndrome de la calotte du Pedoncule cerebral. Les troubles psycho-sensoriels dans les lesions du mésocéphale. Rev Neurol (Paris). 1922;2:1359–65.
41. Kumar R, Behari S, Wahi J, Banerji D, Sharma K. Peduncular hallucinosis: an unusual sequel to surgical intervention in the suprasellar region. Br J Neurosurg. 1999;13(5):500–3.
42. Parisis D, Poulios I, Karkavelas G, Drevelengas A, et al. Peduncular hallucinosis secondary to brainstem compression by cerebellar metastasis. Eur Neurol. 2003;50:107–9.
43. Mauguiere F. Scope and presumed mechanisms of hallucinations in partial epileptic seizures. Epileptic Disord. 1999;1:81–91.
44. Sowa MV, Pituck S. Prolonged spontaneous complex visual hallucinations and illusions as ictal phenomena. Epilepsia. 1989;30(5):524–6.
45. Waters WE, O'Connor PJ. Prevalence of migraine. J Neurol Neurosurg Psychiatry. 1975;38:613–6.
46. Russell MB, Olesen J. A nosographic analysis of the migraine aura in a general population. Brain. 1996;119:355–61.
47. Bliwise DL, Mercaldo ND, Avidan AY, Boeve BF, Greer SA, Kukull WA. Sleep disturbance in dementia with Lewy bodies and. Alzheimer's disease: a multicenter analysis. Dement Geriatr Cogn Disord. 2011;31(3):239–46.
48. Sinforiani E, Terzaghi M, Pasotti C, Zucchella C, Zambrelli E, Manni R. Hallucinations and sleep-wake cycle in Alzheimer's disease: a questionnaire-based study in 218 patients. Neurol Sci. 2007;28(2):96–9.
49. Mignot E, Nishino S. Emerging therapies in narcolepsy-cataplexy. Sleep. 2005;28(6):754–63.
50. Møller LR, Østergaard JR. Treatment with venlafaxine in six cases of children with narcolepsy and with cataplexy and hypnagogic hallucinations. J Child Adolesc Psychopharmacol. 2009;19(2):197–201.
51. Mamelak M, Black J, Montplasir J, Ristanovic RA. A pilot study on the effects of sodium oxybate on sleep architecture and daytime alertness in narcolepsy. Sleep. 2004;27:1327–34.
52. The US Xyrem multicenter study group. A randomized, double blind, placebo-controlled multicenter trial comparing the effects of the three doses of orally administered sodium oxybate with placebo for the treatment of narcolepsy. Sleep. 2002;25:42–9.

Chapter 15
REM Behavior Disorder in Adults

Sujay Kansagra and Bradley V. Vaughn

Introduction

Rapid eye movement (REM) sleep is an active state of the brain characterized by REMs, skeletal muscle atonia, poikilothermia, and plot-like dream content. REM sleep behavior disorder (RBD) is defined by the lack of REM sleep-induced atonia and bouts of motor output consistent with dream enactment. Although some have characterized this condition as a dissociated state in which there is intrusion of elements of one state of being into another, pathology suggests that this condition is related to a malfunctioning of the mechanisms of atonia in REM sleep. In this chapter, we discuss the history and epidemiology of this fascinating disease and then explain the diagnostic criteria and differential diagnosis. The proposed pathophysiology and spectrum of clinical manifestations will be explained. We will conclude with a description of the treatment options and prognosis.

History

In 1965, Michel Jouvet performed a series of cat experiments in which bilateral lesions were made adjacent to the locus coeruleus [1]. These cats then demonstrated notable motor behaviors while in REM sleep. Based on these experiments, Jouvet predicted the existence of the human correlate to this condition.

In the 1970s, reports began to emerge of motor activity during dreaming in patients abusing alcohol and meprobamate [2]. Jouvet's prediction of a human correlate to

S. Kansagra (✉)
Pediatric Neurology Sleep Medicine Program, Duke University Medical Center,
DUMC 3936, Durham, NC 27705, USA
e-mail: sujay.kansagra@duke.edu

B. V. Vaughn
Department of Neurology, CB 7025, University of North Carolina,
Chapel Hill, NC 27599-7025, USA
e-mail: vaughnb@neurology.unc.edu

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_15, © Springer Science+Business Media New York 2013

his cat model was proven correct in 1986 by Schenk and colleagues who reported a series of four patients with abnormal movements in REM sleep. Polysomnography (PSG) revealed lack of chin atonia and a variety of abnormal behaviors during REM sleep without epileptiform correlate [3]. This report and a series of others showed this condition to occur in all ethnicities but more commonly in older males.

Epidemiology

The true incidence and prevalence of RBD is largely unknown. Although underreporting is likely, two phone interview studies screening for violent nighttime behavior suggest a prevalence of less than 1 %. One study of nearly 5,000 individuals from Great Britain found that 2 % of study subjects reported violent behaviors during sleep [4]. However, it was estimated that only 0.5 % of those surveyed actually had RBD based on potential for harm, actual injury, dreams that appeared to be "acted out", and disrupted sleep. No PSG confirmation was performed. Similarly, a phone survey in Hong Kong of 1,034 individuals over the age of 70 found that 0.8 % reported sleep-related injury. These individuals were then evaluated clinically and four subjects were confirmed to have RBD, thereby leading to a prevalence of 0.38 % [5]. Both studies screened for sleep-related injury initially, and therefore, are probably an underestimation of the true prevalence of RBD as the less violent cases were likely missed. Likewise, although there appears to be a male predominance of the disorder, with some studies showing up to 80 % of cases occurring in males, there is likely underreporting in females as their dream reenactment may be less violent and thus less likely to present to a provider [6].

Etiology

The clinical course of RBD can be subdivided into acute, transient episodes and chronic cases. The etiology of acute, transient cases of RBD can usually be attributed to either medications, withdrawal, or in rare cases, exposure to stimulants in food. Chronic cases may be seen in patients with narcolepsy or neurological features that may also serve as harbinger of neurodegenerative diseases. Patients initially labeled as idiopathic in the elderly often subsequently develop a synucleinopathy.

Acute onset RBD (see Table 15.1) may be caused by initiation of medications such as tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors. Studies show an increase in muscle activity during REM in healthy individuals taking TCAs, SNRIs, and SSRIs [7, 8]. Although the mechanism by which these medications induce RBD is unknown, serotonin and norepinephrine have an inhibitory effect on REM sleep mechanisms. Less frequent occurrences of RBD are seen with beta-blockers, selegiline, mirtazapine, anticholinesterase

Table 15.1 Causes of acute RBD

Medication-induced
Selective serotonin reuptake inhibitors
Serotonin-norepinephrine reuptake inhibitors
Tricyclic antidepressants
Beta-blockers
Mirtazapine
Monoamine oxidase inhibitors
Selegiline
Anticholinesterase inhibitors
Antipsychotics
Substance-induced
Alcohol
Caffeine
Chocolate
Withdrawal
Alcohol
Barbiturates
Meprobamate
Nitrazepam

inhibitors, and caffeine [9–12]. Exacerbation of RBD has been reported in one case with chocolate ingestion [13]. Withdrawal from alcohol, barbiturates, nitrazepam, and meprobamate may also lead to this disorder, and some have postulated that delirium tremens have features of RBD [14].

The existence of a truly idiopathic, chronic form of RBD is the subject of debate, particularly since 50–70 % of patients presenting with idiopathic RBD go on to develop a synucleinopathy over 10–15 years [15–20]. Since the onset of RBD may precede other clinical manifestations of neurodegenerative disease by up to 50 years, perhaps all cases of presumed idiopathic RBD are essentially early manifestations of a synucleinopathy, but this has yet to be determined [21]. This notion is further supported by studies showing that the clinical manifestations in idiopathic RBD are identical to those seen in cases secondary to Parkinson's disease or multiple system atrophy [22]. Further, there is a case report in which Lewy body disease was incidentally found during autopsy in a patient with RBD who had no clinical manifestations of parkinsonism [23]. RBD has been reported to occur in one third of patients with Parkinson's disease and close to 70 % of those with multiple system atrophy [24, 25]. See Table 15.2 for full list of causes of chronic RBD.

RBD may also be a secondary manifestation of narcolepsy, with a prevalence of greater than 50 % in those with narcolepsy [26–30]. The occurrence of RBD in young adults should lead to suspicion for narcolepsy. Other disorders that have been linked to RBD include Tourette's syndrome, Machado-Joseph disease, mitochondrial disorders, normal pressure hydrocephalus, cerebellopontine angle tumors, group A xeroderma, multiple sclerosis, cerebrovascular disease, autism, voltage-gated potassium channel autoimmune disease, Möbius syndrome, and Guillain-Barré [14]. These and other cases of acquired RBD suggest any disorder, which may damage the mechanisms in the brainstem that play a role in generating REM sleep atonia, may generate the clinical features of RBD.

Table 15.2 Causes of chronic RBD

Neurodegenerative disorders
Parkinson's disease
Lewy body dementia
Multiple system atrophy
Alzheimer' disease
Corticobasal degenerations
Guadeloupean atypical parkinsonism
Progressive supranuclear palsy
Huntington's disease
Genetic disorders
Parkin gene mutation
Parkinsonism-dementia-amyotrophic lateral sclerosis complex
Type A xeroderma pigmentosum
Focal CNS lesions
Stroke
Tumor
Multiple sclerosis
Other
Encephalitis
Narcolepsy

Pathophysiology

The exact mechanism in which RBD leads to dream reenactment has not been elucidated, largely due to the complex neuronal interactions that mediate REM sleep. However, animal models and human studies have provided for a great deal of insight into the underlying areas within the central nervous system (CNS) that regulate REM and have led to proposed models of the pathophysiology behind RBD.

The finding of REM sleep without atonia (RSWA) on overnight PSG studies is not uncommon (see Fig. 15.1). Yet, only a fraction of these patients go on to have clinical evidence of dream reenactment. This has led to the hypothesis that RBD is a result of dysfunction in two distinctly functioning areas, one area that is responsible for generating atonia of REM sleep and the other which suppresses locomotor activity during REM sleep.

Although the mechanisms by which locomotor activity becomes activated (or uninhibited) in RBD is unclear, most of the animal models have sought to explain the mechanisms that cause lack of atonia in REM sleep. The final common pathway leading to REM atonia found in cats involves projection from the medullary magnocellular reticular formation (MCRF) that forms the ventrolateral reticulospinal tract. This tract hyperpolarizes motoneurons located in the anterior horn cells of the spinal cord, thereby inhibiting motor function and causing atonia. In the cat model, a variety of nuclei and forebrain structures project to or have influence upon the MCRF, thereby influencing downstream control of muscle atonia [1, 31–37]. These areas include the locus coeruleus/subcoeruleus, pedunculopontine nucleus (PPN), laterodorsal tegmental nucleus, substantia nigra, hypothalamus, thalamus, basal forebrain, and frontal cortex, although how each of these affect the MCRF is

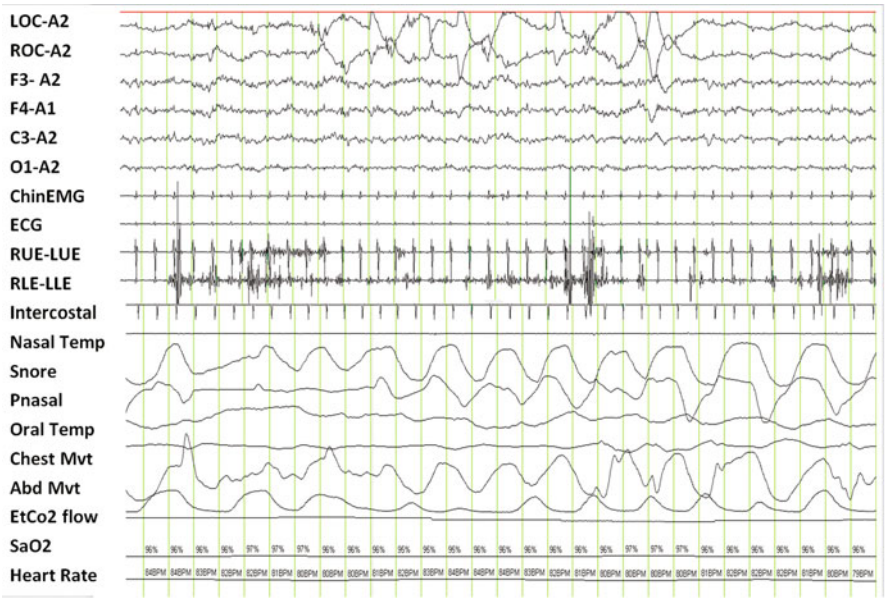


Fig. 15.1 Polysomnogram showing lack of atonia during REM sleep. Note the excessive muscle activity in the RUE-LUE (arms) and RLE-LLE (legs) channels especially during the REMs

unclear. In the cat model, lesions to the MCRF, coeruleus/subcoeruleus, and perhaps even the PPN, lead to RSWA.

Subsequent studies in the rat model have further clarified the complex interaction of these regions in mediating REM sleep [38, 39]. The sublaterodorsal (SLD) nucleus was identified as the key structure in REM sleep. This region is thought to be equivalent to the subcoeruleus area in the cat model. Glutamatergic projections in the rat go directly from the SLD to interneurons within the spinal cord which then hyperpolarize anterior horn cells leading to REM atonia. Lesions to the SLD have led to lack of REM atonia in the rat. There are also projections from the SLD to the MCRF which may also play a role in REM sleep, although not necessary for REM atonia in the rat. In hindsight, the cat experiments in which the MCRF was lesioned may have led to atonia simply because the lesion also disrupted the SLD projections that ran through the MCRF region [40].

Applying these findings to humans, Boeve and colleagues have hypothesized that lesions to the area in humans that is equivalent to the SLD in rats is responsible for RSWA. Two separate pathways from the SLD region may be additive in leading to RSWA: the direct projection from the SLD to the spinal interneurons and a second projection from the SLD to the MCRF which then directly inhibits motoneurons in the spinal cord. The locomotor generators which are presumably activated to produce RBD are yet to be identified, but may involve other central pattern generators or burst of activity from cortical generators.

A link between the proposed pathophysiology of RBD and the temporal relationship to various neurodegenerative processes can be seen in the Braak staging system for Parkinson's disease. In this system, Braak and colleagues showed that Lewy body inclusions are deposited in a topographically predictable manner within the CNS which correlates with clinical findings. In disease stages 1 and 2, the inclusions are confined to the olfactory bulb, anterior olfactory nucleus, medulla, and pons. These stages are thought to be presymptomatic. The inclusions then spread rostrally, and in disease stages 3 and 4, the midbrain, forebrain, and substantia nigra are affected, and parkinsonism may become apparent. In disease stages 5 and 6, the neocortex becomes involved, thereby leading to dementia [41]. This staging system explains why RBD would precede clinical manifestations of the neurodegenerative disorder as the pontine areas that are damaged in early stages may cause RBD, and only later in the course would the inclusions reach more rostral areas causing the clinical presentation of a neurodegenerative disease. Slow progression of the inclusion deposition could allow RBD to precede the clinical manifestations of Parkinson's disease and other synucleinopathies by decades [17, 40, 42].

Clinical Presentation

RBD may present at any age; however, the majority of patients are older than 50 years. The presenting chief complaint is typically the presence of violent behavior during sleep. This behavior tends to be more violent in men than in women. Dream content is also reported to become more violent with RBD onset, and involves the subject being attacked or having to defend a position or others. Although these events are violent, the patient's daytime personality remains unchanged. The nighttime episodes are typically brief, and if speech is present during the episodes, it tends to be clear. Upon awakening, the patient is often able to remember the exact dream, and movement during the dream correlates with dream content. During the episodes, the patient's eyes are typically closed. Interestingly, speed of movements and clarity of speech may be much higher than the patient's baseline abilities while awake. This is especially true for patients with Parkinson's disease, who are typically bradykinetic when awake yet have no bradykinesia during their dream enactment. The episodes of dream reenactment coincide with the time of REM sleep periods, and therefore, are more common in the latter half of the night. Since REM sleep cycles about every 1.5 h, events may occur intermittently throughout the night. The exception is narcolepsy patients who may have early onset REM and express the manifestations of RBD upon going to sleep. Frank dream reenactment may be preceded by bruxism, somniloquy, periodic limb movements, or yelling during sleep. The frequency of events is quite variable, and may occur multiple times each night or only once every few weeks [43]. Most events are very short, lasting only seconds and may last a minute. Patients rarely leave the bedroom. The dream reenactment can be very dangerous. Patients may report diving or trying to tackle or fend off an attacker in their dream. There are case reports of fractures, subdural hematomas, and lacerations

in both patients and their bed partners [44, 45]. Patients often go to extreme measures to prevent injury to themselves and others, including tying themselves to their bed.

A variety of associated clinical problems have been found in patients with idiopathic RBD. Several studies show impairment in olfaction function. A recent study of 54 patients with idiopathic RBD and 54 age- and gender-matched controls showed that 61.1 % of RBD patients had abnormal olfactory function, compared to only 16.6 % of controls [46]. This olfactory dysfunction is similar to that seen in patients with Parkinson's disease, and therefore, may be due to the underlying neurodegenerative process. This olfactory dysfunction was also seen in patients with narcolepsy with and without RBD [47]. This finding was reversed with intranasal orexin A administration [48].

In addition to the olfactory dysfunction, patients with RBD have other neurological features. A study of 17 patients with idiopathic RBD who were compared to matched controls and had neuropsychological measures performed were found to have lower scores on visuoconstructional abilities and visuospatial learning. Similar deficits have been shown in patients with Lewy body dementia, and thus the deficits in patients with RBD may be an early sign of eventual progression to neurodegeneration. Postuma and colleagues also showed that deficits in color vision could predict impending neurodegenerative disease in patients with idiopathic RBD [49]. Additionally, two studies looking at electroencephalography (EEG) findings in patients with idiopathic RBD have shown slowing amongst RBD patients similar to slowing in wake and sleep seen in the early stages of synucleinopathy-mediated neurodegeneration [50, 51].

Recent studies have investigated abnormalities in the autonomic nervous system in patients with idiopathic RBD. There is a higher frequency of clinical symptoms consistent with autonomic dysfunction in these patients, such as constipation, erectile dysfunction, decreased beat-to-beat heart rate variability, and orthostatic blood pressure drops. Miyamoto demonstrated that patients with RBD have impaired uptake labeling of cardiac sympathetic nerves [52]. This finding was confirmed by other investigators suggesting the decline in sympathetic nerves is more striking in those with RBD [53]. Yet, cardiac features may not be a leading indicator of future disease. In a prospective study, Postuma and colleagues attempted to determine if autonomic dysfunction as measured by cardiac autonomic dysfunction could be a predictor of future neurodegeneration. However, beat-to-beat variability based on electrocardiography (EKG) analysis of patients with RBD was unable to predict which patients would go on to develop neurodegeneration [54].

Differential Diagnosis

Many parasomnias can have clinical symptoms that are very similar to RBD, underscoring the need for both clinical and PSG confirmation of the disorder. The differential of RBD includes obstructive sleep apnea (OSA), disorders of arousal, seizure disorders, nocturnal panic disorder, psychogenic dissociative states, delirium,

posttraumatic stress disorder, and malingering [55]. Additionally, variations of RBD such as parasomnia overlap syndrome and agrypnia excitata should be considered.

Sleep apnea can exacerbate and mimic a variety of nocturnal events. OSA has been reported to produce dreamlike enactment, especially when the patient is arousing from REM sleep-related apneas [56]. The clinician should differentiate the presence of sleep apnea in REM sleep as a causative factor for the nocturnal events or an unassociated finding. Thus, polysomnographic recording is essential to diagnose the REM sleep apneic and motor events, with a subsequent recording to evaluate the ongoing absence of atonia after the sleep apnea is appropriately treated.

Disorders of arousals are common non-rapid eye movement (NREM) parasomnias that may mimic RBD. The spectrum of disorders of arousal includes confusional arousals, sleepwalking, and sleep terrors. These events can be triggered by a variety of underlying conditions such as sleep apnea, gastroesophageal reflux, and periodic limb movements. These conditions should be screened in any patient presenting with a parasomnia. Vocalizations during confusional arousals tend to be less distinct and purposeful than during RBD. Patients tend be amnestic to confusional arousals while typically having dream recall if awoken following the dream reenactment of RBD.

Nocturnal seizures are typically stereotyped and tend to occur during NREM sleep. Utilization of a parasomnia-protocoled PSG is imperative to help ensure that there are no epileptiform discharges during the episodes of dream reenactment.

A "parasomnia overlap syndrome" that manifests features of both RBD and sleep terrors or sleepwalking has been reported [55]. The presumed mechanism is through motor disinhibition that is not sleep stage specific. The parasomnia overlap syndrome is considered a variation of RBD. Similarly, agrypnia excitata has elements of RBD, but the overarching feature is one of generalized overactivity and can be seen in conditions such as delirium tremens, Morvan's fibrillary chorea, and fatal familial insomnia [57–59]. In status dissociatus, there is complete breakdown of state distinguishing features. Patients will have unusual behaviors during sleep, such as constant vocalizations and muscle activation. Their sleep studies show lack of clearly defined sleep stages and instead show mixed elements of wakefulness, NREM sleep, and REM sleep.

Work-Up

Evaluation of a patient with abnormal movements at night begins with a detailed history and physical exam. The history should focus on accurate descriptions of the event (typically from a bed partner), with particular emphasis on dream recall, nature of movements, clarity of vocalizations, and timing of events (RBD tends to occur in the latter half of the night when REM sleep predominates). The clinician should also inquire about length and frequency of the events. Careful attention should be drawn to discerning details of stereotypia in the behavior which might indicate epileptic seizures acting as a mimic of RBD [60]. Additionally, the clinician should ask about medications, supplements, and other substances that may provoke the

Table 15.3 Criteria for RBD. (Adapted from ICSD-II [70]. Used with permission of American Academy of Sleep Medicine, Darien, IL, 2012)

Presence of REM sleep without atonia, defined as sustained or intermittent elevation of submental EMG tone or excessive phasic muscle activity in the limb EMG
At least one of the following:
Sleep-related or potentially injurious disruptive behaviors by history
Abnormal REM behaviors documented on polysomnogram
Absence of epileptiform activity during REM sleep unless RBD can be clearly distinguished from any concurrent REM sleep-related seizure disorder
Sleep disturbance not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder

EMG electromyography, *REM* rapid eye movement, *RBD* REM sleep behavior disorder, *ICSD* international classification of sleep disorders

Table 15.4 Indications for PSG in evaluation of nighttime activity

Symptoms of other sleep disorders such as sleep apnea
Dream reenactment
Violent/injurious nighttime behavior
History of synucleinopathy with parasomnia
History of narcolepsy with parasomnia
Stereotyped movements
Sleepwalking/confusional arousals with atypical features (i.e., violent behavior, injury to self or others, clear recollection of dream)

events. The physician may also ask about other features of synucleinopathies, such as constipation, decreased sense of smell, trouble rising from a chair, changes in handwriting, cognitive changes, or changes in gait. The physical exam should focus on clues to why the patient may have nocturnal events. Features of sleep apnea, such as crowded airway, large neck, and elevated blood pressure, should be noted. The clinician should also concentrate on the neurological exam evaluating for features of synucleinopathy: bradykinesia, cranial nerve findings, loss of associated movements of gait, balance issues, and autonomic impairment. PSG should be performed in all patients in whom RBD is considered. This study should look for disorders that may mimic RBD, such as sleep apnea or other parasomnias. The study must also confirm the loss of atonia during REM sleep and therefore include monitoring of all four extremities, especially the wrist extensors and quadriceps. The American Academy of Sleep Medicine (AASM) scoring manual recommends documenting sustained muscle activity if at least 50 % of an epoch or five of the ten 3-s miniepochs contain bursts of transient muscle activity [61]. The manual does not explain how many epochs are needed to make the diagnosis of RSWA. Diagnosis of RBD requires both dream reenactment and PSG confirmation of RSWA (see Table 15.3 for full diagnostic criteria). Table 15.4 lists the reasons to pursue a PSG in the evaluation of unusual nighttime activity.

Following the diagnosis, patients should be considered for magnetic resonance imaging of the brain to look for potential lesions causing the RBD. Additionally, the patient should be followed up by serial neurological exams to monitor further neurological dysfunction.

Treatment

The goal of therapy is to prevent injury to the patient or bed partner while trying to limit any negative psychosocial impact of the disease. All patients should be counseled on environmental safety. Bed partners should consider sleeping in a different room if the disease remains active. The patient's bed should be kept low, with some cases necessitating putting the mattress onto the floor. Windows should be secured, and all objects that can potentially cause injury (i.e., bed posts, night stands, etc.) should be removed from the room.

The decision to pursue pharmacologic treatment depends on the clinical context. Acute RBD that can be attributed to withdrawal is self-limiting and typically does not require medical treatment. Similarly, if RBD is due to initiation of an offending medication, resolution occurs once the medication is discontinued. For chronic disease, there are no large, randomized, placebo-controlled trials on medications for RBD. However, the Standards of Practice Committee of the *Journal of Clinical Sleep Medicine* evaluated the treatment literature in 2010 [62]. This committee assigned a Level B recommendation (defined as "suggested" treatment) to both clonazepam and melatonin, with all other medications receiving lower recommendations. The recommendation for clonazepam was based on 22 studies (16 case series and 6 case reports). This literature is limited in that the majority of studies were done in sleep clinics and thus, may only represent the more severe cases, while some studies did not use PSG to confirm the diagnosis. The recommended dose range for clonazepam is 0.5–2 mg once nightly prior to bedtime. OSA should be ruled out prior to initiating clonazepam. Side effects include sedation, confusion, and memory dysfunction. It should be used cautiously in elderly patients, those with dementia, and those with gait disturbance. Clonazepam has been shown to decrease phasic REM muscle activity but does not affect the tonic increase in electromyography (EMG), indicating that it may act by inhibiting the locomotor activity centers [63]. The recommendation for melatonin was based on five studies (one case report, two open-label prospective case series, and two retrospective case series) for a total of 38 patients, 31 of whom reported improvement. However, six of these patients were also on clonazepam. The recommended dose range is 3–12 mg once nightly. Melatonin likely acts on a different physiologic mechanism than clonazepam, as it decreases the amount of tonic EMG activity [64]. Clinicians overseeing pharmacotherapy of these patients should note a few important points. Minor movements and vocalizations will continue despite pharmacological treatment and bed partners should not be given the expectations that these minor movements will resolve. Also, a good indication that therapy is working is that the dream content will change from attack and confrontational to less violent dreams. As a sidenote, pets that slept in the same bedroom prior to the violent dream enactment may return to the bedroom once the violent activity subsides.

For patients on offending medications that may cause RBD (see Etiology section), these medications should be weaned off whenever possible. Alternatively, patients who cannot tolerate discontinuation of medications (such as SSRIs for depression

or cataplexy) can try the addition of clonazepam or melatonin. Other therapies have been reported as potentially benefiting some patients. Sodium oxybate, donepezil, and pramipexole have case reports suggesting benefit [65–67]. The benefit of the latter two have been debated in other series [68, 69].

Prognosis

The prognosis for disease modification remains favorable in all cases of RBD with appropriate treatment. However, despite adequate control of symptoms, there is still a risk for sporadic episodes of dream reenactment. There is also the possibility of spontaneous improvement of symptoms in cases with neurodegenerative disease as the underlying disease progresses. The reason behind this is unclear.

Conclusion

RBD is a fascinating parasomnia and an area of ongoing research. It represents a unique opportunity to identify patients with possible neurodegenerative disease prior to any cognitive involvement. As the entity becomes better known amongst general practitioners, the accurate diagnosis and treatment of these patients will likely become more expeditious.

Case Example

W. H. is a 72-year-old male brought into the neurology clinic by his wife for abnormal nighttime movements. She reports that for the past 2 years, he has moved violently during his sleep and she is no longer able to sleep in the same bed as the patient due to concern that she may get injured. Last week he jumped out of bed and dislocated his shoulder. The patient recalls that he was "attempting to dive into a pool" during this particular event, and likewise can remember dreaming during many of his prior nighttime movements. He has had no recent medication changes. His exam shows a cognitively intact, mild-mannered gentleman with mild increase in right upper extremity tone and a mildly flatten affect. There is no other evidence of parkinsonism. Polysomnogram reveals evidence of increased tonic EMG activity during REM sleep, but no dream reenactment is captured. No epileptiform activity is seen on the EEG. Due to the clinical history of dream reenactment and PSG showing increased tonic EMG during REM, the patient is diagnosed with RBD and started on melatonin at 3 mg, which leads to resolution of symptoms. He is examined regularly for signs of an underlying synucleinopathy.

Practical Points

- The diagnosis of RBD involves both clinical findings of dream reenactment as well as PSG confirmation of RSWA.
- RBD may be the result of two concurrent areas of dysfunction: (1) in mechanisms that generate REM sleep atonia and (2) in suppression of locomotor activity during REM sleep.
- The mainstay of pharmacologic treatment of RBD includes clonazepam and melatonin.
- Patients with idiopathic RBD are at a high risk of developing a neurodegenerative disease, particularly a synucleinopathy.

References

1. Jouvet M, Delorme F. Locus coeruleus et sommeil paradoxal. C R Seances Soc Biol Fil. 1965;159:895–9.
2. Tachibana M, Tanaka K, Hishikawa Y, et al. A sleep study of acute psychotic states due to alcohol and meprobamate addiction. Adv Sleep Res. 1976;2:177–205.
3. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep. 1986;9(2):293–308 (PubMed PMID: 3505730).
4. Ohayon MM, Caulet M, Priest RG. Violent behavior during sleep. J Clin Psychiatry. 1997 Aug;58(8):369–76; quiz 77 (PubMed PMID: 9515980).
5. Chiu HF, Wing YK, Lam LC, Li SW, Lum CM, Leung T, et al. Sleep-related injury in the elderly—an epidemiological study in Hong Kong. Sleep. 2000 Jun 15;23(4):513–7 (PubMed PMID: 10875558).
6. Bodkin CL, Schenck CH. Rapid eye movement sleep behavior disorder in women: relevance to general and specialty medical practice. J Womens Health (Larchmt). 2009 Dec;18(12):1955–63 (PubMed PMID: 20044857).
7. Passouant P, Cadilhac J, Ribstein M. Sleep privation with eye movements using antidepressive agents. Rev Neurol (Paris). 1972 Jul;127(1):173–92 (PubMed PMID: 4358573. Les privations de sommeil avec mouvements oculaires par les anti-depresseurs).
8. Winkelman JW, James L. Serotonergic antidepressants are associated with REM sleep without atonia. Sleep. 2004 Mar 15;27(2):317–21 (PubMed PMID: 15124729).
9. Onofrj M, Luciano AL, Thomas A, Iacono D, D'Andreamatteo G. Mirtazapine induces REM sleep behavior disorder (RBD) in parkinsonism. Neurology. 2003 Jan 14;60(1):113–5 (PubMed PMID: 12525729).
10. Stolz SE, Aldrich MS. REM sleep behavior disorder associated with caffeine abuse. Sleep Res. 1991;20:341.
11. Iranzo A, Santamaria J. Bisoprolol-induced rapid eye movement sleep behavior disorder. Am J Med. 1999 Oct;107(4):390–2 (PubMed PMID: 10527042).
12. Carlander B, Touchon J, Ondze B, Billiard M. REM sleep behavior disorder induced by cholinergic treatment in Alzheimer's disease. J Sleep Res. 1996;5 Suppl 1:28.
13. Vorona RD, Ware JC. Exacerbation of REM sleep behavior disorder by chocolate ingestion: a case report. Sleep Med. 2002 Jul;3(4):365–7 (PubMed PMID: 14592201).
14. Mahowald MW, Schenck CH. REM sleep parasomnias. In: Kryger M, Roth T, Dement W, editors. Principles and practice of sleep medicine. 5th ed. St. Louis (MO): Elsevier Saunders; 2011. pp. 1083–97.

15. Schenck CH, Hurwitz TD, Mahowald MW. Symposium: Normal and abnormal REM sleep regulation: REM sleep behaviour disorder: an update on a series of 96 patients and a review of the world literature. J Sleep Res. 1993 Dec;2(4):224–31 (PubMed PMID: 10607098).
16. Olson EJ, Boeve BF, Silber MH. Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. Brain. 2000 Feb;123(Pt 2):331–9 (PubMed PMID: 10648440).
17. Schenck CH, Bundlie SR, Mahowald MW. Delayed emergence of a parkinsonian disorder in 38 % of 29 older men initially diagnosed with idiopathic rapid eye movement sleep behaviour disorder. Neurology. 1996 Feb;46(2):388–93 (PubMed PMID: 8614500).
18. Britton TC, Chaudhuri KR. REM sleep behavior disorder and the risk of developing Parkinson disease or dementia. Neurology. 2009 Apr 14;72(15):1294–5 (PubMed PMID: 19164135).
19. Postuma RB, Gagnon JF, Vendette M, Montplaisir JY. Idiopathic REM sleep behavior disorder in the transition to degenerative disease. Mov Disord. 2009 Nov 15;24(15):2225–32 (PubMed PMID: 19768814).
20. Postuma RB, Gagnon JF, Vendette M, Fantini ML, Massicotte-Marquez J, Montplaisir J. Quantifying the risk of neurodegenerative disease in idiopathic REM sleep behavior disorder. Neurology. 2009 Apr 14;72(15):1296–300 (PubMed PMID: 19109537, Pubmed Central PMCID: 2828948).
21. Claassen DO, Josephs KA, Ahlskog JE, Silber MH, Tippmann-Peikert M, Boeve BF. REM sleep behavior disorder preceding other aspects of synucleinopathies by up to half a century. Neurology. 2010 Aug 10;75(6):494–9 (PubMed PMID: 20668263, Pubmed Central PMCID: 2918473).
22. Iranzo A, Santamaria J, Rye DB, Valldeoriola F, Marti MJ, Munoz E, et al. Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD. Neurology. 2005 Jul 26;65(2):247–52 (PubMed PMID: 16043794).
23. Uchiyama M, Isse K, Tanaka K, Yokota N, Hamamoto M, Aida S, et al. Incidental Lewy body disease in a patient with REM sleep behavior disorder. Neurology. 1995 Apr;45(4):709–12 (PubMed PMID: 7723959).
24. Plazzi G, Cortelli P, Montagna P, De Monte A, Corsini R, Contin M, et al. REM sleep behaviour disorder differentiates pure autonomic failure from multiple system atrophy with autonomic failure. J Neurol Neurosurg Psychiatry. 1998 May;64(5):683–5 (PubMed PMID: 9598693, Pubmed Central PMCID: 2170083).
25. Gagnon JF, Bedard MA, Fantini ML, Petit D, Panisset M, Rompre S, et al. REM sleep behavior disorder and REM sleep without atonia in Parkinson's disease. Neurology. 2002 Aug 27;59(4):585–9 (PubMed PMID: 12196654).
26. Bonakis A, Howard RS, Williams A. Narcolepsy presenting as REM sleep behaviour disorder. Clin Neurol Neurosurg. 2008 May;110(5):518–20 (PubMed PMID: 18343568).
27. Mattarozzi K, Bellucci C, Campi C, Cipolli C, Ferri R, Franceschini C, et al. Clinical, behavioural and polysomnographic correlates of cataplexy in patients with narcolepsy/cataplexy. Sleep Med. 2008 May;9(4):425–33 (PubMed PMID: 17681883).
28. Knudsen S, Gammeltoft S, Jennum PJ. Rapid eye movement sleep behaviour disorder in patients with narcolepsy is associated with hypocretin-1 deficiency. Brain. 2010 Feb;133(Pt 2):568–79 (PubMed PMID: 20129934).
29. Dauvilliers Y, Rompre S, Gagnon JF, Vendette M, Petit D, Montplaisir J. REM sleep characteristics in narcolepsy and REM sleep behavior disorder. Sleep. 2007 Jul;30(7):844–9 (PubMed PMID: 17682654, Pubmed Central PMCID: 1978363).
30. Nevsimalova S, Prihodova I, Kemlink D, Lin L, Mignot E. REM behavior disorder (RBD) can be one of the first symptoms of childhood narcolepsy. Sleep Med. 2007 Nov;8(7–8):784–6 (PubMed PMID: 17569582).
31. Hendricks JC, Morrison AR, Mann GL. Different behaviors during paradoxical sleep without atonia depend on pontine lesion site. Brain Res. 1982 May 6;239(1):81–105 (PubMed PMID: 7093693).
32. Lai YY, Siegel JM. Medullary regions mediating atonia. J Neurosci. 1988 Dec;8(12):4790–6 (PubMed PMID: 2904495).

33. Lai YY, Siegel JM. Muscle tone suppression and stepping produced by stimulation of midbrain and rostral pontine reticular formation. J Neurosci. 1990 Aug;10(8):2727–34 (PubMed PMID: 2388085).
34. Lai YY, Siegel JM. Brainstem-mediated locomotion and myoclonic jerks. I. Neural substrates. Brain Res. 1997 Jan 16;745(1–2):257–64 (PubMed PMID: 9037417).
35. Lai YY, Siegel JM. Brainstem-mediated locomotion and myoclonic jerks. II Pharmacological effects. Brain Res. 1997 Jan 16;745(1–2):265–70 (PubMed PMID: 9037418).
36. Morrison AR. The pathophysiology of REM-sleep behavior disorder. Sleep. 1998 Aug 1;21(5):446–9 (PubMed PMID: 9703583).
37. Shouse MN, Siegel JM. Pontine regulation of REM sleep components in cats: integrity of the pedunculopontine tegmentum (PPT) is important for phasic events but unnecessary for atonia during REM sleep. Brain Res. 1992 Jan 31;571(1):50–63 (PubMed PMID: 1611494).
38. Boissard R, Fort P, Gervasoni D, Barbagli B, Luppi PH. Localization of the GABAergic and non-GABAergic neurons projecting to the sublaterodorsal nucleus and potentially gating paradoxical sleep onset. Eur J Neurosci. 2003 Sep;18(6):1627–39 (PubMed PMID: 14511341).
39. Boissard R, Gervasoni D, Schmidt MH, Barbagli B, Fort P, Luppi PH. The rat ponto-medullary network responsible for paradoxical sleep onset and maintenance: a combined microinjection and functional neuroanatomical study. Eur J Neurosci. 2002 Nov;16(10):1959–73 (PubMed PMID: 12453060).
40. Boeve BF, Silber MH, Saper CB, Ferman TJ, Dickson DW, Parisi JE, et al. Pathophysiology of REM sleep behaviour disorder and relevance to neurodegenerative disease. Brain. 2007 Nov;130(Pt 11):2770–88 (PubMed PMID: 17412731).
41. Boeve BF. REM sleep behavior disorder: updated review of the core features, the REM sleep behavior disorder-neurodegenerative disease association, evolving concepts, controversies, and future directions. Ann N Y Acad Sci. 2010 Jan;1184:15–54 (PubMed PMID: 20146689, Pubmed Central PMCID: 2902006).
42. Boeve BF, Silber MH, Ferman TJ, Lucas JA, Parisi JE. Association of REM sleep behavior disorder and neurodegenerative disease may reflect an underlying synucleinopathy. Mov Disord. 2001 Jul;16(4):622–30 (PubMed PMID: 11481685).
43. M Mahowald AC. Rapid eye movement sleep behavior disorder. Medlink; 2010.
44. Dyken ME, Lin-Dyken DC, Seaba P, Yamada T. Violent sleep-related behavior leading to subdural hemorrhage. Arch Neurol. 1995 Mar;52(3):318–21 (PubMed PMID: 7872888).
45. Morfis L, Schwartz RS, Cistulli PA. REM sleep behaviour disorder: a treatable cause of falls in elderly people. Age Ageing. 1997 Jan;26(1):43–4 (PubMed PMID: 9143438).
46. Fantini ML, Postuma RB, Montplaisir J, Ferini-Strambi L. Olfactory deficit in idiopathic rapid eye movements sleep behavior disorder. Brain Res Bull. 2006 Oct 16;70(4–6):386–90 (PubMed PMID: 17027774).
47. Stiasny-Kolster K, Clever SC, Moller JC, Oertel WH, Mayer G. Olfactory dysfunction in patients with narcolepsy with and without REM sleep behaviour disorder. Brain. 2007 Feb;130 (Pt 2):442–9 (PubMed PMID: 17235125).
48. Baier PC, Weinhold SL, Huth V, Gottwald B, Ferstl R, Hinze-Selch D. Olfactory dysfunction in patients with narcolepsy with cataplexy is restored by intranasal Orexin A (Hypocretin-1). Brain. 2008 Oct;131(Pt 10):2734–41 (PubMed PMID: 18718966).
49. Postuma RB, Gagnon JF, Vendette M, Desjardins C, Montplaisir JY. Olfaction and color vision identify impending neurodegeneration in rapid eye movement sleep behavior disorder. Ann Neurol. 2011 May;69(5):811–8 (PubMed PMID: 21246603).
50. Fantini ML, Gagnon JF, Petit D, Rompre S, Decary A, Carrier J, et al. Slowing of electroencephalogram in rapid eye movement sleep behavior disorder. Ann Neurol. 2003 Jun;53(6):774–80 (PubMed PMID: 12783424).
51. Massicotte-Marquez J, Carrier J, Decary A, Mathieu A, Vendette M, Petit D, et al. Slow-wave sleep and delta power in rapid eye movement sleep behavior disorder. Ann Neurol. 2005 Feb;57(2):277–82 (PubMed PMID: 15668971).
52. Miyamoto T, Miyamoto M, Inoue Y, Usui Y, Suzuki K, Hirata K. Reduced cardiac 123I-MIBG scintigraphy in idiopathic REM sleep behavior disorder. Neurology. 2006 Dec 26;67(12): 2236–8 (PubMed PMID: 17190953).

53. Kashihara K, Imamura T, Shinya T. Cardiac 123I-MIBG uptake is reduced more markedly in patients with REM sleep behavior disorder than in those with early stage Parkinson's disease. Parkinsonism Relat Disord. 2010 May;16(4):252–5 (PubMed PMID: 20097595).
54. Postuma RB, Lanfranchi PA, Blais H, Gagnon JF, Montplaisir JY. Cardiac autonomic dysfunction in idiopathic REM sleep behavior disorder. Mov Disord. 2010 Oct 30;25(14):2304–10 (PubMed PMID: 20669316).
55. Schenck CH, Boyd JL, Mahowald MW. A parasomnia overlap disorder involving sleepwalking, sleep terrors, and REM sleep behavior disorder in 33 polysomnographically confirmed cases. Sleep. 1997 Nov;20(11):972–81 (PubMed PMID: 9456462).
56. Iranzo A, Santamaria J, Tolosa E. The clinical and pathophysiological relevance of REM sleep behavior disorder in neurodegenerative diseases. Sleep Med Rev. 2009;13:385–401.
57. Lugaresi E, Provini F. Agrypnia excitata: clinical features and pathophysiological implications. Sleep Med Rev. 2001 Aug;5(4):313–22 (PubMed PMID: 12530995).
58. Montagna P, Lugaresi E. Agrypnia excitata: a generalized overactivity syndrome and a useful concept in the neurophysiopathology of sleep. Clin Neurophysiol. 2002 Apr;113(4):552–60 (PubMed PMID: 11956000).
59. Plazzi G, Montagna P, Meletti S, Lugaresi E. Polysomnographic study of sleeplessness and oneiricisms in the alcohol withdrawal syndrome. Sleep Med. 2002 May;3(3):279–82 (PubMed PMID: 14592220).
60. D'Cruz OF, Vaughn B. Nocturnal seizures mimic REM behavior disorder. Am J Electroneurodiagnostic Technol. 1997;37:258–64.
61. Iber C, Ancoli-Israel S, Chesson A, Quan SF, for the Academy of Sleep Medicine. The AASM manual for scoring of sleep and associated events: rules, terminology and technical specifications. 1sted. Westchester (IL): American Academy of Sleep Medicine; 2007.
62. Aurora RN, Zak RS, Maganti RK, Auerbach SH, Casey KR, Chowdhuri S, et al. Best practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin sleep Med. 2010 Feb 15;6(1):85–95 (PubMed PMID: 20191945, Pubmed Central PMCID: 2823283).
63. Lapierre O, Montplaisir J. Polysomnographic features of REM sleep behavior disorder: development of a scoring method. Neurology. 1992 Jul;42(7):1371–4 (PubMed PMID: 1620348).
64. Takeuchi N, Uchimura N, Hashizume Y, Mukai M, Etoh Y, Yamamoto K, et al. Melatonin therapy for REM sleep behavior disorder. Psychiatry Clin Neurosci. 2001 Jun;55(3):267–9 (PubMed PMID: 11422870).
65. Ringman JM, Simmons JH. Treatment of REM sleep behavior disorder with donepezil: a report of three cases. Neurology. 2000 Sep 26;55(6):870–1 (PubMed PMID: 10994012).
66. Shneerson JM. Successful treatment of REM sleep behavior disorder with sodium oxybate. Clin Neuropharmacol. 2009 May-Jun;32(3):158–9 (PubMed PMID: 19483483).
67. Schmidt MH, Koshal VB, Schmidt HS. Use of pramipexole in REM sleep behavior disorder: results from a case series. Sleep Med. 2006 Aug;7(5):418–23 (PubMed PMID: 16815751).
68. Boeve BF, Silber MH, Ferman TJ. Melatonin for treatment of REM sleep behavior disorder in neurologic disorders: results in 14 patients. Sleep Med. 2003 Jul;4(4):281–4 (PubMed PMID: 14592300).
69. Sasai T, Matsuura M, Inoue Y. Factors associated with the effect of pramipexole on symptoms of idiopathic REM sleep behavior disorder. Parkinsonism Relat Disord. 2013 Feb;19(2):153–7 (PubMed PMID: 22989561).
70. American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic and coding manual. 2nd ed. Westchester (IL): American Academy of Sleep Medicine; 2005. xviii, p. 297.

Chapter 16
REM Behavior Disorder in Children

Sriram Ramgopal, Marcin Zarowski and Sanjeev V. Kothare

Introduction

Rapid eye movement (REM) sleep behavior disorder, sometimes known as REM behavior disorder (RBD), is a relatively rare parasomnia characterized by a loss of REM atonia and the presence of dream-enacting behavior. The condition occurs primarily among elderly males and typically occurs in the context of neurodegenerative disease such as Parkinson's disease or dementia. RBD in the pediatric population is less common. A few reports over the past three decades have documented the presence of these symptoms in the younger population. RBD in this group occurs in the context of various conditions and pathophysiology, despite similar symptomatology and response to treatment. As in adults, RBD can cause daytime tiredness and poor functioning. In addition to being aware of the clinical features, diagnosis, and treatment of RBD, the sleep specialist should also be aware of the existence of this rare condition among children.

S. Ramgopal (✉)
8 Garfield Lane East, Andover, MA 01810, USA
e-mail: Sriram.Ramgopal@childrens.harvard.edu

S. Ramgopal · M. Zarowski
Department of Neurology, Boston Children's Hospital, Boston, MA, USA

M. Zarowski
Polysomnography and Sleep Research Unit, Department of Developmental Neurology, Poznan University of Medical Sciences, 49 Przybyszewskiego STR, 60355 Poznan, Poland
e-mail: marcin.zarowski@gmail.com; zarowski@ump.edu.pl

S. V. Kothare
Center for Pediatric Sleep Disorders, Department of Neurology,
Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, USA
e-mail: sanjeevkothare@hotmail.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_16, © Springer Science+Business Media New York 2013

Case Example

An 8-year-old male child presented to the sleep clinic with complaints of excessive daytime sleepiness over a few months. Narcolepsy with cataplexy was diagnosed on polysomnography (PSG). Incomplete control of hypersomnia and continuing dream enactment was seen on treatment with venlafaxine and modafinil. Two weeks after initiation of therapy, the child developed symptoms of repeated violent behaviors during sleep and complained of nightmares in which the subject was pursued by an attacker. This prompted withdrawal of the venlafaxine and a trial of sodium oxybate. Symptoms of violent dreams and "acting out" behaviors gradually subsided over 2–4 weeks following withdrawal of venlafaxine. Modafinil was gradually withdrawn and the patient was treated on monotherapy with sodium oxybate, with improvement in hypersomnia, and disappearance of the dream enacting behaviors.

Definition

According to a review published by Schenck and Mahowald [1], "REM sleep behavior disorder is a multifaceted parasomnia involving REM sleep and the motor system in which there is problematic behavioral release that is usually experienced by the individual as enactment of distinctly altered, unpleasant and combative dreams." The essential characteristics of RBD are (1) lack of REM atonia, and (2) dream enactment. Dream enactments can take a variety of forms, ranging from simple limb movements to more complex behaviors which can be injurious to self or others, and can be at times potentially life-threatening. RBD was first described in 1986 in five elderly patients with typical clinical features [2].

Demographics

The exact prevalence of RBD in adults or children is not well known. In a telephone study conducted by Ohayon et al. in the UK using the Sleep-EVAL system in 4,972 individuals aged 15–100 years, 2 % of those surveyed had violent behaviors during sleep. Of these, 0.5 % had features suggestive of RBD [3]. In contrast, a study of patients coming for evaluation to Olmsted County, Minnesota, found the incidence of RBD in those with dementia to be 18.5 %, and in those without dementia to be 7.1 % [4]. Because of the rarity of RBD reported among children compared to adults, the incidence of RBD in children is likely much lower than these estimates. However, it is also possible that RBD is under-recognized in the pediatric population.

Etiopathogenesis

Animal Models

Animal models of RBD suggest that the lesion may lie in the dorsolateral pontine tegmental regions. In 1965, Jouvet [5] reported that experimental bilateral lesions caused by electrolysis in the pontine tegmentum have induced symptoms of REM-atonia and dream-enactment in a series of 35 cats. Morrison et al. further elucidated these patterns, finding differences in motor behaviors depending on the exact site of lesion. These findings correspond with case reports of RBD in individuals following pontine strokes [6, 7].

Neurodegenerative Disorders

The occurrence of RBD in elderly adults and often alongside [8, 9] or preceding [10] Parkinson's disease has led to the theory that RBD represents a neurodegenerative process in this population. In a case study of an elderly individual with nocturnal violent behavior during sleep, postmortem histopathological study revealed diffuse Lewy bodies seen in the substantia nigra, paranigral nucleus, supratrochlear nucleus, and mesencephalon [11]. These findings suggest that RBD belongs in the neurodegenerative spectrum characterized by abnormal cholinergic and dopamine signaling, which includes both Lewy body dementia and Parkinson's disease. In this population, RBD may occur secondary to cholinergic dysfunction, as demonstrated in a transcranial magnetic stimulation study [12] and a positron emission tomography (PET) study [13].

Amine Signaling

In the younger population, the etiology for RBD is poorly understood and is probably more varied. One suggested hypothesis involves alterations in amine signaling. Ju et al. [14] observed the high frequency of antidepressant usage among individuals with RBD. This hypothesis stems from a report documenting RBD in a 31-year-old man which began following the initiation of fluoxetine therapy. This patient's RBD persisted for 19 months following discontinuation of therapy [15]. The prevalence of RBD among individuals with psychiatric disturbances is 10 times higher than in the unaffected population. More evidence of the potential role of serotonergic dysfunction in RBD is suggested by its quick and robust responsiveness to clonazepam, which is thought to result partially from its effect on serotonergic receptors, besides its action on the gamma-aminobutyric acid (GABA)-A receptor, where it acts as an agonist [16].

Other Causes

Autoimmune disease has been speculated to increase the risk of RBD. Naturally, this is more often the case in females. According to a single-center study, 20 % of females with RBD were diagnosed to have an autoimmune disease, including a series of females in the 18–29 age group with rheumatoid arthritis [14]. A multicenter case control study, which primarily included adult males, found additional risk factors for RBD, including smoking, alcohol abuse, head injury, pesticide exposure, and farming [17].

Reports of Pediatric RBD in the Literature

The earliest report of RBD in a child was provided by Barros-Ferreira et al. in 1975. The authors reported this condition in an 8-year-old boy with an infiltrating pontine tumor. In addition to other symptoms relating to the space-occupying lesion, the parents reported agitated movements during sleep, described by the parents to be nightmares. A sleep study performed after ventriculo-atrial shunting demonstrated an infrequent and shortened REM atonia. REM sleep was associated with complex mouth movements, talking, laughter, and axial stiffening [18].

In 1989, Blaw et al. presented an 18-month-old boy with reported tongue biting and laceration, screaming, and stiffening during sleep. During monitoring in the video-EEG unit, the child was found to have lack of REM atonia associated with body movements. Clonazepam improved sleep behavior, though segmental myoclonus and tongue-biting persisted [19].

Schenk and Mahowald [20] published a series of 10 patients with narcolepsy who were found to have RBD on multiple sleep latency test (MSLT) and PSG. All patients met the criteria of increased electromyogram (EMG) tone and/or phasic muscle twitching and documented REM behaviors, including truncal jerking and violent behaviors. Three patients in this series were in the pediatric age groups, with ages ranging from 12 to 19 years. Four patients were managed successfully on clonazepam and one was managed with carbamazepine.

A report by Sheldon and Jacobsen [21] documented five children with vivid dreams and motor-behaviors, including limb and body movements. Some of these movements led to injuries due to repeatedly falling out of bed. One patient was known to have narcolepsy. On PSG, these five patients had a significantly shorter REM latency and a greater REM density and EMG phasic density, indicative of increased motor activity during sleep compared to age- and sex-matched controls. Interestingly, all five patients in the series responded well to clonazepam treatment.

Another isolated report was provided by Rye et al. [22] in which RBD occurred concomitantly with juvenile Parkinson's disease. This 18-year-old female patient had a 2-year history of Parkinson's disease and excessive daytime sleepiness. The patient's parent noted the presence of unusual behaviors in the patient, including sleep talking and flailing movements of the limbs. The patient had a significantly

raised EMG activity in both the submental and tibial regions compared to controls, supporting the diagnosis of RBD.

Thirumalai (2002) found a correlation between RBD and autism. In a series of 11 children with autism referred for PSG for disordered sleep, five patients were found to have RBD. The children in this series ranged in ages from 3 to 8 years and 3 of 5 were males. Activities noted to occur during sleep included crying and screaming during sleep, jerking movements, sitting up, bruxism, and wandering around the house [23]. This was the first report to date observing a possible correlation between RBD and autism spectrum disorders.

Another case series, published by Nevsimalova et al. [24] documented two girls with RBD that later evolved into narcolepsy. In a 9-year-old female patient, episodes of harmful behavior during sleep, in which she would aggressively attack her sibling and the wall, occurred for approximately 2 months before she began to develop sleep attacks. MSLT documented the presence of abnormal REM motor control, both clinically and on chin EMG, as well as sleep-onset REM episodes. The patient's symptoms required treatment with both sodium oxybate and clonazepam. In the second patient, a 7-year-old girl, cataplectic attacks and increased sleepiness developed over a 4-month period. During this time, she also developed talking and complex-motor behaviors during sleep. PSG revealed fragmented sleep, abortive SOREMs and phasic muscle activity during sleep. The patient was treated with modafinil and clonazepam.

A larger series by Lloyd et al. [25], reported 13 subjects with RBD and two subjects with REM sleep without atonia. The patients ages ranged from 3 to 17 years. Important comorbidities included anxiety, attention deficit disorder, developmental delay, and narcolepsy. One patient had Smith–Magenis syndrome (intellectual disability, sleep disturbances, craniofacial and skeletal anomalies, and behavioral problems), and another had Moebius Syndrome (congenital bilateral facial paralysis). Three patients in the series were using SSRIs. Treatments included clonazepam in 10 patients, of whom 8 had resolution of diurnal and nocturnal symptoms. Two patients were treated with melatonin, and had resolution of symptoms. One patient was treated by discontinuation of tricyclic antidepressant, which resulted in symptomatic improvement.

Clinical Features

Clinical features of RBD are highly variable. As described, vocal and motor activity during events may range from subtle to gross motor behaviors. The events typically occur in the first 90 min of falling asleep. Affected children also report vivid dreams during these episodes. RBD rarely occurs in isolation in the pediatric group, though this too has been documented. From the available reports however, it can be inferred that RBD may occur more commonly in children with depression on treatment with SSRIs, and in children with narcolepsy or Juvenile Parkinson's disease. In adolescents, substance abuse including alcohol should also be explored. Daytime features

of RBD are similar to those of other sleep disorders and can include poor daytime functioning and fatigue.

Differential Diagnosis

Important differential diagnoses should be considered before making the diagnosis of RBD. Periodic leg movements of sleep may mimic dream-enacting behaviors, as can many cases of focal nocturnal epilepsy. Sleepwalking and bruxism may be mistaken for RBD. Sudden awakenings with obstructive sleep apnea, nightmares, and sleep terrors may occasionally confuse the diagnosis as well.

Diagnostic Criteria

The diagnosis of RBD is the same in children as it is in adults. PSG is an important part of the diagnosis. PSG should be done to monitor for behaviors during sleep, to associate the presence of these behaviors during REM sleep, and to document the lack of REM atonia. Loss of REM atonia may only be intermittent. PSG is also useful in differentiating RBD from nocturnal seizures and periodic leg movements of sleep. The important diagnostic features of RBD, according to the *International Classification of Sleep Disorders, 2nd edition* [26] include:

1. The patient complains of violent or injurious behavior during sleep.
2. Limb or body movement is associated with dream mentation.
3. At least one of the following occurs:
   a. Harmful or potentially harmful sleep behaviors.
   b. Dreams appear to be "acted out".
   c. Sleep behaviors disrupt sleep continuity.
4. PSG monitoring demonstrates at least one of the following electrophysiologic measures during REM sleep:
   a. Excessive augmentation of chin EMG tone.
   b. Excessive chin or limb phasic EMG twitching, irrespective of chin EMG activity and one or more of the following clinical features during REM sleep:
      1. Excessive limb or body jerking.
      2. Complex, vigorous, or violent behaviors.
      3. Absence of epileptic activity in association with the disorder.
5. The sleep disorder is not associated with mental disorders, but may be associated with neurological disorders.
6. Other sleep disorders (e.g., sleep terrors or sleepwalking) can be present but are not the cause of the behavior.

Treatment

A few treatments for RBD have been described in the literature. No treatment has been tested in a prospective manner and treatment suggestions are based on limited case reports. There are less data documenting the treatment of RBD in children. Clonazepam is the most documented form of treatment, and in published reports, is usually effective and well-tolerated. Other treatments which have been reported to be effective include melatonin, pramipexole, paroxetine, acetylcholinesterase inhibitors, benzodiazepines, clozapine, and carbamazepine. Isolated reports have also documented efficacy to L-DOPA, Yi-Gan San, desipramine, and sodium oxybate [27]. Withdrawal of the SSRI often helps in resolving the symptoms of RBD.

Conclusion

The rarity of REM behavior disorder in children makes it hard to identify, diagnose, and treat this condition. The availability of a few case reports over the past two decades, however, confirms the existence of RBD in children. More information is needed to understand the etiologies of this condition in children compared to findings in adults. The sleep physician should be aware of the fact that RBD typically occurs in conjunction with other sleep disorders and only rarely occurs in isolation. The few published reports to date have noted that RBD is generally amenable to treatment, usually with clonazepam.

Practical Points

- RBD is rarer in children than in adults.
- Symptoms of RBD include “acting out” of abnormal dreams.
- The etiology of RBD is associated with a lesion in the region of the pons. The condition may be due to degenerative or autoimmune disease or associated with treatment or withdrawal of drugs. Common causes include narcolepsy, use of an SSRI, rare genetic syndromes, autism, and brainstem tumors or strokes.
- Clinical features of RBD include vivid dreams and violent or self-injurious behaviors during sleep.
- Differential diagnoses include epilepsy, periodic leg movement of sleep, and other parasomnias such as sleepwalking and bruxism.
- Diagnosis can be established by polysomnography documenting lack of REM atonia and varied sleep behaviors.
- Treatment usually includes clonazepam producing good results. No investigations to date have evaluated treatments in a randomized controlled trial.

References

1. Schenck CH, Mahowald MW. REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in SLEEP. Sleep. 2002;25(2):120–38.
2. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep. 1986;9(2):293–308.
3. Ohayon MM, Schenck CH. Violent behavior during sleep: prevalence, comorbidity and consequences. Sleep Med. 2010;11(9):941–6.
4. Rongve A, Boeve BF, Aarsland D. Frequency and correlates of caregiver-reported sleep disturbances in a sample of persons with early dementia. J Am Geriatr Soc. 2010;58(3):480–6.
5. Jouvet M, Delorme F. Locus coeruleus et sommeil paradoxal. C R Soc Biol. 1965;159:859–9.
6. Kimura K, Tachibana N, Kohyama J, Otsuka Y, Fukazawa S, Waki R. A discrete pontine ischemic lesion could cause REM sleep behavior disorder. Neurology. 2000;55(6):894–5.
7. Reynolds TQ, Roy A. Isolated cataplexy and REM sleep behavior disorder after pontine stroke. J Clin Sleep Med. 2011;7(2):211–3.
8. Bjornara KA, Dietrichs E, Toft M. REM sleep behavior disorder in Parkinson's disease—is there a gender difference? Parkinsonism Relat Disord. 2012;19(1):120–2.
9. Nihei Y, Takahashi K, Koto A, Mihara B, Morita Y, Isozumi K, et al. REM sleep behavior disorder in Japanese patients with Parkinson's disease: a multicenter study using the REM sleep behavior disorder screening questionnaire. J Neurol. 2012;259(8):1606–12.
10. Postuma RB, Bertrand JA, Montplaisir J, Desjardins C, Vendette M, Rios Romenets S, et al. Rapid eye movement sleep behavior disorder and risk of dementia in Parkinson's disease: a prospective study. Mov Disord. 2012;27(6):720–6.
11. Uchiyama M, Isse K, Tanaka K, Yokota N, Hamamoto M, Aida S, et al. Incidental Lewy body disease in a patient with REM sleep behavior disorder. Neurology. 1995;45(4):709–12.
12. Nardone R, Bergmann J, Brigo F, Christova M, Kunz A, Seidl M, et al. Functional evaluation of central cholinergic circuits in patients with Parkinson's disease and REM sleep behavior disorder: a TMS study. J Neural Transm. 2012;120(3):413–22.
13. Kotagal V, Albin RL, Muller ML, Koeppe RA, Chervin RD, Frey KA, et al. Symptoms of rapid eye movement sleep behavior disorder are associated with cholinergic denervation in Parkinson disease. Ann Neurol. 2012;71(4):560–8.
14. Ju YE, Larson-Prior L, Duntley S. Changing demographics in REM sleep behavior disorder: possible effect of autoimmunity and antidepressants. Sleep Med. 2011;12(3):278–83.
15. Schenck CH, Mahowald MW, Kim SW, O' Connor KA, Hurwitz TD. Prominent eye movements during NREM sleep and REM sleep behavior disorder associated with fluoxetine treatment of depression and obsessive–compulsive disorder. Sleep. 1992;15(3):226–35.
16. Ferini-Strambi L, Zucconi M. REM sleep behavior disorder. Clin Neurophysiol. 2000;111(Supp 2):S. 136–40.
17. Postuma RB, Montplaisir JY, Pelletier A, Dauvilliers Y, Oertel W, Iranzo A, et al. Environmental risk factors for REM sleep behavior disorder: a multicenter case-control study. Neurology. 2012;79(5):428–34.
18. Barros-Ferreira M, Chodkiewicz J, Lairy GC, Salzarulo P. Disorganized relations of tonic and phasic events of REM sleep in a case of brain-stem tumor. Electroencephalogr Clin Neurophysiol. 1975;38:203–7.
19. Blaw ME, Leroy RF, Steinberg JB, Herman J. Hereditary quivering chin and REM behavioral disorder. Ann Neurol. 1974;26:471.
20. Schenck CH, Mahowald MW. Motor dyscontrol in narcolepsy: rapid-eye-movement (REM) sleep without atonia and REM sleep behavior disorder. Ann Neurol. 1992;32:3–10.
21. Sheldon SH, Jacobsen J. REM-sleep motor disorder in children. J Child Neurol. 1998;13(6):257.
22. Rye DB, Johnston LH, Watts RL, Bliwise DL. Juvenile Parkinson's disease with REM sleep behavior disorder, sleepiness, and daytime REM onset. Neurology. 1999;53(8):1868–70.

23. Thirumalai SS, Shubin RA, Robinson R. Rapid eye movement sleep behavior disorder in children with autism. J Child Neurol. 2002;17(3):173–8.
24. Nevsimalova S, Prihodova I, Kemlink D, Lin L, Mignot E. REM behavior disorder (RBD) can be one of the first symptoms of childhood narcolepsy. Sleep Med. 2007;8(7–8):784–6.
25. Lloyd R, Tippmann-Peikert M, Slocumb N, Kotagal S. Characteristics of REM sleep behavior disorder in childhood. J Clin Sleep Med. 2012;8(2):127–31.
26. American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic and coding manual: American Academy of Sleep Medicine; 2005.
27. Aurora RN, Zak RS, Maganti RK, Auerbach SH, Casey KR, Chowdhuri S, et al. Best practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin Sleep Med. 2010;6(1):85–95.

Part V
Other Parasomnias

Chapter 17
Nocturnal Paroxysmal Dystonia

Joseph Kaleyias, Ruchi Arora and Sanjeev V. Kothare

Introduction

Nocturnal paroxysmal dystonia (NPD) is characterized by nonvoluntary nocturnal movements associated with dystonic and tonic postures and movements of the four limbs and body axis, automatisms, affective mimics, and vocalizations [1]. NPD along with paroxysmal arousals (PAs) and episodic nocturnal wanderings (ENW) comprise the three characteristic manifestations of nocturnal frontal lobe epilepsy (NFLE) [2, 3]. NFLE is an unusual form of partial epilepsy in which seizures, characterized by bizarre motor behavior or sustained dystonic posture, appear exclusively during sleep [4].

The absence of clear-cut epileptic abnormalities on the scalp electroencephalogram (EEG), especially in children with epilepsy that display nocturnal motor attacks, was thought to indicate that the episodes were parasomnias with dystonic posturing out of sleep even when they occurred in epileptic patients [5]. NPD is now believed to be a variant of frontal lobe epilepsy from a deep focus, with minimal to no EEG changes during the event, and normal EEGs in between attacks [6].

Lugaresi and Cirignotta [7] described a group of five patients ranging in age from 7 to 74 years with a history of 2–34 years duration of recurrent brief (< 2 min) motor

J. Kaleyias (✉)
Division of Pediatric Neurology, Department of Pediatrics,
University Hospital of Patras, Rio, 26504 Patras, Greece
e-mail: kaleyias@hotmail.com

R. Arora
Jenny Lind Children's Department, Norfolk and Norwich University Hospital,
Colney Lane, Norwich NR4 7UY, UK
e-mail: ruchi.arora@nnuh.nhs.uk

S. V. Kothare
Center for Pediatric Sleep Disorders,
Department of Neurology, Boston Children's Hospital,
Harvard Medical School, Boston, MA 02115, USA
e-mail: sanjeevkothare@hotmail.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_17, © Springer Science+Business Media New York 2013

attacks arising from non-rapid eye movement (NREM) sleep. All the five patients gave a history of "agitation" during sleep almost every night for many years. The episodes recurred every night or nearly every night a few seconds after an arousal from NREM sleep and were characterized by postures localized in one limb, or involving the entire trunk and all limbs, associated with or alternating with dyskinetic movements. EEG recordings both during sleep and wake-state and during the course of the events were normal in all cases. The uniform clinical behavior and EEG pattern suggested that this syndrome represented a distinct nosological entity. The authors originally used the term hypnogenic paroxysmal dystonia, which they later changed to nocturnal paroxysmal dystonia in 1986 [8]. Four patients in that study had a long follow-up, and all responded well to carbamazepine treatment. At the same time, Peled and Lavie suspected that these recurrent paroxysmal awakenings arising from NREM sleep and associated with daytime sleepiness were of epileptic origin [9].

From NPD to NFLE

The epileptic versus nonepileptic origin of NPD has been extensively debated. The stereotypic motor pattern of the events and the short duration and good response to carbamazepine along with the occurrence of attacks during the day suggested an epileptic origin of the events. In contrast, the absence of clear-cut epileptic ictal and interictal abnormalities made definitive confirmation of the epileptic nature of the attacks difficult. At the same time, the dystonic/dyskinetic motor patterns could also suggest a new kind of movement disorder [6, 8].

Evidence for an epileptic origin of the attacks with the aid of zygomatic and sphenoidal leads was provided by Tinuper et al. [10]. During prolonged video-EEG monitoring, two patients had a convulsive seizure after a typical NPD episode. On both occasions, the EEG showed rhythmic epileptiform discharges that allowed the authors to suggest that short NPD attacks were a form of mesial-orbital frontal epilepsy. The term NFLE was therefore adopted to replace the term NPD.

In 1992, Meierkord et al. [11] attempted to resolve whether NPD is a distinct clinical entity or a type of epilepsy, probably of frontal origin, by comparing clinical and EEG features of patients who fulfilled the criteria for a diagnosis of NPD with those in patients having daytime frontal lobe seizures versus nocturnal motor attacks of epileptic origin. The investigators concluded that the clinical and the ictal motor features did not allow a distinction between the three groups in this study (NPD, nocturnal epilepsy, and daytime frontal lobe epilepsy), and they postulated that these cases are example of epilepsy, presumably of frontal lobe origin in which EEG abnormalities were not evident on the scalp. Despite the aforementioned data, the International Classification of Sleep Disorders (ICSD-2) considers these complex movements as parasomnia [12].

Autosomal Dominant NFLE: An Inherited form of NFLE

NFLE may exist in sporadic, familial, idiopathic, cryptogenic, or symptomatic forms [2, 13, 14]. In 1994, Scheffer et al. described a large Australian family with NFLE inherited in an autosomal dominant pattern and the term autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) was adopted. ADNFLE is the first idiopathic epilepsy for which a genetic basis has been identified [13]. Approximately 25 % of patients have a family history of seizures [15]. Few families have two or more family members with the same seizure type consistent with ADNFLE [15]. Linkage studies have indentified genes for ADNFLE that encode the nicotinic acetylcholine receptor subunits (CHRNA4/CHRNB2) [16]. At least one-third of patients do not have identified genetic mutations (genetic heterogeneity) [16]. Positron emission tomography (PET) studies in ADNFLE patients suggest a hyperactivation of the cholinergic pathway ascending from the brainstem [17]. There is no difference between sporadic NFLE and ADNFLE in the clinical and neurophysiological findings.

Prevalence of NFLE

Definite epidemiological data are lacking because of the rarity of this condition. At the Epilepsy Unit of Strasbourg, 40 patients followed between1985 and 1992 showed symptoms consistent with NPD. These patients represent about 10 % of patients who had been referred for evaluation of nocturnal paroxysmal phenomena [1].

Types of Seizures in NFLE

NFLE comprises a spectrum of distinct phenomena, different in intensity but representing a continuum of the same epileptic condition, as seizures of different intensity could coexist in the same patient [2]. The seizures in NFLE can be grouped into three main categories, based on their semiology and duration, but all with the same underlying epileptic process [3]. PAs, NPD, and ENW are three characteristic manifestations of NFLE [2, 3] (Table 17.1). Patients rarely have only a single type of attack; the brief paroxysmal arousals, which are conceptualized as fragments of larger seizures, and all events are considered to be manifestations of the same underlying epileptic process [3].

Paroxysmal Arousals

PAs [2] consist of abrupt arousal from NREM sleep with vocalization and highly stereotypic motor pattern, often consisting of head movements, frightened or questioned expressions, and dystonic posturing of the limbs, lasting for < 20 s [1].

Table 17.1 Seizure types of nocturnal frontal lobe epilepsy [2, 3]. (Reprinted from Kaleyias and Kothare [37] with permission)

	Paroxysmal arousals (PAs)	Nocturnal paroxysmal dystonia (NPD)	Episodic nocturnal wandering (ENW)
Onset	Abrupt, recurring arousals from non-rapid eye movement (NREM) sleep	Begins as PA; evolves into complex movements	Starts as PA, evolves into NPD, then progresses to hypermotor, agitated wandering
Description	Vocalizations with stereotyped movements. Patient raises head, sit up in bed, looks around, screams	Kicking, bicycling, trunk rocking, tonic or clonic asymmetric, dystonic, or ballistic movements with flailing of limbs	Patient jumps out of bed, ambulates, appears agitated
Consequences	Sleep disruption and daytime sleepiness	Sleep disruption and daytime sleepiness	May lead to injuries
Duration	< 20 s	< 2 min	< 3 min
% of recorded seizures	75	23	2

They occur repetitively, and very frequently throughout the night, and are often underreported [3]. In some rare cases, the awakening is not so sudden, and the pathological hallmark of the attacks can be confirmed by their recurrence with the same stereotyped pattern.

PAs are underestimated on clinical grounds alone, as they are reported by patients only if especially frequent and violent [2]. In some patients with PA only, daytime tiredness, fatigue, and sleepiness were often the main complaint. Patients with PA alone seem to be rare, but this group of patients is characterized by a total absence of daytime seizures and a lack of brain lesions on neuroradiological studies. The stereotypic repetition of the same pattern, sometimes tens of times for long stretches during sleep, and the presence of choreoathetoid and dystonic postures of the limbs help to differentiate the PA from the physiological hypnic jerks or sleep starts upon purely visual inspection alone even when EEG epileptiform activity is not recorded.

Nocturnal Paroxysmal Dystonia

Episodes of NPD begin as paroxysmal arousals but are subsequently associated with more complex movements including bipedal automatisms, rhythmic twisting movements of the trunk and pelvis, vocalization, and tonic or dystonic posturing lasting less than a few minutes [3]. NPDs are accordingly classified as hyperkinetic motor subtype or asymmetric bilateral tonic seizure subtype [18]. Clinical characteristics of NPD are summarized in Table 17.2 [2, 9, 19].

Table 17.2 Clinical features of nocturnal paroxysmal dystonia [2, 9, 19]. (Reprinted from Kaleyias and Kothare [37] with permission)

Feature	
Mean age at onset (range)	14 years (1–64 years)
Male:female ratio	7:3 (high male prevalence)
Seizure type	Usually more than one type; occur in clusters
Clinical presentation	Patients may awaken with choking sensation or shortness of breath
Mean seizure frequency (range)	20/month (1–20/night)
Diurnal and secondarily generalized seizures	One-third of patients
Unawareness of seizures	> 70 %; complaints brought out by families
Consequences	Daytime sleepiness, sleep fragmentation, poor sleep quality reported by many; improves with antiepileptic drug (AED) therapy
Neurologic examination	Normal in 92 %
Neuroradiologic examination	Normal in 86 %

Episodic Nocturnal Wanderings (Agitated Somnambulism)

ENWs begin with a sudden awakening associated with dystonic posture or dyskinetic movements as PA or NPD, followed by agitated somnambulism characterized by jumping out of bed, twitching around, sudden directional changes, and moving around aimlessly as in a grotesque dance. Patients can talk unintelligibly or scream with a terrified expression. Dystonic postures may involve the head, trunk, and limbs [6].

ENWs can mimic sleep walking and confusional arousals, but has accompanying motor patterns and an abnormal EEG not seen with parasomnias [20]. The striking feature of ENWs is the agitated behavior of the patients running about, suddenly changing direction, jumping, screaming, and somersaulting in a kind of disorderly and grotesque dance quite different from the calmer physiological motor pattern of walking in somnambulist patients. Agitated sleepwalking often represents a useful diagnostic clue to NFLE [2].

ENWs are not very frequent and have not been successfully recorded even during polysomnography (PSG) recordings. Daytime somnolence may be the only symptom reported by patients with recurrent paroxysmal awakenings during the night.

EEG and Video-Polysomnographic Findings

Interictal and even ictal EEGs are uninformative, being either normal or marked by muscular artifacts in a substantial percentage of patients with NFLE [2, 21]. The percentage of epileptiform abnormalities in interictal wakefulness EEG range from 12 to 33 %, in interictal sleep EEG from 16 to 50 %, and in ictal EEG from 36 to 56 % (Fig. 17.1) [2, 22–24].

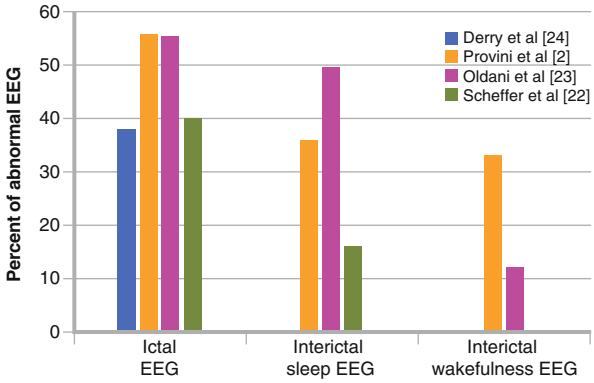


Fig. 17.1 Role of the EEG in the NFLE diagnosis. (Reprinted from Kaleyias and Kothare [37] with permission)

Only in some of the patients, sphenoidal EEG electrodes were shown to be useful. Thirteen patients in the study by Provini et al. had ictal EEG activity detected by these electrodes [2]. The insufficient accuracy of scalp EEGs emphasizes the need for depth electrode studies in these patients if surgery is indeed planned [25].

Tharp described [26] orbital frontal seizures in a series of three patients with a unique EEG pattern characterized by periodic frontal sharp and slow waves resembling the periodic activity of subacute sclerosing panencephalitis (SSPE). The seizures were associated with prominent autonomic disturbance, loud vocalization, and automatisms. It is speculated that this unique clinical pattern is due to seizure discharges arising in the orbital frontal region with a spread to subcortical areas, particularly the hypothalamus and the temporal lobe.

Polygraphic recordings indicate that these attacks generally occurred during stages 2, 3, and 4 of slow-wave sleep. Seizures appeared between 1 and 558 min after sleep onset (mean 207 ± 133 min). Ninety-seven percent of the attacks appeared during NREM sleep; 69 % during light (stage 1–2) and 28 % deep sleep (3–4) [2]. Initially, an EEG arousal and autonomic changes (tachycardia and tachypnea or bradycardia and apnea) were observed. During the actual attack, only artifacts were seen on the recordings. There was no postictal EEG suppression.

Anatomo-Electro-Clinical Correlations of NFLE: Frontal and Extrafrontal Origins of Seizures

A network including frontal and possible extrafrontal limbic structures is involved in the genesis of the complex epileptic manifestations of NFLE [21, 27]. Patients with asymmetric tonic posturing showed an early activation of supplementary motor area with a varying degree of involvement of the intermediate mesial frontal cortex

and the frontal cingulate gyrus [28]. This category includes asymmetric, bilateral tonic seizures with sudden asymmetric tonic/dystonic posturing assumed by the four limbs and sometimes maintained by the oral and facial muscles for a few seconds. Normally the patient remains alert and some vocalization may occur but he/she is unable to speak [29].

Patients with hyperkinetic ictal behavior showed the involvement of either mesial-dorsolateral, orbitopolar, opercular, or larger cortical regions [28]. In the hypermotor seizures, a sudden awakening associated with an intense autonomic activation and dystonic posture characterizes seizure onset. Thereafter, widespread massive extrapyramidal activation with violent and arrhythmic choreoathetoid and ballismic movements and strange emotional behaviors follow. Patients with ENW showed an activation of anterior cingulate, orbitopolar, and temporal regions [20].

Patients with NFLE may occasionally present with seizures of extrafrontal origin. Seizures from temporal lobe may also mimic hyperkinetic semiology [30], whereas seizures from the insula may mimic asymmetric tonic posturing.

The term frontal lobe epilepsy does not signify that the seizures originate from this lobe alone, as other lobes could present with the same semiology but with a common pathway for discharges originating elsewhere. Thus, the term NFLE refers to a syndromic entity whose hallmark is the recurrence of hypermotor seizures during sleep, but does not define the epileptic zone. Therefore, an invasive monitoring is always needed if surgical treatment is considered. The term NPD is a comprehensive definition of different complex seizures regardless of the site of the epileptic zone [21].

Co-Occurrence of NFLE and Parasomnias

The familial nature of both parasomnias and NFLE is widely recognized [21]. Recently, we have started recognizing the co-occurrence of NFLE with parasomnias. While the prevalence of arousal disorders in the general population is only 1–6 %, almost one-third of patients with NFLE have a history of parasomnia (mostly arousal disorders) [2]. Approximately 50 % of patients with NFLE have a family history of parasomnia including arousal disorder, rapid eye movement (REM) behavior disorder (RBD), primary enuresis, and rhythmic movement disorders [2].

Bisulli et al. [31] recently undertook a prospective familial aggregation study on a population with established NFLE proven by video-polysomnographic recordings of attacks. They compared patients with NFLE with a control population and found statistically higher lifetime prevalence of arousal parasomnias among NFLE probands (OR = 6.3) and their relatives (OR = 4.7). These findings indicate a true link between the arousal parasomnias and NFLE. The cholinergic system and related pathways could represent a model unifying the pathogenesis of arousal parasomnias and NFLE [21]. Till date, genetic analysis has failed to disclose a common ground between NFLE and parasomnias [32].

A plausible hypothesis [2, 33] is that parasomnias typical for childhood are substituted by NFLE later in life in predisposed individuals. The morphogenetic role

of acetylcholine (ACh) in the development of the frontal cortex [34] may represent a common mechanism in the arousal parasomnias and NFLE that could share an abnormal development of the frontal cortical architecture [32].

Another hypothesis is that a pathological phenomenon (epileptic discharge or a pathological arousal) may activate the central pattern generators (CPGs) in the brainstem, triggering repetitive motor patterns characterizing NFLE and some parasomnias [35, 36].

Differential Diagnosis

Frontal lobe seizures, which display a wide range of frequently bizarre clinical features often combined with normal or nonspecific interictal and ictal EEG findings can be a source of diagnostic confusion [3, 37, 38].

Epileptic Disorders

Hyperkinetic seizures associated with affective symptoms are considered a typical manifestation of NFLE [39]. Patients with *nocturnal temporal lobe epilepsy* (*NTLE*) with mainly sleep-related seizures have been described; however, they commonly lack hyperkinetic activity and their daily seizure frequency outside the sleep is low. Mai et al. [40] examined 25 patients with sleep-related hyperkinetic epileptic seizures, with a frontal lobe onset in 18 cases and a temporal lobe onset in 7 cases. Patients with sleep-related hyperkinetic seizures with temporal lobe origin had amnesia, and their clinical features were strikingly similar to those with a frontal onset, with agitated movements, high seizure frequency, and no history of febrile convulsions. The authors concluded that this kind of epileptic manifestation is not specific to frontal lobe epilepsy only. The comparison between NFLE and NTLE is shown in Table 17.3 [40].

Sleep-related seizures similar to those observed in people with NLFE may have an *extrafrontal origin* and the etiologic substrate may play a role in facilitating the occurrence of seizures during sleep [30, 41–43]. In both frontal and extrafrontal cases of surgically treated drug-resistant sleep-related epilepsy (SRE), Taylor's type focal cortical dysplasia (TFCD), a disorder of cortical malformation [44], has been shown to be the most frequent finding at histopathologic examination [30]. Nobili et al. [45] have statistically confirmed a strong association between SRE (sleep-related epilepsy) and TFCD in a population of drug-resistant epileptic patients. Significantly higher proportion of TFCD was documented in the frontal lobe (67.6 % in the frontal lobe versus 33.3 and 37.5 in the temporal and posterior quadrant, respectively). One of every two patients with a TFCD, independent of its location, had an SRE confirming the effect of TFCD as an independent risk factor for SRE. The diagnosis of TFCD increases the risk of SRE 14-fold. The investigators concluded that TFCD should be considered as the potential etiological factor when evaluating a drug-resistant patient

Table 17.3 Comparison between nocturnal frontal and nocturnal temporal lobe epilepsy [40]. (Reprinted from Kaleyias and Kothare [37] with permission)

	Nocturnal frontal lobe epilepsy ($N = 18$)	Nocturnal temporal lobe epilepsy ($N = 7$)
Male:female ratio	10:8	2:5
Mean age of onset, years (range)	6.3 (1–24 years)	5.6 (1–17)
Neurologic examination	Normal	Normal
Family history of epilepsy	7 (38.8 %)	2 (28.5 %)
Median frequency of seizures per month	35	42
EEG background activity normal	14 (77.8 %)	1 (14.3 %)
EEG focal spikes/sharp waves	7 (38.8 %)	7 (100 %)
EEG ictal		
Negative	5 (27.8 %)	1 (14.3 %)
Frontal uni- or bilateral fast activity	5 (27.8 %)	0
Frontotemporal fast activity	8 (44.4 %)	3 (42.9 %)

with SRE, even if findings are absent on the MRI. In addition, surgical treatment of TFCD-associated SRE provides excellent results [30].

Sleep Disorders

The behavioral presentations of NREM arousal parasomnias, REM behavior disorder, and NFLE can be similar [21]. Several sleep phenomena may occur during nighttime that can mimic seizures. Sleep-related paroxysmal disorders of infancy and childhood present a significant challenge for the clinician, with the distinction of nocturnal epilepsy from nonepileptic sleep disorders often being the primary concern [3, 37, 38]. Although in some patients, diagnosis is easy to establish, other cases may require a video-EEG recording of the episodes because of the similarities between the nonepileptic events and epileptic seizures [46].

In the International Classification of Sleep Disorders, 2nd edition (ICSD-2) (AASM, 2005), the disorders mimicking epilepsy have been categorized into parasomnias, sleep-related breathing disorders, sleep-related movement disorders, and "others" [12]. In addition, certain sleep phenomenon can occur during wakefulness in the daytime, thus mimicking epilepsy. These phenomena have been summarized in Fig. 17.2 [3, 12].

Differential diagnosis for episodes of sudden arousal from sleep accompanied by motor activity and often dramatic or bizarre behaviors include: NREM arousal parasomnias, REM sleep behavior disorder, and nocturnal panic attacks.

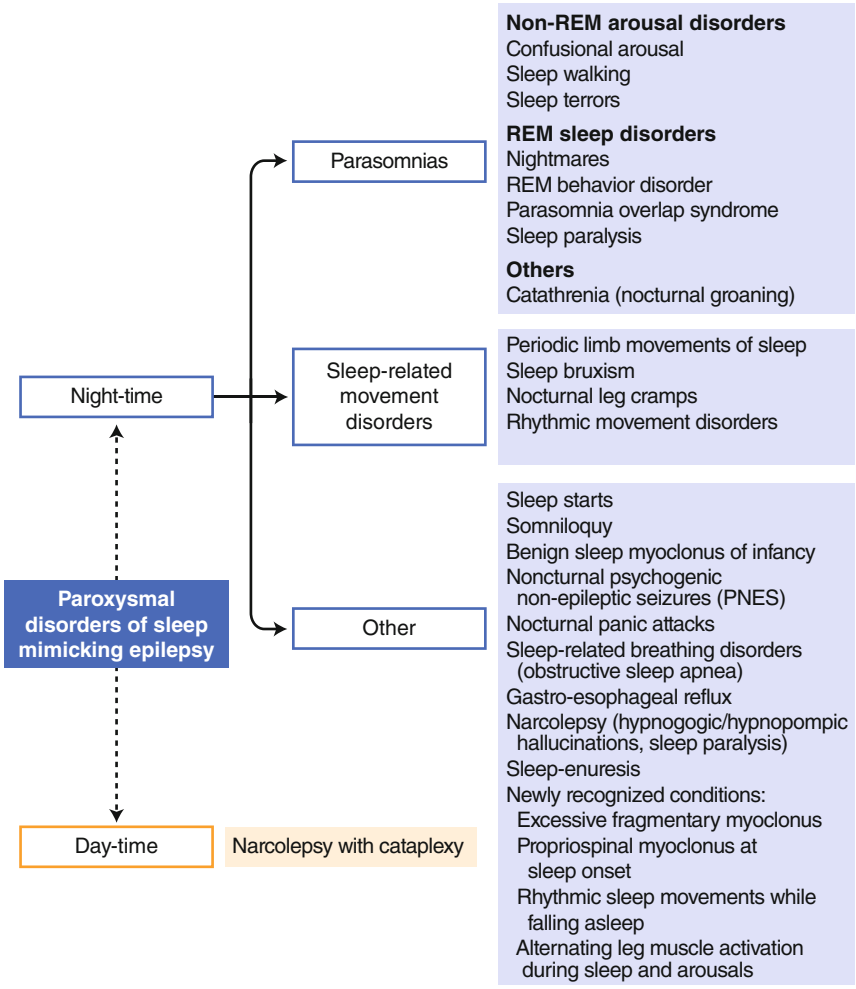


Fig. 17.2 Paroxysmal disorders of sleep mimicking epilepsy (ASDA, 2005) [3, 12]. (Reprinted from Kaleyias and Kothare [37] with permission)

Differential Diagnosis of NFLE

Parasomnias

More than 80 % of preschool-age children experience parasomnias, which can be difficult to differentiate from nocturnal seizures [40, 41]. Non-REM arousal parasomnias are paroxysmal behaviors without conscious awareness, usually arising from stage 3 or 4 non-REM sleep. On the basis of the occurrence of motor activity and the autonomic involvement, they are classically subdivided into three main

forms: confusional arousals (little motor or autonomic involvement), somnambulism (mainly motor activity but little autonomic involvement), and sleep terrors (prominent autonomic involvement with variable motor activity) [12]. While parasomnias are generally benign, frequent or unusual episodes may sometimes be confused with epilepsy, particularly NFLE [3, 24, 47, 48]. Various parasomnias have been discussed in detail in other chapters in this book. In addition, parasomnias can coexist with frontal lobe epilepsy. Features differentiating them from seizures will be addressed here and are summarized in Table 17.4 [3, 24]. Disorders of arousal tend to arise earlier in childhood and disappear over the years. In addition, these episodes are isolated and rare (1 every 1–4 months) without the stereotypic extrapyramidal patterns (dystonic posturing, hemiballismic movements, or tremors choreoathetosis) [6]. NFLE is more likely than arousal disorder when the attacks recur several times during the same night, when they occur in a stereotyped fashion, when they arise or persist into adulthood, and when tremor dystonia, ballism, or abnormal movements are present during the attack.

REM Sleep Behavior Disorder

Later life onset (around 60 years) and complex behavior associated with dream mentation along with the typical polygraphic findings of REM sleep without atonia is the hallmark of this condition and has been described elsewhere in this book.

Nocturnal Panic Attacks

These are also characterized by a sudden awakening from sleep with dramatic agitation and a sensation of imminent death [6]. The episodes usually arising in adolescence or middle age often recur several times a night and are prolonged (24 min as a mean). They are accompanied by symptoms of choking and breathlessness and by daytime panic attacks.

NPD of Variable Duration [8]

Short-lasting NPD shows many similarities with paroxysmal kinesigenic dystonia (the short duration, the responsiveness to carbamazepine, and the common occurrence of sporadic seizures of definite epileptic origin, in some cases), which makes differentiation between a movement disorder and seizure difficult. NPD of intermediate duration (3–5 min) triggered by arousal during sleep and by protracted exercise during wakefulness differ from NFLE in their duration, triggering effect of exercise, and above all the peculiar motor patterns (asynchronous jerks of head, trunk, and limbs, making the patient look like a puppet on strings). Long-lasting NPD (2–50 min) arising from light sleep, recurring several times per night, and resistant to antiepileptic drugs (AEDs) was recently described in two patients. The long duration, the inefficacy of AED, and the link with Huntington's disease in one patient

Table 17.4 Comparison of clinical and video-EEG/PSG features of parasomnias versus NFLE and important quantitative and qualitative features that can be used in the positive identification of parasomnias [3, 24]

	Parasomnias	Nocturnal frontal lobe epilepsy (NFLE)
Age at onset	Usually < 10 years	Variable; usually childhood or adolescence
Family history	60–90 %	≤ 40 %
Attacks per night (mean)	1 or 2	> 3
Episode frequency/mo	< 1–4	20–40
Clinical course (over years)	Trends to disappear by adolescence	Often stable with increasing age
Disease duration (mean)	~ 7 years	~ 20 years
Episode duration (mean)	Seconds to 30 min	Seconds to 3 min (often < 2 min)
Semiology of movements (*for details, see next part of this table*)	Variable complexity; not highly stereotyped (on video)	Highly stereotyped on video monitoring; often vigorous movements
Trigger factors	Sleep deprivation, febrile illness, alcohol, stress	Often not identified
Associated conditions	Obstructive sleep apnea	Often not identified
Ictal electroencephalogram (EEG)	Slow waves, no epileptiform features	Often normal or obscured by movements. Frankly epileptiform ictal rhythms in < 10 %
Time of episodes during sleep	First third of the night, but usually after 90 min of sleep	Any time, but may occur in first 30–60 min
Polysomnographic sleep stages when events occur	Non-rapid eye movement sleep stage 3 or 4	Usually non-rapid eye movement sleep stage 1, occasionally 3 or 4
Important quantitative and qualitative features that can be used in the positive identification of parasomnias		
Features *strongly favoring* parasomnias	Features *moderately favoring* parasomnias	Features that *do not discriminate* between parasomnias and NFLE
Yawning	Tremor/trembling	Brevity
Scratching and prominent nose-rubbing	Myoclonic jerks	Sitting
Rolling over in bed	Coughing	Standing or walking[a]
Internal or external trigger (noise, cough, snore)	Semipurposeful behaviors, fumbling, manipulation of nearby objects	Preceding "normal" arousal
Waxing and waning pattern	Variability/absence of stereotypy	Brief arousals (up to 10 s) without definite semiological features of epilepsy
Physical or verbal interaction	No events recorded on first night of monitoring	Fearful emotional behavior
Sobbing, sad emotional behavior	Few events recorded in total (less than 3)	
Indistinct offset		

Table 17.4 (continued)

	Parasomnias	Nocturnal frontal lobe epilepsy (NFLE)
Failure to fully arouse after event with complex behavior		
Prolonged duration (> 2 min)		
Discordance between severity and duration of *reported* event and *recorded* event		

[a] Standing and walking do not, in usual circumstances, discriminate between parasomnias and NFLE. However, in individuals who rouse to full wakefulness after their events, and in whom events have an indistinct offset, standing or walking suggests a diagnosis of parasomnias over NFLE

suggests a basal ganglia involvement. NPD with long-lasting attacks has many similarities with paroxysmal dystonic choreoathetosis because of the long duration of the attacks, the ineffectiveness of AEDs, and the absence of epileptic antecedents.

Pathophysiology

Nocturnal and Periodic Occurrence of the Attacks

Attacks could assume a quasiperiodic occurrence during some portion of NREM sleep [10, 49] occurring every 20–40 s that reflects the pulsatility of arousal mechanisms. K complexes are a characteristic feature of stage 2 sleep, arising in the prefrontal cortex [3], which often coincide with or immediately precede the seizure onset, suggesting that K complexes may trigger epileptic seizures [6, 50]. Deep cortical hyperpolarization–depolarization sequences characterizing K complexes may provoke a cortical arousal mainly in the frontal cortex and trigger an epileptic discharge in a predisposed individual. The epileptic discharges may then spread to limbic cortical and subcortical circuits provoking sudden vigilance and autonomic changes along with the peculiar motor patterns [2]. This hypothesis is also supported by the fact that the seizures tend to recur with the same periodicity as that of K complexes in physiological conditions [6].

Seizures with Primitive Stereotyped Behavior

The cortical discharges are not merely confined to the orbitofrontal or mesiofrontal regions but may also act (by disinhibition) on other cortical-subcortical networks, involving the limbic system, thus explaining primitive behaviors [51, 52]. The complex, semipurposeful, sometimes primitive, motor behaviors like screaming, grasping, implorations, imprecations, spitting and whistling, rocking and rolling, and compulsive

wandering are more difficult to ascribe to a specific cortical frontal area. The dystonic/dyskinetic features often observed during seizures suggest an involvement of subcortical structures like the basal ganglia, the ventral striatopallidal system, and the brainstem (CPGs of emotional and instinctive behavior) [32].

The observation that similar motor features can accompany both arousal disorder parasomnias and seizures, including those of NFLE, has led to the hypothesis that both phenomena may indicate a release of normal neocortical inhibition of CPGs in mesencephalon, pons, and/or spinal cord [35, 53, 54]. CPGs are neuronal aggregates responsible for coordinated motor routines of innate behaviors [55]. The locomotor activity that occurs in both NFLE and NREM arousal parasomnias may indicate convergent disinhibition of locomotor CPGs during seizure activity (in NFLE) or a different pathological disinhibition mechanism relating to arousal (in NREM parasomnias) [54].

The Role of Nicotinic Acetylcholine Receptor

The ACh acts as a possible common pathogenic mechanism that is supported by recent experimental data showing that nicotine-stimulated locomotion depends on activation of mesolimbic dopaminergic system [56]. A recent PET study disclosed that ADNFLE patients with alpha four mutation of nicotinic acetylcholine receptor (nAChR) had reduced D1 receptors in the striatum [57]. Therefore, alterations in mesostriatal dopaminergic circuits with an increase of dopamine in the striatum and prefrontal cortex and a reduced inhibition of excitatory thalamocortical projections to frontal lobes may contribute to the nocturnal paroxysmal activity observed in ADNFLE [56].

Diagnostic Tools

Clinical History and Diagnostic Criteria

A reliable description of nocturnal motor events is difficult to collect from a witness. The semiological subjective elements are often absent in all types of motor events during sleep. The standard criteria for diagnosing NFLE are still lacking [21]. However, the NFLE study groups [2, 3, 23] around the world utilize different operative criteria that can be summarized as:

a. History: Nocturnal paroxysmal episodes consistent with NFLE.
b. Video-polysomnography: Positive ictal EEG; or if EEG is negative, the clinical features of PAs, NPD, or ENWs must be present.

The Frontal Lobe Epilepsy and Parasomnias Scale

Derry et al. have developed the frontal lobe epilepsy and parasomnias (FLEP) scale as a method to distinguish NFLE from parasomnias [58]. The scale was found to be associated with a risk of misdiagnosis in some patients especially with ENW, which were misinterpreted as arousal parasomnias [59], indicating a low sensitivity of the scale. In one-third of parasomnia patients who belonged to an RBD group, the scale indicated a misleading diagnosis of epilepsy, which showed its low specificity. Despite the above limitations, FLEP is a useful screening tool, but it may need a video or polysomnographic recording for the assessment of more complex behaviors [59].

Video-Polysomnography

Video-EEG polysomnography (VPSG) is the gold standard for the diagnosis of paroxysmal nocturnal events. However, it has a sensitivity of less than 100 % (especially in patients with rare seizures) and a theoretical 100 % specificity is flawed by an unsatisfactory interobserver agreement [21, 60].

In a recent paper, Derry et al. [24] systematically evaluated semiological features of 120 events recorded on the video-EEG monitoring (57 parasomnias, 63 NFLE seizures) from 44 subjects in order to identify features that can be used to reliably distinguish parasomnias from NFLE. The clinical features that strongly favored parasomnias included interactive behavior, failure to wake after event, and indistinct offset. While sleep stage at onset was discriminatory (82 % of seizures occurred during stage 1 or 2 sleep, with 100 % of parasomnias occurring from stage 3 or 4 sleep), ictal EEG features were less useful. A video analysis of parasomnias identified three principal behavioral patterns: arousal behavior (92 % of events); nonagitated motor behavior (72 %); and distressed emotional behavior (51 %). An algorithm generated from these data correctly classified 94 % of events. While sleep stage at onset was discriminatory (82 % of seizures occurred during stage 1 or 2 sleep, with 100 % of parasomnias occurring from stage 3 or 4 sleep), ictal EEG features were less useful. Physiological stimuli (external or internal) or subclinical seizure discharges can induce indistinguishable arousal behaviors during sleep. In parasomnias, these may evolve to a clinical parasomnia and terminate with return to sleep or with a full awakening. In individuals with nocturnal epilepsy, clinically evident seizures with distinguishing characteristic behaviors and marked stereotypy may occur, or the event may terminate with full waking or return to sleep (Fig. 17.3) [24]. The algorithm based on video features only is shown in Fig. 17.4 [24]. In this study, the proposed algorithm correctly classified 113 of 120 (94 %) of events. The comparison of clinical and video-EEG/PSG features of parasomnias versus NFLE that can be used for the positive identification of parasomnias are shown in Table 17.4 [3, 24].

If events are stereotypic or repetitive, occur frequently (minimum two events per week), and the history is suggestive of potential epileptic seizures, the patients should be considered for the video-EEG monitoring in a sleep laboratory (with extended

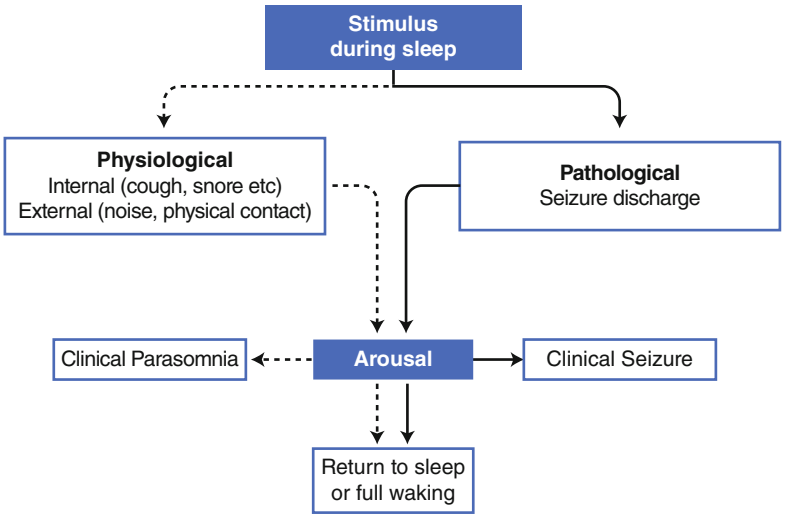


Fig. 17.3 Relationship of arousal behavior to parasomnias and nocturnal seizures. (Reprinted from Kaleyias and Kothare [37] with permission)

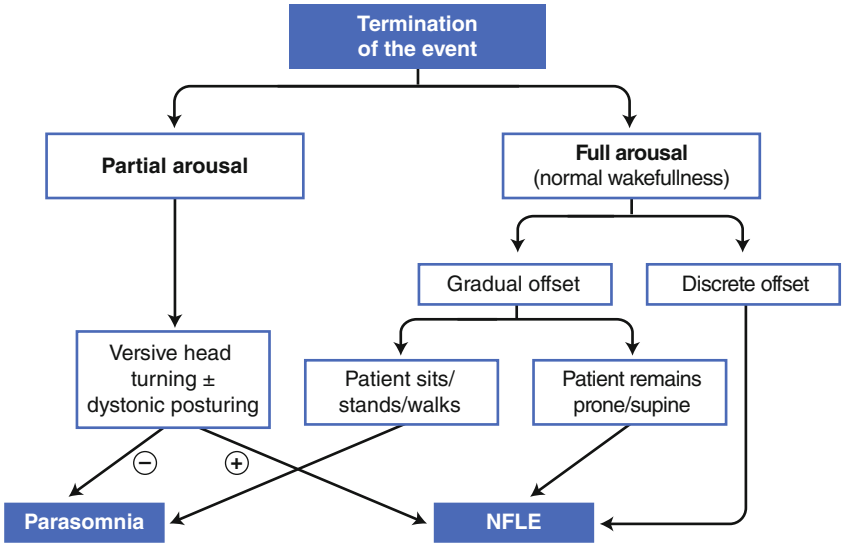


Fig. 17.4 Algorithm for the differential diagnosis of nocturnal arousals. (Reprinted from Kaleyias and Kothare [37] with permission)

multichannel scalp EEG, electromyographic monitoring of all four extremities, and continuous, time-synchronized audiovisual recording). Scalp EEG recording even during an episode is of limited diagnostic value, because in about half of NFLE seizures, ictal EEG fails to disclose any paroxysmal abnormality [2, 18].

Homemade Video Recordings

A homemade video is a useful adjunct to aid the diagnosis. It can be a valuable option in cases of infrequent episodes not caught during video-EEG monitoring or when having few to none interictal EEG findings [21].

Treatment

Treatment with the small doses of carbamazepine was effective in all patients described by Lugaresi and Cirignotta in 1981 [7], with an efficacy of 70 % in controlling seizures [19]. Approximately one-third of the patients, usually with a high seizure frequency, are drug-resistant [6, 19]. The percentage of drug-resistant patients is similar to those found in other forms of epilepsy [61]. The claimed "benign" nature of NFLE is thought to be due to the limited social impact of nocturnal seizures on the daytime functioning and the quality of life [6]. Refractory seizures should, however, be worked up for surgical treatment [1].

Circadian distribution of seizures may provide an opportunity for the assessment and therapeutic interventions in specific populations of patients [62, 63]. In their recent study, Guilhoto et al. demonstrated an improved seizure control with a differential AED dosing schedule adjusted for seizure timing, with the fewer side effects in selected patients [62]. They described 17 children with nocturnal or early-morning seizures who were switched to a proportionally higher evening dose of AEDs. Differential dosing led to seizure freedom in 64.7 % (11/17) of patients, and 88.2 % (15/17) experienced $\geq$ 50 % reductions in seizures. Therefore, in patients with NFLE, use of individually tailored AED dosing, that is, higher doses of AEDs in the evening, may be helpful.

Up to one-third of patients with epilepsy may have obstructive sleep apnea (OSA), a common disorder that results in sleep disruption and sleep deprivation [64]. In patients with epilepsy, improvement in seizure control with treatment of coexisting OSA has been reported. Vendrame et al. [65] showed that epilepsy patients with OSA who were compliant with continuous positive airway pressure (CPAP) for a minimum of 6 months had a better seizure control than those who were noncompliant with CPAP. Tonsillectomy and adenoidectomy as treatment of OSA may decrease seizure frequency, especially in children with elevated body mass index scores and of younger age at the time of surgery [66].

Safety Issues

An agitated and violent motor behavior of the ENWs that presents with running about, sudden change in direction, or jumping may lead to severe self-injuries [2, 6]. It has been demonstrated that complex, violent acts arising from sleep without conscious awareness may cause injuries such as ecchymosis, abrasions, lacerations,

fractures, burns, cranial trauma, self-mutilation, and assaults on others [67]. Thus, measures to ensure safety of the environment should be considered, such as removal of obstructions in the bedroom, securing windows, installing locks or alarms on the outside doors, covering windows with heavy curtains. In cases of violence inflicted on self or others, forensic evaluation may be necessary to assess legal responsibility of the involved individual [68].

Conclusions

In the last two decades, paroxysmal nocturnal motor events have been the topic of intensive studies. NFLE should always be suspected in the presence of paroxysmal nocturnal events characterized by a high frequency of similar-night or inter-night repetition, occasionally persistence into adulthood, "extrapyramidal features" or agitated behavior, and stereotypy of the attacks [6]. An apparently low prevalence of NFLE may be due to the fact that diagnosis is seldom made without audiovisual recording [2, 6].

The diagnosis of NFLE remains a powerful challenge. The use of video-EEG and PSG technology has resulted in considerable progress in defining the spectrum of nocturnal motor paroxysmal events. NFLE can be misdiagnosed as an NREM arousal parasomnia; less commonly as a REM behavior disorder or nocturnal panic attack [2, 6, 19].

The recording of episodes by using video-EEG/PSG may be required to make a definite diagnosis, although this may be difficult to achieve. Important quantitative and qualitative features can be used for the positive identification of parasomnias. NFLE is usually managed with small doses of the antiepileptic drugs, but many patients are resistant to AED therapy; fortunately, the social impact of seizures is limited, as they are confined to sleep. The locomotor activity that occurs in both NFLE and NREM arousal parasomnias may indicate convergent disinhibition of locomotor CPGs during seizure activity (in NFLE) or can have a different pathological disinhibition mechanism related to arousals (in NREM parasomnias) [54].

Future research should clarify the physiopathogenetic and molecular substrates underlying the mechanisms leading to nonepileptic paroxysmal disorders and epileptic seizures during sleep. The understanding of the mechanisms through which the sleep–wake cycle controls NPDs should help in designing new therapeutic strategies [18]. Future research should define reliable criteria for the diagnosis of NFLE and explore genetic aspects and epidemiology NFLE and parasomnias in order to better understand the links between epileptic and nonepileptic nocturnal motor events.

Practical Points

- Paroxysmal arousals (PAs), nocturnal paroxysmal dystonia (NPD), and episodic nocturnal wanderings (ENW) are three characteristic manifestations of nocturnal frontal lobe epilepsy (NFLE).

- NFLE should be suspected when stereotyped paroxysmal agitated nocturnal motor behavior reoccurs many times during the night or multiple times per month and when onset starts or persists into adulthood.
- Interictal and even ictal scalp electroencephalogram (EEG) recording often fails to disclose paroxysmal abnormalities in NFLE in up to 20 % of cases. Video-polysomnographic recording of the attack during sleep is the gold standard for the diagnosis. A home video is a useful adjunct in establishing the diagnosis.
- NFLE patients respond to antiepileptic drugs, especially carbamazepine.
- NFLE must be distinguished from arousal disorders in children.
- NREM parasomnias are more common in NFLE than in normal healthy population. They coexist in almost 30 % of patients with NFLE and in their families.
- Similar motor features can accompany both arousal disorder parasomnias and seizures, including those of NFLE. This observation has led to the hypothesis that both phenomena may indicate a release of normal neocortical inhibition of central pattern generators in mesencephalon, pons, and/or spinal cord.

Case Example

A 14-year-old boy started experiencing thrashing movements in sleep, occurring nightly and often several times per night. Video-EEG monitoring showed no clear EEG correlate of the events captured during the monitoring, and magnetic resonance imaging (MRI) of the brain (on a 1.5-T magnet) was unremarkable. The events were thought to be NREM parasomnias, on the spectrum of paroxysmal nocturnal dystonia. Family history was unremarkable. Multiple AEDs failed to control these events. A repeated evaluation at a tertiary care epilepsy center showed that on a 3.0-T magnet with epilepsy protocol, a subtle focal cortical dysplasia (FCD) was detected deep in the mesial frontal lobe on the MRI and ictal single-photon emission computed tomography (SPECT) scan showed hyperintense focus in the same area. Resection of the FCD led to the complete resolution of the nocturnal events.

References

1. Hirsch E, Sellal F, Maton B, Rumbach L, Marescaux C. Nocturnal paroxysmal dystonia: a clinical form of focal epilepsy. Neurophysiol Clin. 1994;24:207–17.
2. Provini F, Plazzi G, Tinuper P, Vandi S, Lugaresi E, Montagna P. Nocturnal frontal lobe epilepsy. A clinical and polygraphic overview of 100 consecutive cases. Brain. 1999;122(Pt 6):1017–31.
3. Derry CP, Duncan JS, Berkovic SF. Paroxysmal motor disorders of sleep: the clinical spectrum and differentiation from epilepsy. Epilepsia. 2006;47:1775–91.
4. Bazil CW. Nocturnal seizures. Sem Neurol. 2004;24:293–300.
5. Tassinari CA, Mancia D, Bernardina BD, Gastaut H. Pavor nocturnus of non-epileptic nature in epileptic children. Electroencephalogr Clin Neurophysiol. 1972;33:603–7.
6. Provini F, Plazzi G, Lugaresi E. From nocturnal paroxysmal dystonia to nocturnal frontal lobe epilepsy. Clin Neurophysiol. 2000;111:S2–8.

7. Lugaresi E, Cirignotta F. Hypnogenic paroxysmal dystonia: epileptic seizure or a new syndrome? Sleep. 1981;4:129–38.
8. Lugaresi E, Cirignotta F, Montagna P. Nocturnal paroxysmal dystonia. J Neurol Neurosurg Psychiatry. 1986;49:375–80.
9. Peled R, Lavie P. Paroxysmal awakenings from sleep associated with excessive daytime somnolence: a form of nocturnal epilepsy. Neurology. 1986;36:95–8.
10. Tinuper P, Cerullo A, Cirignotta F, Cortelli P, Lugaresi E, Montagna P. Nocturnal paroxysmal dystonia with short-lasting attacks: three cases with evidence for an epileptic frontal lobe origin of seizures. Epilepsia. 1990;31:549–56.
11. Meierkord H, Fish DR, Smith SJ, Scott CA, Shorvon SD, Marsden CD. Is nocturnal paroxysmal dystonia a form of frontal lobe epilepsy? Mov Disord. 1992;7:38–42.
12. American Academy of Sleep Medicine. International classification of sleep disorders, 2nd ed. Diagnostic and coding manual. Westchester, IL: American Academy of Sleep Medicine; 2005
13. Scheffer IE, Bhatia KP, Lopes-Cendes I, Fish DR, Marsden CD, Andermann E, et al. Autosomal dominant nocturnal frontal lobe epilepsy. A distinctive clinical disorder. Brain. 1995;118:61–73
14. Combi R, Dalpra L, Tenchini ML, Ferini-Strambi L. Autosomal dominant nocturnal frontal lobe epilepsy-a critical overview. J Neurol. 2004;251:923–34.
15. Ryvlin P, Rheims S, Risse G. Nocturnal frontal lobe epilepsy. Epilepsia. 2006;47(Supl 2):83–6.
16. Phillips HA, Scheffer IE, Crossland KM, Bhatia KP, Fish DR, Marsden CD, et al. Autosomal dominant nocturnal frontal-lobe epilepsy: genetic heterogeneity and evidence for a second locus at 15q24. Am J Hum Genet. 1998;63:1108–16.
17. Picard F, Bruel D, Servent D, Saba W, Fruchart-Gaillard C, Schöllhorn-Peyronneau MA, et al. Alteration of the in vivo nicotinic receptor density in ADNFLE patients: a PET study. Brain. 2006;129(Pt 8):2047–60.
18. Tinuper P, Provini F, Bisulli F, Vignatelli L, Plazzi G, Vetrugno R, et al. Movement disorders in sleep: Guidelines for differentiating epileptic from non-epileptic motor phenomena arising from sleep. Sleep Med Rev. 2007;11:255–67.
19. Provini F, Plazzi G, Montagna P, Lugaresi E. The wide clinical spectrum of nocturnal frontal lobe epilepsy. Sleep Med Rev. 2000;4:375–86.
20. Plazzi G, Tinuper P, Montagna P, Provini F, Lugaresi E. Epileptic nocturnal wanderings. Sleep. 1995;18:749–56.
21. Bisulli F, Vignatelli L, Provini F, Leta C, Lugaresi E, Tinuper P. Parasomnias and nocturnal frontal lobe epilepsy (NFLE): lights and shadows—controversial points in the differential diagnosis. Sleep Med. 2011;12 (Suppl 2):S27–32.
22. Scheffer IE, Bhatia KP, Lopes-Cendes I, Fish DR, Marsden CD, Andermann F, et al. Autosomal dominant frontal epilepsy misdiagnosed as sleep disorder. Lancet. 1994;343(8896):515–7.
23. Oldani A, Zucconi M, Ferini-Strambi L, Bizzozero D, Smirne S. Autosomal dominant nocturnal frontal lobe epilepsy: electroclinical picture. Epilepsia. 1996;37:964–76.
24. Derry CP, Harvey AS, Walker MC, Duncan JS, Berkovic SF. NREM arousal parasomnias and their distinction from nocturnal frontal lobe epilepsy: a video EEG analysis. Sleep. 2009;32:1637–44.
25. Williamson PD, Spencer DD, Spencer SS, Novelly RA, Mattson RH. Complex partial seizures of frontal lobe origin. Ann Neurol. 1985;18:497–504.
26. Tharp BR. Orbital frontial seizures. An unique electroencephalographic and clinical syndrome. Epilepsia. 1972;13:627–42.
27. Proserpio P, Cossu M, Francione S, Gozzo F, Lo Russo G, Mai R, et al. Epileptic motor behaviors during sleep: anatomo-electro-clinical features. Sleep Med. 2011;12 (Suppl 2):S33–8.
28. Ryvlin P, Minotti L, Demarquay G, Hirsch E, Arzimanoglou A, Hoffman D, et al. Nocturnal hypermotor seizures, suggesting frontal lobe epilepsy, can originate in the insula. Epilepsia. 2006;47:755–65.
29. Provini F, Tinuper P, Bisulli F, Lugaresi E. Arousal disorders. Sleep Med. 2011;12 (Suppl 2):S22–6.
30. Nobili L, Cossu M, Mai R, Tassi L, Cardinale F, Castana L, et al. Sleep-related hyperkinetic seizures of temporal lobe origin. Neurology. 2004;62:482–5.

31. Bisulli F, Vignatelli L, Naldi I, Licchetta L, Provini F, Plazzi G, et al. Increased frequency of arousal parasomnias in families with nocturnal frontal lobe epilepsy: a common mechanism? Epilepsia. 2010;51:1852–60.
32. Tinuper P, Bisulli F, Provini F, Montagna P, Lugaresi E. Nocturnal frontal lobe epilepsy: new pathophysiological interpretations. Sleep Med. 2011;12 (Suppl 2):S39–42.
33. Tinuper P, Provini F, Bisulli F, Lugaresi E. Hyperkinetic manifestations in nocturnal frontal lobe epilepsy. Semeiological features and physiopathological hypothesis. Neurol Sci. 2005;26 (Suppl 3):S210–4.
34. Hohmann CF. A morphogenetic role for acetylcholine in mouse cerebral neocortex. Neurosci Biobehav Rev. 2003;27:351–63.
35. Tassinari CA, Rubboli G, Gardella E, Cantalupo G, Calandra-Buonaura G, Vedovello M, et al. Central pattern generators for a common semiology in fronto-limbic seizures and in parasomnias. A neuroethologic approach. Neurol Sci. 2005;26 (Suppl 3):S225–32.
36. Parrino L, Halasz P, Tassinari CA, Terzano MG. CAP, epilepsy and motor events during sleep: the unifying role of arousal. Sleep Med Rev. 2006;10:267–85.
37. Kaleyias J, Kothare SV. Sleep and epilepsy. In: Kothare SV, Kotagal S, editors. Sleep in childhood neurological disorders. New York, NY: Demos Medical Publishing; 2011. p. 71–96.
38. Kothare SV, Kaleyias J. Sleep and epilepsy in children and adolescents. Sleep Med. 2010;11:674–85.
39. Salanova V, Morris HH, Van Ness P, Kotagal P, Wyllie E, Lüders H. Frontal lobe seizures: electroclinical syndromes. Epilepsia. 1995;36:16–24.
40. Mai R, Sartori I, Francione S, Tassi L, Castana L, Cardinale F, et al. Sleep-related hyperkinetic seizures: always a frontal onset? Neurol Sci. 2005;26 (Suppl 3):S220–4.
41. Nobili L, Francione S, Cardinale F, Lo R. Epileptic nocturnal wanderings with a temporal lobe origin, a stereo-EEG study. Sleep. 2002;25:669–71.
42. Dobesberger J, Ortler M, Unterberger I, Walser G, Falkenstetter T, Bodner T, et al. Successful surgical treatment of insular epilepsy with nocturnal hypermotor seizures. Epilepsia. 2008;49:159–62.
43. Kaleyias J, Loddenkemper T, Vendrame M, Das R, Syed TU, Alexopoulos AV, et al. Sleep-wake patterns of seizures in children with lesional epilepsy. Pediatr Neurol. 2011;45:109–13.
44. Taylor DC, Falconer MA, Bruton CJ, Corsellis JA. Focal dysplasia of the cerebral cortex in epilepsy. J Neurol Neurosurg Psychiatry. 1971;34:369–87.
45. Nobili L, Cardinale F, Magliola U, Cicolin A, Didato G, Bramerio M, et al. Taylor's focal cortical dysplasia increases the risk for sleep-related epilepsy. Epilepsia. 2009;50:2599–604.
46. Fusco L, Specchio N. Non-epileptic paroxysmal manifestations during sleep in infancy and childhood. Neurol Sci. 2005;26 (Suppl 3):S205–9.
47. Nobili L, Francione S, Mai R, Cardinale F, Castana L, Tassi L, et al. Surgical treatment of drug-resistant nocturnal frontal lobe epilepsy. Brain. 2007;130:561–73.
48. Montagna P. Nocturnal paroxysmal dystonia and nocturnal wandering. Neurology. 1992;42 (Suppl 6):61–7.
49. Sforza E, Montagna P, Rinaldi R, Tinuper P, Cerullo A, Cirignotta F, et al. Paroxysmal periodic motor attacks during sleep: clinical and polygraphic features. Electroencephalogr Clin Neurophysiol. 1993;86:161–6.
50. Lugaresi E, Coccagna G, Mantovani M, Lebrun R. Some periodic phenomena arising during drowsiness and sleep in man. Electroencephalogr Clin Neurophysiol. 1972;32:701–5.
51. Tassinari CA, Gardella E, Meletti S, Rubboli E. The neuroethological interpretation of motor behaviours in "nocturnal-hyperkinetic-frontal seizures": emergence of "innate" motor behaviours and role of central pattern generators. In: Beaumanoir A, Andermann F, Chauvel P, Mira L, Zifkin B, editors. Frontal seizures and epilepsies in children. London: John Libbey Eurotext; 2003. pp. 43–8.
52. Tinuper P. Parasomnias versus epilepsy: common grounds and a need to change the approach to the problem. Epilepsia. 2007;48(5):1033–4.
53. Berkovic SF, Crompton DE. The borderland of epilepsy: a clinical and molecular view, 100 years on. Epilepsia. 2010;51 (Suppl 1):3–4.

54. Crompton DE, Berkovic SF. The borderland of epilepsy: clinical and molecular features of phenomena that mimic epileptic seizures. Lancet Neurol. 2009;8:370–81.
55. Grillner S. The motor infrastructure: from ion channels to neuronal networks. Nat Rev Neurosci. 2003;4:573–86.
56. Ferrari R, Le Novère N, Picciotto MR, Changeux JP, Zoli M. Acute and long-term changes in the mesolimbic dopamine pathway after systemic or local single nicotine injections. Eur J Neurosci. 2002;15:1810–8.
57. Fedi M, Berkovic SF, Scheffer IE, O'Keefe G, Marini C, Mulligan R, et al. Reduced striatal D1 receptor binding in autosomal dominant nocturnal frontal lobe epilepsy. Neurology. 2008;71:795–8.
58. Derry CP, Davey M, Johns M, Kron K, Glencross D, Marini C, et al. Distinguishing sleep disorders from seizures: diagnosing bumps in the night. Arch Neurol. 2006;63:705–9.
59. Manni R, Terzaghi M, Repetto A. The FLEP scale in diagnosing nocturnal frontal lobe epilepsy, NREM and REM parasomnias: data from a tertiary sleep and epilepsy unit. Epilepsia. 2008;49:1581–5.
60. Vignatelli L, Bisulli F, Provini F, Naldi I, Pittau F, Zaniboni A, et al. Interobserver reliability of video recording in the diagnosis of nocturnal frontal lobe seizures. Epilepsia. 2007;48:1506–11.
61. Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med. 2000 Feb 3;342(5):314–9.
62. Guilhoto LM, Loddenkemper T, Vendrame M, Bergin A, Bourgeois BF, Kothare SV. Higher evening antiepileptic drug dose for nocturnal and early-morning seizures. Epilepsy Behav. 2011;20:334–7.
63. Loddenkemper T, Lockley SW, Kaleyias J, Kothare SV. Chronobiology of epilepsy: diagnostic and therapeutic implications of chrono-epileptology. J Clin Neurophysiol. 2011;28:146–53.
64. Manni R TM, Arbasino C SI, Galimberti CA, Tartara A. Obstructive sleep apnea in a clinical series of adult epilepsy patients: frequency and features of the comorbidity. Epilepsia. 2003;44:836–40.
65. Vendrame M, Auerbach S, Loddenkemper T, Kothare S, Montouris G. Effect of continuous positive airway pressure treatment on seizure control in patients with obstructive sleep apnea and epilepsy. Epilepsia. 2011;52:e168–71.
66. Segal E, Vendrame M, Gregas M, Loddenkemper T, Kothare SV. Effect of treatment of obstructive sleep apnea on seizure outcomes in children with epilepsy. Pediatr Neurol. 2012;46:359–62.
67. Schenck CH, Pareja JA, Patterson AL, Mahowald MW. Analysis of polysomnographic events surrounding 252 slow-wave sleep arousals in thirty-eight adults with injurious sleepwalking and sleep terrors. J Clin Neurophysiol. 1998;15:159–66.
68. Guilleminault C, Leger D, Philip P, Ohayon MM. Nocturnal wandering and violence: review of a sleep clinic population. J Forensic Sci. 1998;43:158–63.

Chapter 18
Sleep Related Dissociative Disorders

Keith R. Warren

Introduction

Sleep related dissociative disorders are characterized by dissociative episodes that emerge during the normal sleep period near sleep–wake transitions. Unlike other parasomnias, sleep related dissociative episodes occur during well-established EEG wakefulness. For this reason, they are also referred to as dissociative pseudoparasomnias. Other names include nocturnal (psychogenic) dissociative disorder and hysterical somnambulistic trance [1].

Dissociation is a primitive psychological defense that occurs in the setting of overwhelming stress or trauma. It serves to protect the individual from the distressing experience by removing it from consciousness. This also results in a failure to integrate the experience into one's life and thus recover from the stressor. Dissociation results in the formation of a parallel consciousness, which may reexperience or attempt to cope with previous stressors [2, 3].

Diagnostic Criteria

Sleep related dissociative disorders are a variant of dissociative disorders, which are defined by the Diagnostic Statistical Manual of Mental Disorders (Fourth Edition, Text Revision; DSM IV-TR) as disruptions in the usually integrated functions of consciousness, memory, identity, or perception of the environment. DSM IV-TR lists five major dissociative categories:

- *Dissociative Amnesia* is characterized by an inability to recall important personal information, usually of a traumatic or stressful nature, that is too extensive to be explained by ordinary forgetfulness.

K. R. Warren (✉)
Department of Sleep Medicine, Chicago Sleep Group, Winfield, IL, USA
e-mail: keith.warren@sublung.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_18, © Springer Science+Business Media New York 2013

- *Dissociative Fugue* is characterized by sudden, unexplained travel away from home or one's customary place of work, accompanied by an inability to recall one's past and confusion about personal identity or the assumption of a new identity.
- *Dissociative Identity Disorder* (formerly Multiple Personality Disorder) is characterized by the presence of two or more distinct identities or personality states that recurrently take control of the individual's behavior accompanied by an inability to recall important personal information that is too extensive to be explained by ordinary forgetfulness.
- *Depersonalization Disorder* is characterized by persistent or recurrent feeling of being detached from one's mental process or body that is accompanied by intact reality testing.
- *Dissociative Disorder Not Otherwise Specified* is characterized by a disorder with dissociation as its predominant feature that does not meet the criteria for any specific dissociative disorder.

Of the five categories, three categories of dissociative disorders (dissociative identity disorder, dissociative fugue, and dissociative disorder NOS) have been identified with sleep related dissociative disorders [1, 4, 5]. The similarity of the behaviors found with nocturnal dissociative disorders to the behaviors found with other parasomnias warrants their inclusion as a parasomnia [1].

The International Classification of Sleep Disorders, 2nd ed. (ICSD-2) lists the following diagnostic criteria for sleep related dissociative disorders:

1. A dissociative disorder must fulfill Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV), criteria and emerges in close association with the main sleep period.
2. One of the following is present:
    a. PSG demonstrates a dissociative episode or episodes that emerge during sustained EEG wakefulness, either in the transition from wakefulness to sleep or after an awakening from NREM or REM sleep.
    b. In the absence of a PSG-recorded episode of dissociation, the history provided by observers is compelling for a sleep-related dissociative disorder, particularly if the sleep-related behaviors are similar to observed daytime dissociative behaviors.
3. The sleep disturbance is not better explained by another sleep disorder, a medical or neurologic disorder, mental disorder, medication use, or substance use disorder.

Notice that while EEG recording may be the only objective means of confirming these disorders, it is not necessary to establish a diagnosis. When EEG recording is available, EEG wakefulness is present throughout the dissociative episode, as opposed to a mixture of sleep–wake features typically seen in arousal parasomnias such as sleepwalking, confusional arousals, and sleep terror. The time interval between EEG arousal and observed behavior can also help distinguish a dissociative episode from an arousal parasomnia, since arousal parasomnias begin almost immediately after an arousal, whereas with sleep related dissociative disorders may lag by 15–60 s [1].

Clinical Features

Most patients with sleep related dissociative disorders also have corresponding daytime dissociative disorders and have past or current histories of physical abuse, sexual abuse, or other overwhelming stressors. Dissociative disorders have been associated with child abuse [6], interpersonal violence [7], combat [8], and natural disasters [9]. Common psychiatric comorbidities include posttraumatic stress disorder, major depressive disorder, anxiety disorders, borderline personality disorder, and substance abuse. Patients may also have a history or self-mutilating behaviors, suicide attempts, and multiple psychiatric hospitalizations. Nevertheless, a sleep related dissociative disorder can occur as an isolated condition without a daytime component and without a history of trauma, abuse, or significant psychiatric comorbidities [1, 10, 11].

The clinical presentation of sleep related dissociative episodes can vary greatly. Cases have been reported in children and adults. Episodes can last from minutes to hours. Activities range from semipurposeful movements during which the individual appears asleep to complex and even bizarre goal-directed behaviors. Patients may show marked agitation and violence during episodes leading to significant injury. Events can take the form of a dissociative fugue involving driving an automobile great distances or flying on an airplane. Some may assume a different personality or the characteristics of an animal. Dissociative episodes may represent reenactments of previous physical and sexual abuse, and be associated with sexualized behavior during which the patient appears distressed. Eating uncooked food or binge eating high-calorie food can occur during dissociative episodes. By definition, episodes occur during EEG wakefulness, but may be recounted as a "dream" when the individual "wakes up" and is no longer in a dissociative state. Others may be completely amnestic of the dissociative event [11, 12].

Epidemiology and Course

While general population studies cite a 5 % prevalence rate of diurnal dissociative symptoms in adults, the prevalence of sleep related dissociative disorder is unknown. In a study of 150 consecutive patients presenting to a sleep disorders center for evaluation of repeated sleep related injuries, polysomnographic evaluations identified 8 cases (5.3 %) associated with sleep related dissociative disorder, there was a strong female predominance (87.5 %), and the mean age at referral was 29.5 years [11]. In case reports, age of onset ranges from childhood to middle adulthood. Onset can be gradual and sporadic or abrupt and fulminant. Episodes often occur several times weekly to multiple times nightly. As with most dissociated disorders, the course tends to be chronic and severe. The greatest risk factors include a history of physical, sexual, or emotional abuse combined with severe and chronic psychiatric disorders. Complications include repeated injuries to self or bed partner from the dissociative behaviors and can result in ecchymoses, fractures, lacerations, self-mutilations, and burns.

Etiology

Trauma or extreme stress, especially in childhood, is thought to be a precipitant for most dissociative disorders. It is not clear why some patients display a sleep related variant of dissociative disorders. One mechanism proposed is that a functional disconnection or loss of integration among various brain regions occurs in psychogenic dissociation. Sleep–wake transitions may increase one's vulnerability to dissociate due to sensory misperceptions and dissociative phenomena that can occur at these times [1, 13, 14]. If the original trauma occurred in a bed, as is likely with sexual abuse, the bed or sleep environment may also serve as a trigger for dissociation.

Differential Diagnosis

Sleep-related dissociative disorders share features with NREM parasomnias (sleepwalking, confusional arousals and sleep terrors), REM parasomnias (REM behavior disorder or nightmares), nocturnal seizures, altered states of consciousness due to a medical condition (hypoglycemia, hepatic encephalopathy, infection, CNS pathology, etc.) or the effects of a medication or substance (alcohol, hypnotics, etc.).

Non-REM arousal parasomnias include sleepwalking, confusional arousals, and sleep terrors. These usually occur in slow-wave sleep during the first third of the night, but can also arise from any stage of NREM sleep and may occur late in the sleep period [15]. These disorders are characterized by incomplete transition from NREM sleep, automatic behavior, and an altered state of consciousness. They usually peak at 8–12 years, do not have a gender bias, and often are associated with a positive family history [16]. Treatment typically involves reassurance, optimizing safety in the sleep environment, maintaining good sleep hygiene, avoiding sleep deprivation, and evaluating for other medical conditions or medications that may increase arousals. Sleep-related dissociative episodes may appear similar to NREM arousal parasomnias, but are usually associated with daytime dissociative features, often occur in the setting of trauma or significant psychiatric illness, and if EEG monitor is done, episodes arise from well-established wakefulness.

REM behavior disorder (RBD) is a parasomnia that occurs due to loss of normal REM sleep atonia. It is associated with dream enactment that is often violent, and can result in serious injuries to the patient and bed partner. RBD has a male predominance, begins in middle to late age, and often precedes neurodegenerative conditions, such as Parkinson's disease. It is rarely seen in children or females, as opposed to sleep related dissociative disorder that has a female predominance and may present in childhood. Serotonin medications, such as SSRIs, may be associated with developing RBD. Clonazepam and melatonin are usually effective treatments for RBD [17].

Nocturnal seizures may also be mistaken for other parasomnias, including sleep related dissociative disorder. Nocturnal frontal lobe epilepsy (NFLE) can present with arousals, stereotypic movements (head elevation, sitting, pelvic rocking, kicking,

and dystonic posturing), appearing confused or frightened, screaming and agitated somnambulation. A differentiating feature is that the events are relatively brief, lasting from seconds to a few minutes [18], while dissociative episodes are typically longer. Mean age of onset for NFLE is 10–12 years, and is typically associated with a previously normal psychomotor development. Establishing the diagnosis by EEG abnormalities can be difficult. Events usually respond to anticonvulsant therapy.

Certain medications have been associated with complex sleep related behaviors with dissociative features. Activities include nocturnal eating, cooking, sexual intercourse, driving, and bizarre behavior. Multiple reports involve the use of zolpidem [19]. Risk of sleep related behaviors was increased with higher doses of zolpidem and with female gender [20]. Other psychotropic medications, including antipsychotics, antidepressants, anxiolytics, and mood stabilizers, have also been associated with nocturnal amnestic activities and parasomnias [20–23].

Treatment

As dissociative disorders are usually associated with significant psychopathology, treatment typically consists of a combination of prolong psychotherapy and medications to treat comorbid psychiatric conditions. Psychotherapy is directed toward the effects of a patient's trauma history and can include a mix of psychodynamic therapy, cognitive behavioral therapy (CBT), insight-oriented therapy, dialectical behavioral therapy (DBT), hypnotherapy, and eye movement desensitization and reprocessing (EMDR). Therapy needs to be conducted carefully by skilled clinicians to prevent retraumatization. For dissociative symptoms in children, early intervention is important and treatment may involve forms of play and creative art therapy. A stable living environment without risk of future trauma is also essential.

The International Society for the Study of Trauma and Dissociation has published guidelines to phase-oriented treatment in adults as well as children and adolescents that are widely used in the field of dissociative treatment [24]. The first phase of therapy focuses on relieving distressing symptoms related to dissociative disorders, ensuring the individual safety, improving the patient's ability to form and maintain healthy relationships, and improving general daily life functioning. Comorbid disorders such as substance abuse and eating disorders are addressed in this phase of treatment. The second phase focuses on stepwise exposure to traumatic memories while reducing future dissociation. The final phase focuses on reintegrating the dissociative states into a single functioning identity with all its memories and experiences intact.

Case Example 1

Molaie and Deutsch report the case of a 10-year-old boy who began to experience nocturnal enuresis [25]. He was also noted to have sleepwalking and occasionally would exhibit violent behavior during sleep, including kicking and punching his

parents. His mother reported that he tried to jump out of a window of their apartment during one episode. Parents reported no snoring, coughing, vomiting, or loss of bowel control. The episodic events would last up to 30 min and could occur several times during one night with no recollection by the patient.

Two weeks prior to nocturnal enuresis, he moved to a new residence away from his grandmother, who was a primary caregiver to him. At the same time, his father began to work longer hours and he was transferred to a new school.

He was diagnosed with sleepwalking and night terrors. Magnetic resonance imaging (MRI) and EEG were normal. Treatment with imipramine and clonazepine were not effective. There was no known prior psychiatric history or evidence of preexisting disorder. Past developmental history and academic history were normal. There was no reported history of physical or sexual abuse. Family history was negative for psychiatric illness, epilepsy, and parasomnias.

Continuous video/EEG monitoring revealed several events that occurred exclusively at night, lasting from 2 min to 3.5 hours. Complex behaviors included punching, kicking, attempting to bite nursing staff and jumping out of bed. During these episodes, his eyes were closed, and he remained unresponsive to external stimuli. He denied dreaming and had no recollection of the events. All episodes arose from EEG wakefulness.

He was diagnosed with adjustment disorder with depressed mood. Treatment involved individual and family psychotherapy with a focus on reestablishing the relationship of the child with his parents and in particular with his father. The episodes ceased after therapy.

Case Example 2

Schenck et al. report the case of a 34-year-old woman who was referred for evaluation of sleep-related behaviors [11]. Sleep history was unremarkable until five months prior when major stressors triggered an abrupt onset of the behaviors. Within a 9-day period, the patient's father suddenly died of a myocardial infarction, the patient had her eighth miscarriage (at 16 weeks gestation), her mother committed suicide, and her second husband left her. She had received a diagnosis of Post-Traumatic Stress Disorder (PTSD) and major depression. She refused psychiatric hospitalization and failed to engage in ongoing psychotherapy despite seeing various psychologists, due to the fear that "they would die on me like my father did." The sleep-related episodes occurred at least twice weekly, and occasionally daily, generally beginning more than 2 h after perceived sleep onset. Several episodes involved driving to an airport, appropriately dressed but without luggage, purchasing a ticket and boarding flights to distant cities. She would then "awaken" en route in the setting of a panic attack and would be confused as to where she was. Upon landing, she boarded a return flight home, and resumed her life, with complete amnesia for how she had left home and boarded an airplane.

She would also drive great distances, only to "come to" at a remote gas station. Other episodes involved wandering around her yard and neighborhood in a nightgown, crashing through a glass door, breaking windows, and running into furniture. Self-sustained injuries included ecchymoses and lacerations. Other bizarre behavior included cutting her hair in an odd fashion, shredding her daughter's snowsuit, ripping sweaters, and tearing down drapes.

Relevant history includes the death of her first husband in an accident, multiple separations from her second husband, a sister dying in an automobile accident two months prior to referral. She was intelligent, had a master's degree and was employed in a technical field.

At the time of referral, psychiatric diagnoses included PTSD, major depression, panic disorder, thanatophobia (fear of dying), and dissociative disorder. On interview, she appeared depressed, tearful, and had several panic attacks. There was no evidence of psychosis. PSG studies performed during her usual sleeping hours did not reveal seizure activity, behaviors arising from NREM sleep, or abnormality of REM sleep. Periodic limb movements were elevated though. PSG identified two behavior episodes that arouse from unequivocal EEG wakefulness. The first occurred approximately 1 h after initial sleep onset, during which the patient wandered into a hallway and appeared confused. The second episode involved sitting up suddenly, hyperventilating and not being able to speak for a few minutes.

Psychotherapy was attempted but the patient declined as she was convinced that her therapist "will die too since he is the same age my father was when he died." Medication treatments were partially effective for anxiety symptoms, but had no effect on sleep related episodes. The patient's dissociative events progressed to include three distinct personalities ranging from childlike, to highly competent, to rageful. Eventually, it was discovered that she had been a victim of repeated incest by the father and at age 14 became pregnant and subsequently delivered a son-brother, who twenty years later, still lived in close proximity to her. The sexual abuse occurred not only with the mother's knowledge, "but with her approval." Dissociative episodes fulfilled criteria for dissociative identity disorder and dissociative fugue.

Case Example 3

Another report from Schenck et al. is the case of a 19-year-old male who had nocturnal episodes of assuming the characteristics of a large cat [11]. Episodes involved prowling around the house on all four limbs while growling, hissing, leaping about and biting objects in the manner of a large jungle cat for periods of up to 1 h. Episodes terminated by an abrupt collapse and unresponsiveness. The patient was amnestic of his actions, but would recall a recurrent "dream" of being a lion or tiger attempting to grab a "piece of raw meat" but was held back by an invisible force field, which made him feel "disappointed" and "frustrated". The "dream" always ended with "someone shooting a tranquilizer gun at me" resulting in him falling down and becoming unconscious. He remained unresponsive to family members during these episodes,

and his posturing and behavior was consistent with that of a large cat. He commonly opened the refrigerator with his mouth, put uncooked bacon between his teeth and then proceed to prowl around the house. He had injured his lips and gingiva on numerous occasions from biting sharp objects, and also had ecchymoses and lacerations on his trunk and limbs. Nocturnal activity was also associated with excessive daytime sleepiness. The onset of this disorder had no recognized precipitant. Shortly after the onset, he had a psychiatric hospitalization and was diagnosed with depression. His history was pertinent for premature birth, postpartum respiratory distress syndrome, and multiple severe cognitive impairments. He was adopted at 10 months, and was reported to have an excessive attachment to his mother, exhibiting intense separation reactions whenever she slept away from home. There was no history of physical or sexual abuse since the time of his adoption at 10 months, with the antecedent history being unknown. PSG studies documented the characteristic episodes occurring during well-established EEG wakefulness.

Summary

Sleep related dissociative disorders are a variant expression of diurnal dissociative disorders. Episodes occur in well-established EEG wakefulness. Trauma, especially in childhood, is a common finding. Age of onset can range from childhood to adulthood and females are more commonly affected. Common comorbidities include depression, anxiety disorders, PTSD, borderline personality disorder, and substance abuse. The associated behaviors can be bizarre or violent and may contain reenactments of previous traumas. Differential diagnosis includes NREM parasomnias, REM parasomnias, nocturnal seizures, and behaviors due to medical condition or medication. Treatment is typically prolong, and includes appropriate therapy and medication for dissociative disorders and comorbid conditions.

Practical Points

- Sleep related dissociative disorders are a variant of diurnal dissociative disorders.
- Episodes occur in well-established EEG wakefulness.
- Trauma, especially in childhood, is a common finding.
- Age of onset can range from childhood to adulthood.
- Females are more commonly affected.
- Common comorbidities include depression, anxiety disorders, PTSD, borderline personality disorder, and substance abuse.
- Associated behaviors can be bizarre or violent and may contain reenactments of previous traumas.
- Differential diagnosis includes NREM parasomnias, REM parasomnias, nocturnal seizures, and behaviors due to medical condition or medication.
- Treatment is typically prolong, and includes appropriate therapy and medication for dissociative disorders and comorbid conditions.

References

1. American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic and coding manual. 2nd ed. American Academy of Sleep Medicine: Westbrook (IL); 2005.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Washington, DC: American Psychiatric Association; 2000.
3. Sadock B, Kaplan SV. Delirium, dementia, and amnestic and other cognitive disorders. In: Sadock's synopsis of psychiatry. 10th ed. Philidelphia: Lippincott, Williams, & Wilkins; 2007. pp. 665–79.
4. Schenck C, Milner D, Hurwitz T, Bundlie S, Mahowald M. A polysomnographic and clinical report on sleep-related injury in 100 patients. Am J Psychiatry. 1989;146:1166–73.
5. Mason TBA, Pack AI. Pediatric parasomnias. Sleep. 2007;28:140–50.
6. Chu JA, Dill DI. Dissociative symptoms in relation to childhood physical and sexual abuse. Am J Psychiatry. 1990;147:882–92.
7. Feeny N, Zoellner L, Fitzgibbons L, Foa E. Exploring the roles of emotional numbing, depression, and dissociation in PTSD. J Trauma Stress. 2000;13:489–98.
8. Bremner JD, Southwick S, Brett E, Fontana A, Rosenheck R, Charney DS. Dissociation and posttraumatic stress disorder in Vietnam combat veterans. Am J Psychiatry. 1992;149:328–32.
9. Cardena E, Speigel D. Dissociative reactions to the San Francisco Bay Area Earthquake of 1989. Am J Psychiatry. 1993;150:474–8.
10. Molaie M, Deutsch GK. Psychogenic events presenting as parasomnia. Sleep. 1997;20:402–5.
11. Schenck C, Milner D, Hurwitz T, Bundlie S, Mahowald MW. Dissociative disorders presenting as somnambulism: polysomnographic, video and clinical documentation (8 cases). Dissociation: Progress in the Dissociative Disorders. 1989;2(4):194–204.
12. Schenck C, Milner D, Hurwitz T, Bundlie S, Mahowald M. A polysomnographic and clinical report on sleep-related injury in 100 patients. Am J Psychiatry. 1989;146:1166–73.
13. Mahowald MW, Schenck CH. Evolving concepts of human state dissociation. Archives. Italiennes de Biologie. 2001;139:269–300.
14. Mahowald M, Schenck C. Nocturnal dissociation—awake? asleep? both? or neither? Sleep Hypnosis. 2001;3:129–30.
15. Naylor MW, Aldrich MS. The distribution of confusional arousals across sleep stages and time of night in children and adolescents with sleep terrors. Sleep Res. 1991;20:308.
16. Mahowald MW, Bornemann MAC. Non-REM arousal parasomnias. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 5th ed. St. Louis: Elsevier; 2011. pp. 1075–82.
17. Aurora RN, Zak RS, Maganti RK, Auerbach SH, Casey KR, Chowdhuri S, et al. Practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin Sleep Med. 2010;6(1):89–90.
18. Provini F, Plazzi G, Tinuper P, Vandi S, Lugaresi E, Montagna P. Nocturnal frontal lobe epilepsy: a clinical and polygraphic overview of 100 consecutive cases. Brain. 1999;122:1017–31.
19. Hwang TJ, Ni HC, Chen HC, Lin YT, Liao SC. Risk predictors for hypnosedative-related complex sleep behaviors: a retrospective, cross-sectional pilot study. Clin J Psychiatry. 2010;71:1331–5.
20. Inagaki T, Miyaoka T, Tsuji S, Inami Y, Nishida A, Horiguchi J. Adverse reactions to zolpidem: case reports and a review of the literature. Prim Care Companion J Clin Psychiatry. 2010;12(6):PCC.09r00849.
21. Paquet V, Strul J, Servais L, Pelc I, Fossion P. Sleep-related eating disorder induced by olanzapine. J Clin Psychiatry. 2002;63(7):597.
22. Pressman M. Factors that predispose, prime and precipitate NREM parasomnias in adults: clinical and forensic implications. Sleep Med Rev. 2007;11(1):5–30.

23. Cartwright RD. Parasomnias due to medications or substances. In: Thorpy MJ, Plazzi G, editors. The parasomnias and other sleep-related movement disorders. Cambridge: Cambridge University Press; 2010. pp. 42–53.
24. International Society for the Study of Trauma and Dissociation. Guidelines for treating dissociative identity disorder in adults, third revision. J Trauma Dissociation. 2011;12(2):188–212.
25. Molaie M, Deutsch GK. Psychogenic events presenting as parasomnia. Sleep. 1997;20(6): 402–5.

Chapter 19
Sleep Bruxism

Umakanth Khatwa and Sanjeev V. Kothare

Bruxism: Definition

The term 'la bruxomanie' was first introduced by Marie Pietkiewicz in 1907. It was later adopted as 'bruxism' to describe gnashing and grinding of the teeth occurring without a functional purpose [1]. Bruxism is an involuntary, nonfunctional repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible. Teeth grinding may have phasic (rhythmic), tonic (sustained), or mixed (both types) jaw muscle contractions. Bruxism is also defined as 'the parafunctional grinding of teeth'. Parafunctional activities are nonfunctional oromandibular and/or lingual activities that usually include jaw clenching, bruxism, tooth grinding, tooth tapping, cheek biting, lip biting, and object biting.

Bruxism has two distinct circadian manifestations: it can occur during sleep (indicated as sleep bruxism) or during wakefulness (indicated as awake bruxism) [2]. The ICSD-2 lists sleep bruxism among the sleep related movement disorders (which in previous version was listed as a parasomnia) [3]. The condition is defined as 'an oral activity characterized by grinding or clenching of the teeth during sleep, usually associated with electro-cortical (EEG) arousals'. Sleep bruxism (SB) differs in terms of etiology from daytime bruxism and hence should be distinguished from teeth clenching, bracing, or gnashing while being awake which may be purely behavioral in some patients. Some authors have suggested a clinical diagnostic grading system for sleep bruxism such as "possible", "probable", and "definite" [2].

U. Khatwa (✉)
Sleep Laboratory, Division of Respiratory Diseases,
Boston Children's Hospital, 333 Longwood Ave, LO 486, Boston, MA 02115, USA
e-mail: umakanth.khatwa@childrens.harvard.edu

S. V. Kothare
Center for Pediatric Sleep Disorders,
Department of Neurology, Boston Children's Hospital,
Harvard Medical School, Boston, MA 02115, USA
e-mail: sanjeevkothare@hotmail.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_19, © Springer Science+Business Media New York 2013

Epidemiology

Most studies have reported a prevalence from the self-reported symptoms of tooth grinding during sleep rather than any diagnostic testing. SB is common in the general population and represents the third most frequent sleep-related movement disorder. Large number of adults with bruxism also had childhood history of bruxism.

Bruxism is common during infancy and typically follows eruption of deciduous incisors, however infantile bruxism is considered clinically not significant. The prevalence of sleep bruxism during infancy and preadolescent age group is about 14–20 %, in adolescents and adults is about 8 %, and in older persons is around 3.6 % [4]. SB occurs equally between men and women. In comparison to sleep bruxism, thumb sucking is noted in 21 %, while snoring is reported in 14 % of the children. However concomitant oral activity such as nail biting is also noted in 9–28 % of those reporting SB [5].

Etiology

The etiology of sleep bruxism is multifactorial and multiple causes can coexist. The various risk factors of sleep bruxism are listed in Table 19.1. Common sleep disorders such as obstructive sleep apnea (OSA), restless leg syndrome (RLS), and periodic limb movement of sleep (PLMS) are thought to be associated with SB. Sometimes, bruxism may be incidentally noted during sleep studies done for evaluation of other sleep disorders and the patient may not be aware of these symptoms. SB can be idiopathic and may not have a clearly identifiable cause. Cigarette smoking, excessive caffeine intake, and use of some recreational drugs is associated with increase in SB. It can also be induced iatrogenically as a side effect of various medications (see Table 19.1) used in treatment of neurological and psychiatric disorders. Whenever SB is suspected or diagnosed, screening for the common risk factors needs to be undertaken because these factors should be treated for effective management of SB. SB is commonly associated with nocturnal gastroesophageal reflux disease (GERD) in adults.

In a large population study by Guilleminault et al., subjects with obstructive sleep apnea syndrome (odds ratio [OR], 1.8), loud snorers (OR, 1.4), subjects with moderate daytime sleepiness (OR, 1.3), heavy alcohol drinkers (OR, 1.8), caffeine drinkers (OR, 1.4), smokers (OR, 1.3), subjects with a highly stressful life (OR, 1.3), and those with anxiety (OR, 1.3) were at higher risk of reporting sleep bruxism [6].

Table 19.1 Risk factors for bruxism and medications causing bruxism. (Source: Modified from Kyger MH [15])

Sleep disorders	Sleep disordered breathing
	Periodic limb movement of sleep
	Restless leg syndrome
	REM behavior disorder
	Nocturnal seizure disorder
	Night terrors
	Nocturnal gastroesophageal reflux
	Confusional arousals
	Fragmentary sleep myoclonus
Neurological disorders	Tardive dyskinesia
	Cerebral palsy
	Developmental delay
	Tics disorder
	Parkinsonism
	Shy–Drager syndrome
Psychiatric disorders	Dementia
	Anxiety disorder
	Stress
Medications	Serotonin reuptake inhibitors
	Haloperidol
	Lithium
	Methylphenidate
	Nicotine
	Cocaine
	Alcohol
	Caffeine
	Methylphenidate
	Flunarizine

Familial Pattern

SB tends to occur in families and approximately 20–50 % of patients have at least 1 relative with history of tooth grinding. Bruxism is more common among first-degree relatives and monozygotic twins [7].

There are no genetic marker identified that are associated with sleep bruxism. The pattern of inheritance is also unknown.

Pathophysiology

There are several theories postulated to explain bruxism and these are a matter of controversy in the current literature; no single mechanism is able to fully explain this phenomenon. The pathophysiological disturbances causing SB may depend on the underlying etiology. The common explanation described in literature is based on three possible mechanisms which include central causes, peripheral causes, and psychosocial factors.

The central theory is loosely based on imbalance in neuronal plasticity in the basal ganglia. A neurotransmitter such as dopamine is implicated, and it is hypothesized that the direct and indirect pathways of the basal ganglia nuclei involved in the coordination of movements are disturbed in these patients [8]. Nicotine stimulates central dopaminergic action and this may explain why bruxism is more common in smokers than nonsmokers [8]. Serotonin reuptake inhibitors (SSRIs), which exert an indirect influence on the dopaminergic system may cause SB after long term use [9].

As bruxism commonly occurs during sleep, the physiology of sleep has been extensively studied to identify any pathophysiological explanation. The common sleep disorders such OSA, RLS, and PLMS are associated with SB. Hence some authors have termed sleep bruxism as a "parasomnia" triggered by sleep fragmentation. SB is also frequently associated with common childhood sleep disorders such as night terrors, nightmares, sleep walking, and nocturnal enuresis. The mechanism which might trigger these parasomnias may also be involved in inducing SB, and hence this may potentially explain high prevalence of SB in young children with disorders of arousals [10].

The second theory which is commonly discussed in the literature is the role of peripheral factors. It has been postulated that tooth malocclusion and other occlusal inferences have been associated with jaw grinding and teeth clenching. The lack of occlusal equilibrium can stimulate masticatory muscle activity through periodontal nerve receptors and may lead to frequent teeth grinding [4].

The last theory which is implicated in bruxism is psychosocial factors and coping mechanisms. A stressful life is considered as a big risk factor for SB [6]. Individuals with poor coping mechanisms, anxiety, and depression are particularly at higher risk for SB.

Effect of Bruxism on Sleep

As mentioned above, the American Academy of Sleep Medicine (AASM) (International Classification of Sleep Disorders, Second Edition [ISCD II]), classifies sleep bruxism as a sleep related movement disorder [3]. The characteristic electromyographic (EMG) feature of sleep bruxism is repetitive and recurrent episodes of masticatory muscle activity (RMMA) of temporalis and masseter muscles and is usually associated with electrocortical (EEG) arousals [3]. RMMA has a frequency of 1 Hz and occurs during sleep in association with many other orofacial motor activities such swallowing, lip smacking, coughing, smiling, and jaw movements. The RMMA is associated with tooth grinding sounds in approximately half of all cases as reported by their bed partners, parents, and/or self-reports. Compared to healthy individuals, patients with SB have normal sleep stage architecture, distribution, and cycling, and their sleep efficiency and macro sleep architecture is usually normal [11]. Most of these patients are good sleepers. Like OSA, SB is more common in supine position [12]. Recurrent SB is known to cause sleep disturbances in the patient and/or their bed partner due to sound of tooth grinding. It may also cause headaches

and jaw pain in the morning and rarely SB may trigger another parasomnia such as sleep terror, sleep talking or confusional arousal especially in children. In a study by Kothare et al. in children with sleep bruxism, the investigators did not find any difference of sleep architecture between patients and controls, except for a higher arousal index for the bruxism group (36.7 vs. 20.7, $p < .007$). Sleep bruxism occurred more frequently in stage 2 and rapid eye movement sleep, with arousals in 66 % of the cases. They also did not find any relationship of bruxism to gastroesophageal reflux or intelligence [13].

Effect of Sleep on Bruxism

The similar mechanism which causes periodic limb movement of sleep (PLMS), which is another type of sleep-related movement disorder may be involved in SB. Sleep bruxism can also occur after a physiologic event during sleep such as change in body position or yawning. About 80–90 % of RMMA episodes may result in EEG arousal during sleep. SB may be secondary to exaggerated transient motor and autonomic nervous system activation in relation to EEG arousals. Investigators have postulated that rather than triggering EEG arousals per se, SB may represent a series of an event occurring along the sequence of physiologic activations associated with micro-arousals during sleep [14]. There is a change in autonomic activity in moments preceding bruxism followed by increase in EEG alpha activity, increase in tidal volume of breathing and jaw-opening followed by jaw contraction [15]. This may be part of the central pattern generator (CPG) activity which may trigger these events. Frequency of RMMA activity is modulated by cyclical alternating pattern (CAP) during NREM sleep which is characterized by alternating periods of stable and unstable sleep [16, 17]. Most of the RMMA activities are seen in lighter stages of sleep (stage N1, N2) and during sleep stage transition from NREM to REM but rarely during REM sleep.

Clinical Presentation

The diagnosis of sleep bruxism should be based on criteria proposed by the AASM (see Table 19.2). The tooth grinding sounds during sleep is the pathognomonic sign of SB. Most of RMMA activities are associated with tooth grinding sounds during sleep but the patient may not be aware of this. Some patients may present to the dentist with complaints of tooth, jaw, and temporal mandibular pain which may be worse on awakening in the morning. Sometimes, these patients may have symptoms of sleep disturbances such as frequent nighttime awakenings and excessive daytime sleepiness, behavioral problems, and inattention or hyperactivity, thus mimicking ADHD. In a study to assess daytime cognitive performance and behavior in children with bruxism, Kothare et al. reported that 40 % of their patients had elevated scores

Table 19.2 Sleep bruxism: AASM clinical diagnostic criteria [3]

Diagnostic criteria
Reports of tooth-grinding sounds during sleep reported by patient, parent or bed partner for at least 3–5 nights per week in last 3–6 months
One or more of the following:
Abnormal wear of the teeth
Hypertrophy of masseter muscle on voluntary forceful clenching
Discomfort, fatigue, pain in the jaw (and transient morning headaches and or jaw pain)
Jaw muscle activity cannot be explained by any other current sleep, medical, neurological or psychiatric disorders and or use of medication or substance usage

Table 19.3 Questionnaire for detecting if a patient has bruxism [1]

Has anyone heard you grinding your teeth at night?
Is your jaw ever fatigue or sore on awakening in the morning?
Are you teeth or gums ever sore on awakening in the morning?
Do you ever experience temporal headache on awakening in the morning?
Are you ever aware of grinding your teeth during the day?
Are you ever aware of clenching your teeth during the day?

on the Achenbach Child Behavior Checklist, indicating significant attention and behavior problems, and there were moderate correlations between the arousal index and several of the behavior-problem scales from the Achenbach Child Behavior Checklist (0.5 to 0.6) [13].

All patients should be screened for nocturnal GE reflux symptoms as these are commonly associated. Symptoms of restless leg syndrome and use of any recreational drugs and/or medications should also be questioned. Table 19.3 lists a set of commonly asked questionnaires to patient for evaluation of bruxism.

Examination

On physical examination, there may be signs of tooth grinding activity such as tooth wear, tooth tenderness, tongue indentation, tooth fractures, hypertrophy of masseter and temporalis muscles, and jaw tenderness on digital palpation [18]. Although these signs are highly suggestive of bruxism, none are a direct evidence of concurrent bruxism. There may also be signs of increased upper airway resistance like Malampatti score 3 and 4, adenotonisllar hypertrophy, micrognathia, and nasal allergies, all of which increase the risk for OSA which in turn is a risk factor for SB. A neurological examination and temperomandibular joint examination is essential to evaluate secondary causes. Newly erupted permanent teeth may not show the wear and tear signs of bruxism.

Table 19.4 Diagnosis of bruxism

Patient questionnaires
Clinical diagnosis
Clinical history
Assess for risk factors (noted in Table 19.1)
Tooth examination for wear
Diagnostic criteria for sleep bruxism [3]
Tests
Measurement of pressure exerted on occlusal splints
Electromyography of masticatory muscles
Polysomnography

Table 19.5 Polysomnographic diagnostic criteria for sleep bruxism. (Source: Modified from references [3] and [15])

Mean SB EMG potentials:>10 or 20 % of the maximal clench while awake
Masseter muscles SB event episodes types are scored on PSG
Phasic (rhythmic): > 3 EMG bursts, separated by 2 interburst pauses, in masseter or temporalis muscle, each burst lasting > 0.25 and < 2.0 s
Tonic (sustained): 1 EMG burst lasting > 2.0 s
Mixed: both phasic and tonic types
Data are expressed in index as
Number of SB events per hour of sleep
Number of SB bursts (contractions) per hour of sleep
Number of SB episodes per night
Duration of SB EMG activity per hour of sleep

Diagnosis

Sleep bruxism diagnosis may be confirmed by using single ambulatory EMG recording to monitor master muscle activity during sleep or multichannel recording for EEG, EMG, ECG, movements and respiration [19]. Table 19.4 lists the diagnostic approach for SB. Although these testing are cheap and can be used in home setting, they are limited by multiple artifacts and lack of audio-video recording. Alternatively polysomnogram (PSG) may be considered for diagnosing sleep bruxism, which will also help to assess associated sleep disorder like OSA, PLMS and/or confusional arousals. As chin EMG alone may not be sufficient to diagnose SB, additional EMG leads on both masseter muscles may also be employed. Figure 19.1 shows characteristics PSG findings of sleep bruxism. The AASM diagnostic criteria for sleep bruxism on a sleep study have been listed in Table 19.5.

Long Term Consequences

The potential long term adverse effect of untreated bruxism includes dental erosion, tooth damage, tooth fracture, tooth sensitivity, headaches, orofacial pain, and temperomandibular disorders (TMD). More than 2/3rd of patients with SB report orofacial pain [20]. Children with SB have higher instances of behavioral and attentional problem [13].

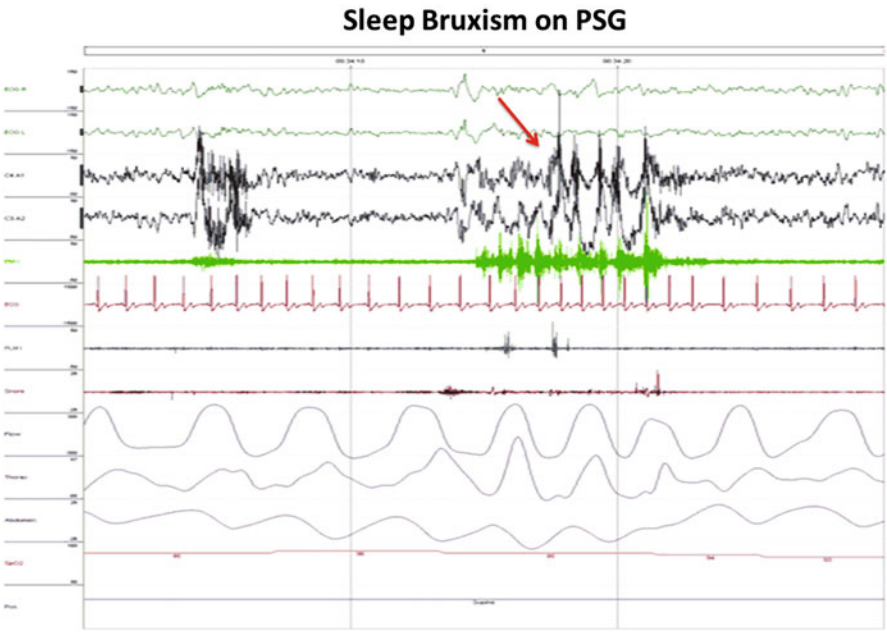


Fig. 19.1 Sleep bruxism on PSG

Table 19.6 Management of sleep bruxism. (Source: Modified from [15, 18])

Behavioral strategies
Avoid cigarette smoking, excessive caffeine, recreational drugs
Good sleep hygiene
Relaxation techniques, better coping skills
Hypnotherapy and biofeedback
Cognitive behavioral therapy
Oral appliances
Occlusal splints
Mandibular advancement devices
Pharmacotherapy
Clonazepam
Clonidine
Gabapentin
Botulinium toxin injection

Management

There is currently no cure for bruxism. The treatment approach aims at evaluation and treatment of risk factors and helps prevent harmful consequences of sleep bruxism. Table 19.6 lists all the treatment strategies for SB. In adults, identifying and avoiding risk factors is an important step toward treating SB. These include avoiding cigarette smoking, excessive caffeine intake, and recreational drugs. Management of stress and

poor coping skills with relaxation techniques, biofeedback, and cognitive behavioral therapy may also be helpful [18].

If bruxism is suspected or diagnosed, referral to dentist should be considered. Treatment with oral appliances such as oral and stabilization splints have been extensively used in dental clinical practice. The main purpose to use these modalities includes protecting the dental surfaces, preventing dental erosion, and relaxing the masseter muscle. By using occlusal splints, bruxism actually may not decrease as shown by RMMA activity, but the wear and tear and dental damage due to SB will be prevented. The teeth grinding noise with SB will also decrease with oral devices and hence may not cause sleep disturbances to the patients' bed partner. Patient with TMD will also find relief with occlusal splints [21]. For sleep bruxism, it is important to limit their use as a habit management aid and to prevent dental damage. Physiotherapy targeting the masseter muscle may also help relax the muscle and decrease SB. In patients with OSA and SB, the mandibular advancement appliances (MAA) may be helpful in increasing the upper airway patency, decreasing apnea–hypopnea index (AHI) and preventing dental damage due to SB. MAA is typically used to treat snoring and mild-to-moderate OSA; short term use of the adjustable MAA has also been demonstrated to be effective in treatment of SB in one crossover sleep laboratory study [22]. Therefore, MAA be an option in a subpopulation of patients with concomitant mild-to-moderate OSA and significant SB.

Pharmacotherapy should be considered if SB persists or oral appliances are not tolerated and associated with adverse consequences such as significant sleep fragmentation, excessive daytime sleepiness, recurrent parasomnias, behavioral and cognitive problems, dental damage, headaches, orofacial pain, and temperomandibular disorder. There are several medications that have been shown to reduce the RMMA and severity of SB which in turn help in supporting the central theory of its pathogenesis. Clonazepam, a benzodiazepine, hypnotic, anxiolytic, and myorelaxant drug is commonly used for treatment of sleep disorders such as parasomnias and sleep related movement disorders, and has been shown to be effective in reducing SB in a recent placebo-controlled study [23]. In addition, clonidine, an alpha-2 adrenergic agonist, a medication commonly used for treatment of insomnia in children is shown to reduce SB [24], however it has the potential side effect of drowsiness and hypotension and is not routinely used.

Botulinum toxin (Botox) injections can reduce the frequency of bruxism events, along with reducing bruxism-induced pain levels. In comparison with oral splints, botulinum toxins are equally effective on bruxism. Use of botulinum toxin injections at a dosage of < 100 U are safe in otherwise healthy patients and is a safe alternative in these patients [25].

Summary

Sleep bruxism is a common sleep related movement disorder which is prevalent in all age groups. It can be asymptomatic and is suspected on dental evaluation due to dental erosion or fractures and/or may be highly distressing to patients due to

tooth erosion, orofacial pain, headaches, sleep disturbances, and TMD. In children, it may be the cause of secondary parasomnia as well as behavioral and cognitive deficits. If SB is suspected or diagnosed, the patient needs to be screened for other risk factors such as nocturnal reflux, OSA, anxiety disorders, neurological disorders, use of medications such as SSRI and or recreational drugs. These patients should be referred to a dentist for further evaluation and treatment. When oral appliances fail or are not tolerated, pharmacotherapy should be considered in carefully selected patient populations. Alternatively, recent data suggest that botulinium toxin injections may be a safe option in otherwise healthy adult patients.

Practical Points

- Sleep bruxism is classified as a sleep related movement disorder
- It is common and seen across all age groups (infants–old age) and prevalence decreases with age
- There are multiple risk factors that are associated with sleep bruxism
- More than 2/3rd of the sleep bruxism episodes are associated with EEG arousal leading to sleep fragmentation
- Usually diagnosis is based on history and clinical examination finding of tooth damage, and jaw pain
- Children with sleep bruxism have higher incidence of daytime behavioral and cognitive problems
- Polysomnogram can be used to confirm diagnosis and a special masseter muscle electrode may need to be used
- Treatment involves referral to dentist, oral splint and mandibular advancement devices
- Pharmacotherapy is effective in treatment of SB in selected population

Case Example

A 28-year-old male presents to a dentist's office with tooth pain and headaches in the morning. This has been happening for several months and he recently fractured a tooth while biting on a walnut. On examination, he has significant erosion of this tooth and loss of molar cusps. There were several cracks visible and tooth tenderness with masseter muscle hypertrophy. Based on this, he was diagnosed with sleep bruxism. On further questioning, he had history of anxiety, heartburn, and was on Zantac as needed. He also has history of loud snoring and excessive daytime sleepiness. He underwent a sleep study which revealed moderate OSA with RDI of 15/h and had several instances of sleep bruxism noted during sleep stage transition and had an EEG arousal index of 30/h. He was recommended CPAP but had difficulty tolerating it. He was referred back to the dentist and was fitted with mandibular advancement

device. He had a sleep study with this oral device and his OSA was well controlled with residual RDI of 2/h and the EEG arousal index was 9/h. On 3-month follow up, his compliance was good and his symptoms had resolved. This oral appliance had helped him control his OSA and help prevent further tooth damage from sleep bruxism.

References

1. Shetty S, Pitti V, Babu CLS, Kumar GPS, Deepthi BC. Bruxism: a literature review. J Indian Prosthodont Soc. 2010;10(3):141–8.
2. Lobbezoo F, Ahlberg J, Glaros AG, Kato T, Koyano K, Lavigne GJ, et al. Bruxism defined and graded: an international consensus. J Oral Rehabil. 2013 Jan;40(1):2–4.
3. American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic and coding manual. 2nd ed. Westchester: American Academy of Sleep Medicine; 2005. xviii, p. 297.
4. Behr M, Hahnel S, Faltermeier A, Bürgers R, Kolbeck C, Handel G, et al. The two main theories on dental bruxism. Ann Anat. 2012;194(2):216–9.
5. Laberge L, Tremblay RE, Vitaro F, Montplaisir J. Development of parasomnias from childhood to early adolescence. Pediatrics. 2000;106(1 Pt 1):67–74.
6. Ohayon MM, Li KK, Guilleminault C. Risk factors for sleep bruxism in the general population. Chest. 2001;119(1):53–61.
7. Hublin C, Kaprio J, Partinen M, Koskenvuo M. Sleep bruxism based on self-report in a nationwide twin cohort. J Sleep Res. 1998;7(1):61–7.
8. Lobbezoo F, Van Der Zaag J, Naeije M. Bruxism: its multiple causes and its effects on dental implants—an updated review. J Oral Rehabil. 2006;33(4):293–300.
9. Lobbezoo F, van Denderen RJ, Verheij JG, Naeije M. Reports of SSRI-associated bruxism in the family physician's office. J Orofac Pain. 2001;15(4):340–6.
10. Lavigne GJ, Guitard F, Rompré PH, Montplaisir JY. Variability in sleep bruxism activity over time. J Sleep Res. 2001;10(3):237–44.
11. Lavigne GJ, Rompre PH, Montplaisir JY. Sleep bruxism: validity of clinical research diagnostic criteria in a controlled polysomnographic study. J Dent Res. 1996;75(1):546–52.
12. Miyawaki S, Lavigne GJ, Pierre M, Guitard F, Montplaisir JY, Kato T. Association between sleep bruxism, swallowing-related laryngeal movement, and sleep positions. Sleep. 2003;26(4):461–5.
13. Herrera M, Valencia I, Grant M, Metroka D, Chialastri A, Kothare SV. Bruxism in children: effect on sleep architecture and daytime cognitive performance and behavior. Sleep. 2006;29(9):1143–8.
14. Kato T, Rompré P, Montplaisir JY, Sessle BJ, Lavigne GJ. Sleep bruxism: an oromotor activity secondary to micro-arousal. J Dent Res. 2001;80(10):1940–4.
15. Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 5th ed. Philadelphia: Elsevier; 2011.
16. Huynh N, Kato T, Rompré PH, Okura K, Saber M, Lanfranchi PA, et al. Sleep bruxism is associated to micro-arousals and an increase in cardiac sympathetic activity. J Sleep Res. 2006;15(3):339–46.
17. Parrino L, Ferri R, Bruni O, Terzano MG. Cyclic alternating pattern (CAP): the marker of sleep instability. Sleep Med Rev. 2012;16(1):27–45.
18. Carra MC, Huynh N, Lavigne G. Sleep bruxism: a comprehensive overview for the dental clinician interested in sleep medicine. Dent Clin North Am. 2012;56(2):387–413.
19. Gallo LM, Lavigne G, Rompré P, Palla S. Reliability of scoring EMG orofacial events: polysomnography compared with ambulatory recordings. J Sleep Res. 1997;6(4):59–63.

20. Bader G, Lavigne G. Sleep bruxism; an overview of an oromandibular sleep movement disorder. Sleep Med Rev. 2000;4(1):27–43.
21. Dao TT, Lavigne GJ. Oral splints: the crutches for temporomandibular disorders and bruxism? Crit Rev Oral Biol Med. 1998;9(3):345–61.
22. Landry-Schonbeck A, de Grandmont P, Rompré PH, Lavigne GJ. Effect of an adjustable mandibular advancement appliance on sleep bruxism: a crossover sleep laboratory study. Int J Prosthodont. 2009;22(3):251–9.
23. Saletu A, Parapatics S, Anderer P, Matejka M, Saletu B. Controlled clinical, polysomnographic and psychometric studies on differences between sleep bruxers and controls and acute effects of clonazepam as compared with placebo. Eur Arch Psychiatry Clin Neurosci. 2010;260(2):163–74.
24. Carra MC, Macaluso GM, Rompré PH, Huynh N, Parrino L, Terzano MG, et al. Clonidine has a paradoxical effect on cyclic arousal and sleep bruxism during NREM sleep. Sleep. 2010;33(12):1711–6.
25. Long H, Liao Z, Wang Y, Liao L, Lai W. Efficacy of botulinum toxins on bruxism: an evidence-based review. Int Dent J. 2012;62(1):1–5.

Chapter 20
Nocturnal Enuresis

Ronald E. Becker

Introduction

Nocturnal enuresis (also known as "sleep enuresis" or "bedwetting") is a common occurrence among children, and is considered by some to be a physiologic variant until age seven. Micturition during sleep is present in 100 % of infants, but often resolves about the same time as daytime continence of urine is achieved. When achieving night time urinary continence lags behind daytime continence, there is a developmental trajectory of ongoing resolution in about 15 % of these children per year. At age seven and a half there is a 15.5 % prevalence [1] and at age 18 there is a 1 % prevalence of nocturnal enuresis.

Although proper evaluation of any individual with nocturnal enuresis includes thorough assessment for comorbid medical conditions, the majority of children with nocturnal enuresis will not have any other medical problem.

Therefore, nocturnal enuresis can be considered a medically benign condition. However, there are number of reasons why it properly deserves clinical attention. First, nocturnal enuresis has long been associated with social stigma and has been unduly associated with behavioral or emotional disorders. The social stigma of nocturnal enuresis is often based on incorrectly equating enuresis with the failure to achieve an emotional maturational stage. Because of this stigma, the presence of nocturnal enuresis can negatively affect self-esteem. Secondly, the presence of nocturnal enuresis can interfere with access to social events such as sleepovers or overnight camps. Lastly, there is a significant inconvenience and financial cost to families associated with the need to protect bedding and mattresses from urine.

The potential for nocturnal enuresis to dramatically affect a child and family is great, and at the same time, the stigma can sometimes inhibit the family from seeking professional help.

R. E. Becker (✉)
Harvard Medical School, Center for Pediatric Sleep Disorders, Boston Children's Hospital, FEGAN 10, 300 Longwood Avenue, 02115 Boston, MA, USA
e-mail: ronald.becker@childrens.harvard.edu

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_20,

Definition

There is no single agreed-upon definition for Nocturnal enuresis, but there are essential features for which there is consensus. The diagnosis is made when there is episodic wetting of the bed after an age or developmental stage at which the child would be expected to be dry, typically considered to be 5 years of age. Diagnostic criteria require a minimum of two events per month, or a single event per month after the age of seven. However, there may be clinical implications of wetting episodes even if they are less frequent.

The American Academy of Sleep Medicine's *International Classification of Sleep Disorders-2* prefers the term "Sleep Enuresis" and categorizes it as "Other Parasomnia." From a diagnostic perspective, a polysomnogram is not required, but if done, it can identify the presence of urination, and must demonstrate the absence of seizure activity [2].

The wetting cannot be the consequence of an identified medical issue such as untreated diabetes, anomaly of the urinary tract, seizures, or the use of medications with diuretic properties. When other urinary symptoms are absent, some authors will refer to "mono-symptomatic" enuresis.

The most clinically relevant distinction to make is between **primary** and **secondary** nocturnal enuresis. Primary nocturnal enuresis refers to micturition in sleep in which the individual has not had a significant intervening period of (medication-free) dryness. Secondary enuresis refers to situations where there has been a dry period of 3–6 months before wetting began again.

The diagnostic criteria which are most available to non-sleep specialists are similar to the International Classification of Sleep Disorders (ICSD) criteria but can be misleading as they link the disorder to mental health and behavioral disorders. This includes listings in the Diagnostic and Statistical Manual-IV (DSM-IV) of the American Psychiatric Association and in the International Classification of Diseases (ICD-10) by the World Health Organization [3, 4].

Pathophysiology

The rate at which urine is produced is under circadian control and typically the rate of urine production should diminish at night. However, there is a flow of urine from the kidneys to the bladder that is continuous through the night. The sensation of an expanding bladder is transmitted to the central nervous system, but the signal must be received and interpreted properly during sleep. When most young children are dry at night they do not wake to go the bathroom, but rather are able to hold their urine through the entire night. Thus, they are able to inhibit bladder contractions and elicit sphincter control without full conscious arousal. Any condition interfering with these steps can result in nocturnal enuresis.

Enuretic events tend to occur in the first half of the night, and are not necessarily associated with any specific stage of sleep. An autonomic arousal, with elevated heart

rate, is often present prior to the enuretic event, but there is no associated alertness or activation of the urinary sphincters [5]. There is no difference in the circadian flow of urine nor the bladder capacity in children with enuresis compared to controls [6].

Broadly speaking, nocturnal enuresis is an imbalance between the automatic functioning of the urinary system and the ability of the child to alert sufficiently to exert sphincter control. The high rate of success of bladder training using alarm systems suggests that for most children the primary issue leading to nocturnal enuresis is the inability to arouse sufficiently at night to control bladder contraction rather than anomalies of urine production or bladder size.

Secondary nocturnal enuresis, that which begins after at least 3 months of dryness, likely has a somewhat different natural history and etiology set than primary enuresis. Specifically, secondary enuresis is more likely to be associated with a specific medical cause than is primary enuresis. There is a strong association with constipation, and the constipation symptoms may be occult [7]. Other potential causes of secondary enuresis are myriad, and include urinary tract infections, diabetes, seizures, or trauma to the urinary system.

The Relationship with Obstructive Sleep Apnea

There are number of plausible mechanisms by which obstructive sleep apnea (OSA) could increase the risk of nocturnal enuresis. OSA may, through its tendency to fragment sleep, increase sleep pressure and raise the arousal threshold, thereby increasing enuresis. The possibility that brain natriuretic peptides (BNPs) may be elevated in the setting of sleep-disordered breathing has also been explored. It is hypothesized that the cardiac distension associated with increased respiratory effort may trigger an increase in circulating plasma BNPs and that this can account for increased risk of enuresis in this population. However, BNPs are found to be elevated in all children with nocturnal enuresis compared to those who remain dry at night, regardless of whether they snore or have apnea [8].

Although there may be an association between OSA and nocturnal enuresis, the relationship is in fact a complicated one. Although there is a greater risk of enuresis for children with apnea, children with sleep apnea do not uniformly have nocturnal enuresis and the vast majority of youngsters with nocturnal enuresis do not snore nor have signs of sleep apnea. Within a clinically referred population, a higher rate of enuresis is present for children with a respiratory distress index (RDI) > 1 compared with children with an RDI ≤ 1 [9]. However, in a more recent community-based sample, the risk of nocturnal enuresis was not increased for school-aged children with OSA [10].

Genetics

It has long been understood that family history is a factor in nocturnal enuresis. The handful of studies performed have shown higher concordance among monozygotic versus dizygotic twins [11]. It has also been well established that having one or

both parents with delayed dryness at nighttime significantly increases the risk of a child having the same difficulty [1]. Studies attempting to find specific genes have not yet yielded clinically relevant information, although one study has implicated a polymorphism on a gene for a 5-hydroxytryptamine receptor [12].

Treatment

When considering treatment for nocturnal enuresis, it is helpful to recall that the option of not to treat can be a legitimate course. Approximately 15 % of 5-year-olds will still be wetting the bed. Bed wetting will spontaneously remit in about 15 % of affected children each year. For some families there is little to no concern for the events and no apparent impact on self-esteem or quality of life. In these cases, especially when a parent recalls becoming dry at night at a later age, watchful waiting can be appropriate and most often will eventually be successful. It is also necessary to state, however briefly, that approaches involving punishment or shaming must be avoided.

Treatment options can be divided into those that are nonpharmacologic, pharmacologic, and those that have a basis in complementary and alternative medicine (CAM) practices. Treatment can target the rate of bladder filling, the propensity of the bladder wall to contract, or the ability for the individual to arouse and suppress micturition at night.

Nonpharmacologic Treatment

Fluid Restriction

Reducing fluid intake just before bed can certainly be effective in improving enuresis. This method reduces the demand on the bladder capacity. However, this approach is also quite intuitive and most often would have been tried at some point if any attempt at getting a dry bed was made. However, after initially trying to reduce fluids without success, some families will have abandoned this portion of the training. When attempting treatment using other methods, it is still important to consider the amount of fluids taken just before bed.

Enuresis Alarm

Among all available treatment options, the most effective and lasting approach is the use of an enuresis alarm (sometimes referred to as “bell and pad devices.”). This approach can usually be implemented successfully after a typically developing child reaches the age of seven. Younger children, or children with developmental concerns, at times can achieve success with an alarm with additional parental support. The overall success rate with alarms is 55–75 %, with a low relapse rate [13, 14].

The alarm is a moisture sensor, ideally affixed to an undergarment so as to remain in position. Bell-pad systems which employ a pad on the bed which is also moisture sensing can be successful, but a child can roll off the sensitive area. The alarm itself does not reduce wetting, it is an adjunct to a behavioral program in which the child learns about basic bladder function. Hearing the alarm means that urine has escaped and that the child should quickly stop the stream of urine. As with any behavioral training, there will be swifter success if there are more frequent training events. Therefore any medication for treating enuresis should be discontinued. Absorptive garments interfere with training in two ways—they can directly interfere with the response to the alarm and they continue the child's feeling of being protected against wetting, which may cause disregard at night to signals of voiding. Some would choose to "overlearn" by increasing a child's fluid intake before bed. Relapse rates may be lower if overlearning is added at the end of standard training [13].

The motivation for arousal must overcome the motivation to disregard the internal signals of bladder distension and remain asleep. A stronger signal, such as the alarm provides, helps overcome that motivation threshold. Reviewing the nighttime plan and practicing that plan before bed helps the child remember to hold their urine on waking. Contingent reinforcement for dry nights can also be a helpful part of this plan, but for children who are already well-motivated, tracking progress might be sufficient.

Start-Stop Exercises

Children can be taught to stop their urinary stream. It is unlikely that this "strengthens" muscles, but does likely help them develop conscious awareness of this muscle group. Practicing start-stop exercises can be a helpful addition to the use of an alarm, since stopping the urinary stream at night is the first task once the alarm rings.

Scheduled Wakings ("Lifting")

Parents can bring children to the bathroom in the middle of the night (the child may be awake or only partially awake.) By urinating at this time, they reduce the volume in the bladder and therefore reduce the likelihood of enuretic events. There is very limited research in this area. However, in clinical practice, this is not highly effective and tends to result in sleep disruption for parents and children.

Pharmacologic Treatment

Medications can have a role in treating nocturnal enuresis. They have the potential benefit of working quickly, and can be used on an as needed basis for social events such as sleepovers. Medications are associated with a high relapse rate when discontinued, but if treatment persists long enough, the normal maturation process might

result in ongoing dryness. Medications typically used to treat nocturnal enuresis fall into three main categories: (1) Agents that reduce the flow of urine. (2) Agents that reduce bladder contractility. (3) Agents that affect the arousal system, such as the stimulant medicines (used less frequently).

Medication treatment of enuresis has focused mainly on medications that affect the urinary system directly. The early mainstay treatment was the use of tricyclic antidepressants which were presumably effective for their anticholinergic properties, relaxing the bladder wall musculature and possibly reducing the flow of urine into the bladder. However, it is not impossible that there would have been a secondary effect on sleep/arousal patterns, sleep stage cycling, or other neurologic aspects of the sleep process that is just less well defined. At this time, the side effect profile of the tricyclics relegates them to second- or third-line agents.

Similarly, oxybutynin, used primarily for bladder wall relaxation for children and adults with daytime bladder instability, can be used for treatment of nocturnal enuresis. However, it is less likely to be successful and carries risk of anticholinergic side effects. [15, 16]

Desmopressin (also known as DDAVP) is a synthetic modified form of vasopressin which came into use for nocturnal enuresis once it could be easily synthesized. It works by reducing the volume of urinary production by the kidneys. It is currently prescribed in tablet form after cases of water intoxication were reported with use of the nasal spray form. Alterations of sodium balance remain a potential side effect of this medication, but this has likely become less common with elimination of the indication for the nasal spray. Desmopressin has a similar rate of improving enuresis symptoms as the enuresis alarm, but there is a higher rate of relapse for desmopressin compared to an alarm if discontinued [17].

Complementary/Alternative Medicine

Complementary approaches to treating nocturnal enuresis might include hypnosis, acupuncture, herbal remedies, chiropractic treatment, homeopathy, or dietary manipulations. The literature in this area is especially sparse, and no evidence currently exists to support these approaches [18].

Case Example 1

JL is an 8-year-old boy seen in consultation having been referred by his primary care pediatrician because of nightly bedwetting. His parents feel that JL is a very deep sleeper, and has been so for his whole life. JL wears an absorptive undergarment to bed, but not infrequently wets through. He has turned down several invitations to sleepover at friends' houses because of this issue. He is surprised to hear that he is most likely not the only third-grader at his school with this problem, until he

realizes that the other children with this problem are probably not talking about it either. JL takes no medications, has no medical problems, and his sleep history is fully unremarkable. Specifically, there is no snoring present. There is no concern for daytime wetting, he has been toilet trained while awake since he was 3.5 years old.

Comprehensive examination is undertaken, but with specific interest in assuring that there is no evidence of constipation. The structure of the external genitalia are normal. The lower extremity reflexes, strength, coordination, and balance are fully normal and symmetric. The spine is closely examined and free of evidence of skin stigmata of possible occult spinal dysraphism (spina bifida occulta). A urinalysis is normal.

JL's presentation is classic for primary (monosymptomatic) nocturnal enuresis. Following a discussion of the options, the family seeks treatment with an alarm system. JL is present for the discussion and seems eager to try the alarm. As he is a "deep sleeper", his parents are told that they should first help by entering his room when the alarm rings to help assure that he has woken. Before bed he will practice by listening to the alarm sound, and verbally reviewing the plan. "If my alarm goes off at night, I need to stop peeing, stop the alarm, go to the bathroom to finish peeing and then clean up and put the alarm back on." His family will track his dry nights for two reasons: to mark progress and to know when to stop using the alarm (after 2 weeks of uninterrupted dryness.)

At follow-up in 6 weeks, he has been dry for the past 3 weeks and there has been no relapse. He sleeps through the night and has not needed to wear the protective undergarments for the past week.

Case Example 2

SM is a 6-year-old girl seen by her primary care pediatrician. She had been fully dry at day and night since she turned three, but has started wetting the bed about three times per week over the past month. Her parents initially attributed this change to the arrival of a new baby sister, who is now 3 months old. However, the enuresis has not resolved and SM gives no other indication of distress over her sister's arrival, in fact she seems eager to take on the role of "big sister." SM is otherwise healthy, and developmentally normal. There is no daytime wetting. Physical examination is fully normal, but there is a suggestion of left-lower fullness in her abdomen. On questioning, her parents do reflect that the arrival of an infant has meant some change in diet for the whole family. SM denies symptoms of constipation and her parents no longer monitor her frequency of bowel movements. To be thorough, a urinalysis is performed in the office and is normal.

SM's presentation is one of secondary nocturnal enuresis. Her parents are counseled to refocus on fiber-containing foods and a mild stool softener is recommended for daily use. Ten days later, her father calls to report that the night wetting has stopped. The stool softener is also stopped and no further relapse occurs.

Practical Points

- Ask all patients over 7 years of age about night time wetting. They may not report it on their own, and may not be aware that treatment is available.
- Assure that constipation is adequately treated. Clinically significant constipation can be present even in the absence of parent/patient report. This is especially true for secondary enuresis, and for older enuretics, but it can play a role even in primary enuresis.
- Resolution of nighttime wetting is usually associated with holding the urine through the night rather than waking for a trip to the bathroom.
- Basic enuresis alarms are usually adequate, "special features" are not necessary. An alarm which is worn has advantages over pad systems that are stationary on the bed.
- Effective treatment with an alarm system also must incorporate behavioral factors; simply placing the alarm is usually inadequate to achieve success. The child should understand that the alarm sounds when wetness is detected. The alarm sound at night means that they should stop the urine stream. Review and practice before bed can help the child comply when woken at night by the alarm.
- Alarm should be worn for at least 2 weeks after last wetting episode. If possible, the alarm should be retained by the family for a while in the case of a brief relapse.

References

1. von Gontard A, Heron J, Joinson C. Family history of nocturnal enuresis and urinary incontinence: results from a large epidemiological study. J Urol. 2011;185(6):2303–6.
2. American Academy of Sleep Medicine. International classification of sleep disorders. 2nd ed. Westchester: American Academy of Sleep Medicine; 2005.
3. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, D.C.; 2000.
4. World Health Organization. International classification of diseases. Geneva: World Health Organization; 1993.
5. Bader G, Neveus T, Kruse S, Sillen U. Sleep of primary enuretic children and controls. Sleep. 2002;25(5):579–83.
6. Van Hoeck K, Bael A, Lax H, Hirche H, Van Dessel E, Van Renthergem D, et al. Urine output rate and maximum volume voided in school-age children with and without nocturnal enuresis. J Pediatr. 2007;151(6):575–80.
7. Hodges SJ, Anthony EY. Occult megarectum—a commonly unrecognized cause of enuresis. Urology. 2012;79(2):421–4.
8. Sans Capdevila O, Crabtree VM, Kheirandish-Gozal L, Gozal D. Increased morning brain natriuretic peptide levels in children with nocturnal enuresis and sleep-disordered breathing: a community-based study. Pediatrics. 2008;121(5):e1208–14.
9. Brooks LJ, Topol HI. Enuresis in children with sleep apnea. J Pediatr. 2003;142(5):515–8.
10. Su MS, Li AM, So HK, Au CT, Ho C, Wing YK. Nocturnal enuresis in children: prevalence, correlates, and relationship with obstructive sleep apnea. J Pediatr. 2011;159(2):e1238–42.
11. Hublin C, Kaprio J, Partinen M, Koskenvuo M. Nocturnal enuresis in a nationwide twin cohort. Sleep. 1998;21(6):579–85.

12. Wei CC, Wan L, Lin WY, Tsai FJ. Rs 6313 polymorphism in 5-hydroxytryptamine receptor 2A gene association with polysymptomatic primary nocturnal enuresis. J Clin Lab Anal. 2010;24(6):371–5.
13. Glazener CM, Evans JH, Peto RE. Alarm interventions for nocturnal enuresis in children. Cochrane database of systematic reviews. 2005(2):CD002911.
14. Butler RJ, Holland P, Gasson S, Norfolk S, Houghton L, Penney M. Exploring potential mechanisms in alarm treatment for primary nocturnal enuresis. Scand J Urol Nephrol. 2007;41(5):407–13.
15. Lovering JS, Tallett SE, McKendry JB. Oxybutynin efficacy in the treatment of primary enuresis. Pediatrics. 1988;82(1):104–6.
16. Montaldo P, Tafuro L, Rea M, Narciso V, Iossa AC, Gado RD. Desmopressin and oxybutynin in monosymptomatic nocturnal enuresis: a randomized, double-blind, placebo-controlled trial and an assessment of predictive factors. BJU Int. 2012;110(8 Pt B):E381–6.
17. Kwak KW, Lee YS, Park KH, Baek M. Efficacy of desmopressin and enuresis alarm as first and second line treatment for primary monosymptomatic nocturnal enuresis: prospective randomized crossover study. J Urol. 2010;184(6):2521–6.
18. Huang T, Shu X, Huang YS, Cheuk DK. Complementary and miscellaneous interventions for nocturnal enuresis in children. Cochrane database of systematic reviews. 2011(12):CD005230.

Chapter 21
Sleep-Related Eating Disorders: A Separate Entity or Part of the NES Clinical Spectrum?

Orna Tzischinsky, Pierguiseppe Vinai, Michael J. Howell and Yael Latzer

Introduction

Eating and sleeping are two basic needs of the human body that are essential for normal development and existence. These needs are directly connected and mutually influence one another. Every situation that involves a physiological and mental imbalance manifests itself in eating and sleeping patterns. The intensity and nature of the reaction differ from one person to another and is affected by age, gender, individual genetic predisposition, personality, length and magnitude of the change, and the social and cultural environment. These relationships are manifested in normal as well as disturbed eating and sleeping patterns.

Studies have suggested that nutritional factors play a role in the sleep disturbances seen in people with psychiatric and psychological disorders, such as depression [1, 2], posttraumatic stress disorder (PTSD), anxiety, and EDs including night eating

Y. Latzer (✉)
Faculty of Social Welfare and Health Sciences,
University of Haifa, Haifa, Israel

Eating Disorder Clinic, Rambam Medical Center, Haifa University,
Mount Carmel, Haifa 31905, Israel
e-mail: latzer@zahav.net.il

O. Tzischinsky
Department of Psychology, Emek Yezreel Academic College,
Emek Yezreel, 19200 Israel
e-mail: orna@yvc.ac.il

P. Vinai
Studi Cognitivi Research Group, GNOSIS Non-profit Research Group,
v Langhe 64, Magliano Alpi, 12060 Italy
e-mail: piervinai@tin.it

M. J. Howell
Department of Neurology, University of Minnesota Medical Center,
717 Delaware St., SE, Rm. 5106, Minneapolis,
Minnesota 55414-2959, USA
e-mail: howel020@umn.edu

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_21, © Springer Science+Business Media New York 2013

syndrome (NES). Sleep disturbances occurring together with such psychological disorders may cause parasomnia, insomnia, or hypersomnia [3].

These relationships are apparent during the daytime and nighttime. Normal sleep time is characterized by a continued period of fasting that differs metabolically from not eating during the day in the awake state [4]. The fasting during sleep time is balanced due to several reasons. First, there is an equilibrium between the leptin (satiety signal) and the ghrelin hormones (hunger signal) [5], as well as between the growth hormone that is secreted after sleep onset and the cortisol hormone before wake-up time [6, 7]. There is also a decrease in the peripheral and brain metabolic rate [8, 9], as well as changes in insulin release that stabilizes glucose levels [7].

Nighttime eating and drinking is a common symptom of two clinical conditions with suggested different pathogenesis. The first is labeled as sleep-related eating disorders (SRED) and is considered to be a parasomnia. The second is termed as night eating syndrome (NES) and is considered to be an eating disorder [10]. The level of awareness during the nocturnal eating episodes represents the main differentiating feature between NES and SRED, with SRED characterized by a lack of awareness during eating episodes and NES characterized by full awareness [11]. These differences between NES and SRED, whether they are opposite poles in the continuum of the clinical spectrum of EDs or separate syndromes but with similar pathology are still controversial.

SRED is a parasomnia frequently associated with other sleep disorders, such as sleepwalking and hypersomnia, and often associated with restless legs syndrome (RLS) and obstructive sleep apnea [12, 13]. In contrast, NES is considered as an abnormality in the circadian rhythm of mealtime, with a normal circadian timing of sleep onset. A recent study [11] found an overlap between the symptomatology and the polysomnographic alpha rhythms of the two disorders, confirming the need for refining the diagnostic criteria of SRED to better differentiate the syndromes.

This chapter will first review the diagnostic features of NES with its final proposed diagnostic criteria [10], prevalence, clinical characteristics, and psychopathology. The second part will review the relationship between NES and EDs, including anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED). The third part will focus on SRED, including its historical background, definition, epidemiology, clinical characteristics, and the relationship between SRED and sleep abnormalities, such as amnesia, RLS, and sleepwalking. Finally, we will conclude by considering the relationship between SRED and NES and discuss the controversial issues surrounding the question of whether SRED is in the continuous clinical spectrum of NES or a separate sleep disorder.

Diagnostic Criteria and Prevalence of Night Eating Syndrome: A Historical Overview

NES was firstly described by Stunkard in 1955 in a sample of obese patients [14]. Core characteristics were morning anorexia, evening hyperphagia (EH) (25 % of daily food had to be eaten after 7 p.m.), insomnia, depressed mood (worsening in the

evening), and emotional distress [14]. These diagnostic criteria have been modified many times and until recently, almost 20 different sets of diagnostic criteria have been used to diagnose the syndrome.

In 1986, Kuldau and Rand [15] suggested the addition of two diagnostic criteria: feeling tense, upset or anxious as bedtime nears, and having difficulties going to sleep. In 1996, Stunkard et al. [16] further modified the amount of food intake needed to be diagnosed as NES, increasing it to at least 50 % of daily calories after 7 p.m. Emotional distress, a core characteristic of Stunkard's original definition, was not a diagnostic requirement until Rand et al. [17] recommended it again as part of the diagnostic criteria in 1997. Until 1999, the presence of night-time awakenings with nocturnal ingestions (NIs) was not required. In that year, Birketvedt et al. [18] added this symptom and excluded distress from the criteria, but not all researchers have included this behavior in their diagnostic sets or even assessed it descriptively [19, 20].

One key question has involved the cut-off time for the diagnosis of EH. Some reports have used 7 p.m. [17], 8 p.m. [18], or after dinner [21, 22]. Experts from European countries noted that the hour of the evening meal differs cross-culturally and thus suggested [23] modifying the diagnostic criteria as follows: usual consumption of some food just before going to sleep or waking up during sleep to eat. Cerú-Björk et al. in 2001 [24] defined nocturnal eating as eating during the sleep period and night eating as eating before bedtime. To make this distinction clearer, Allison et al. [21, 25] in 2006 suggested the term for food intake during the sleep period as "nocturnal ingestions" (NI) and the term for overeating after the evening meal as "evening hyperphagia" (EH). These two definitions are currently used by researchers and clinicians.

To further confound the field, the American Sleep Disorders Association in 1990 included among the sleep disorders a syndrome termed night eating and drinking syndrome (NEDS), characterized by "*frequent and recurrent awakenings to eat and normal sleep onset following ingestion of the desired food*" [26] and thus with a symptomatology very similar to that of NES. The NEDS definition (often referred to as nocturnal eating syndrome) was used in several studies [27–29], sometimes synonymously with NES [27, 29, 30]. This overlap convinced the sleep disorders experts to no longer include NEDS in the second edition of the International Classification of Sleep Disorders (ICSD) in 2005 [31].

An attempt to clarify the diagnostic criteria of the syndrome was made in 2008 during the first international conference on NES in Minneapolis by the International NES Working Group, with sleep and EDs experts reaching a consensus on a set of diagnostic criteria that were published in 2010 [10], and proposed for inclusion in the American Psychiatric Association's (APA) diagnostic criteria DSM-V edition [10]. The diagnostic criteria are characterized by a significantly increased intake in the evening and/or nighttime, with at least 25 % of food intake, and/or at least two episodes of nocturnal eating per week. Awareness and recall of evening and nocturnal eating episodes are present. In addition, the daily pattern manifested by at least three of the following features: morning anorexia, strong urge to eat between dinner and sleep onset and/or during the night, insomnia, a belief that one must eat in order to

sleep, and depressed and/or mood worsens in the evening. The disorder is associated with significant distress, maintained at least 3 months, and not secondary to medical or psychiatric disorder. These newly proposed criteria currently represent the most updated instrument used to diagnose this syndrome. Despite the proliferation of diagnostic criteria since its original description, only nine reports were published on NES between 1955 and 1991, seven of which were case reports [30]. Night eating appeared to be nothing more than a curiosity. Since the beginning of the 1990s, interest in this syndrome has again risen, and currently a Medline search identified 128 papers on NES (16 only in 2012). This rise is due to the increasing prevalence of obesity in Western countries and the clarification of the latest diagnostic criteria. Although there have been a few significant studies on the prevalence of NES, all reports show that the disorder is common among overweight and obese people. In the general population, about 1.5 % of adults are affected by NES [17], but amongst people seeking weight loss treatment, the disorder is much more prevalent (8.9 % in an obesity clinic) [16]. Among patients seeking treatment for EDs: BN, BED, and AN, the prevalence rates for NES were 9, 16, and 0 % respectively [32]. In a psychiatric population, Lundgren et al. [33] found a prevalence of 12.3 % for NES.

Night Eating Syndrome Among Patients with Eating Disorders

EDs are considered a major disease of the modern world and are among the most prevailing public health problems in female adolescents and young adults in recent decades, reaching epidemic proportions in many Western countries [34]. The main disorders are AN, BN, BED, and eating disorders not otherwise specified (EDNOS). EDs are still highly misunderstood disorders and likely reflect complex interdependent multidimensional causalities, including genetic, biological, psychological, familial, and socio-cultural factors.

All EDs occur primarily in young females, with only 5–10 % of the patients being males [34]. In Western countries, the lifetime prevalence of AN, BN, and BED is estimated to be between 0.3–1.20 %, 1–1.5 %, and 3–3.5 %, respectively among females, and 0.3, 0.7, and 2 %, respectively among males [34, 35]. The prevalence of EDNOS is in the range of 3–22 % [36].

The standardized mortality rates for AN are 5–10 times higher than for normal controls [37] and are considerably higher than those reported for most other psychiatric disturbances, with the highest rates found in the binging–purging type of AN. By contrast, relatively low mortality rates (0.3–3 times greater than controls) have been reported in BN [37]. AN and BN represent chronic disorders, with recovery typically occurring after 4–10 years from the start of the illness [38, 39].

NES was not included in the American Association of Psychiatric diagnostic criteria [40], however, a new NES diagnostic criteria has been proposed for the forthcoming DSM-5 [10].

The last 2 decades have seen an abundance of research in many aspects related to EDs, including varied SREDs and NES. However, little is yet known about the

relationship between NES and EDs, and there is continuous debate in the literature regarding the relationship between the two. Some conceptualize NES as a subtype of obesity, while others relate to it as a variant of other EDs, in particular BN and BED. Others see NES as a separate syndrome among EDs, and still others view it as a variant of sleep disorders, termed in the literature as SRED [41]. The documented prevalence of NES among patients with EDs ranges from 5 to 43.4 %, depending on the sample population, the diagnostic categories, and the recruitment setting (ED, sleep disorder, or weight loss centers).

Most of the research on NES has focused on an overweight and obese female population with and without BED [16]. Only a few studies have been conducted on NES among BN patients [18, 32, 42–48], in addition to the two early case reports describing NES in this patient population [49, 50]. Likewise, very little research has examined NES in patients with AN [32, 43, 45, 51, 52].

Night Eating Syndrome in Patients with Binge Eating Disorder

Of the many studies conducted on the relationship between NES and BED, some have focused on the distinctions between the two [21, 53], while others have reported on the overlap between them [16, 20, 27, 53, 54]. Each study has used varying criteria for identifying NES. Stunkard et al. [16] first described BED and NES according to the DSM-IV criteria for BED. Results indicated that there was little overlap between the two disorders.

Some studies have focused on the differences in eating patterns [20, 21, 27, 55, 56] or sleeping patterns [32], while others have examined the differences in psychopathology and emotional distress in BED and NES [16, 19, 21, 27, 32, 53, 54, 56–58]. The first case report on NES and BED described an unclear relationship between obesity, BED, NI, and SRED [59]. One year later, Greeno et al. [27] examined the prevalence of NES in 40 women with BED who were overweight and 39 overweight controls. Fifteen percent of the women with BED reported NES-NI, while none from the control group had NES-NI. In this study, NES-NI was associated more with EDs than with overweight. A few studies examined the psychological and behavioral characteristics associated with NES (EH and/or NI) and BED and found similar results [55, 60]. They observed that individuals with BED have higher psychopathology, both in terms of eating patterns and emotional level, than individuals with NES. The authors suggested that NES should be considered as a separate diagnostic subcategory from BED.

Grilo & Masheb [54] examined the frequency of NES-NI and its correlates with BED. They found no significant differences in the number of days or number of binge eating episodes between NES-NI and NES-EH and BED groups. They suggested that the ambiguity and overlap around the differences between BED and NES-NI needed to be further explored. Colles et al. [56] investigated the differences in psychological distress between the three subgroups of NES-EH, NES-NI, and BED. They found that individuals with comorbid NES and BED reported similarly elevated psychological

distress as the other groups. NES-EH was not associated with psychological distress. Those with NES-NI who consumed nocturnal snacks reported poorer mental health-related quality of life and greater depressive symptoms and hunger than others with NES-EH. Recent studies have added that night eating behavior in patients with NES is associated with nocturnal mental anxiety, whereas night eating behavior in patients with BED is associated with diurnal anxiety [56, 58]. Stunkard et al. [61] noted that BED is not associated with a circadian delay of food intake, which is characteristic of individuals with NES.

In their examination of patients with BED and NES-NI seeking treatment for EDs, Tzischinsky & Latzer [32] found that traumatic life events, in particular sexual and physical abuse, coincided closely with the onset of NES-NI binge eating episodes, as well as a high level of psychiatric comorbidity (64 %), anxiety, or depression. In addition, they reported on a high frequency of sleep disorders, including a low level of alertness, mid-sleep awakenings, and excessive daytime sleepiness. Similarly, Allison et al. [57] found a higher prevalence of emotional and sexual abuse, emotional and physical neglect, and depression in BED and NES groups than in individuals with overweight. These results emphasize that BED patients with NES, in particular NES-NI, who are seeking treatment for EDs may have high rates of traumatic life events, as well as high levels of loneliness, psychological distress, and psychiatric comorbidity.

Even after more than half a century of the initial research on NES, there is still considerable debate about whether NES represents a distinct entity or whether it is a variant of BED in which the binges occur in the evening after dinner or at night after sleep onset. Few studies of patients with obesity who have additionally been assessed for BED have found that NES (defined as both NI and/or EH) and binge eating behavior commonly co-occur. Although these behaviors may well overlap, it is suggested that NES and BED have different underlying behavioral constructs. According to the literature reviewed, we suggest the concept that BED only, BED with NES, and NES only constitute a psychopathology continuum, with BED accompanied by NES involving higher psychopathology and NES only indicative of lower psychopathology. In addition, we suggest that patients with NES-EH may be related to a variant of BED. However, NES-NI patients with BED represent a distinct entity.

Night Eating Syndrome in Patients with Bulimia Nervosa

Only a few studies have been conducted on NES among patients with BN, mostly with patients seeking treatment for sleep disorders. The prevalence rate of NES among patients with BN ranges from 9 to 47.1 % [32, 43, 47]. Two case studies from the late 1980s provided initial reports on the clinical and psychological characteristics of patients with BN who also suffer from NES [49, 50]. The authors described binge eating episodes as somnabulistic bulimia.

Subsequently, a few studies with more participants described NES-NI among patients with BN who woke up during the night and experienced a binge episode

with little or no awareness at least two to three times in the previous month ([44, 48]). The authors related to this behavior as SRED and suggested that SRED is a relatively homogeneous syndrome associated with significant chronicity and morbidity, which combines parasomnia and daytime EDs.

According to the current diagnostic criteria, these behaviors would be considered as SRED among patients with BN. This approach is supported by previous polysomnographic data showing that SRED is composed of patients with a number of underlying sleep disorders [29, 51]. However, it is noted that the question of awareness of SRED among ED patients is still unclear, as there is variability reported in the degree of awareness of NES-NI episodes. Thus, excluding SRED from the latest NES diagnostic criteria [10] may call for further consideration and clarification. Different observations were described in several studies of patients with BN and NES-NI seeking treatment for EDs, as all of the patients were aware of their NI binge episodes and were diagnosed as NES-NI rather than SRED [32, 47, 62]. They reported high sleep disorders, including a low level of alertness, midsleep awakenings, and excessive daytime sleepiness. However, all of them were aware of the NI binge episodes. In addition, the results indicated that traumatic life events, in particular sexual and physical abuse coincided closely with the onset of NES-NI binge eating episodes, as well as a high level of psychiatric comorbidity (82 %), anxiety, or depression [32].

It is important to note that patients with BN (mostly binge–purge type) tend to engage in compensatory behavior (e.g., self-induced vomiting, excessive exercise, dietary restrictions) following binges during the evening time [63]. It is suggested that the delayed eating (i.e., skipping breakfast) found in NES patients is a kind of compensatory mechanism following the night eating binge episodes and not just a circadian delay in eating. It may also be possible that overeating during the evening hours represents a variant of BN, rather than a distinct entity of NES-EH [47]. The differences between BN patients with or without NES-NI are still unclear.

Night Eating Syndrome in Patients with Anorexia Nervosa

Only a few studies have been conducted on NES among patients with AN. The first three studies examined NES in patients seeking treatment for sleep disorders [43, 51, 52], whereas another three examined patients seeking treatment for EDs [32, 44, 45]. With regard to patients with AN and sleep disorders, about 70 % of them were diagnosed with sleepwalking, 13 % with RLS, and 10 % with obstructive sleep apnea, all based on polysomnographic data. In another study, nearly all of the patients, including AN and sleep disorder patients, reported NI (1–6 episodes per night) after sleep onset; 66 % reported binge episodes during night time; and over 90 % reported that they were half-awake/half-asleep and unaware during the nocturnal eating. Nearly 50 % were diagnosed as having somnambulism [43, 44].

With regard to patients seeking treatment for EDs, Tzischinsky & Latzer [32] assessed the prevalence of NES-NI and found that none of the patients with AN reported on NI episodes. In a recent study examining the prevalence and characteristics

of NES in a sample of patients being treated for ED, NES was diagnosed in 25 % of all the patients and 9.4 % of the patients with AN (not clear if it was NI or EH) [47].

In conclusion, patients with AN were significantly less likely to report night eating behavior than patients with BN or BED and in particular EH [47]. However, most of those diagnosed with NES were found to have additional sleep disorders and can be considered as part of the SRED subgroup.

Sleep-Related Eating Disorders

Humans maintain an overnight sleep-related fast by alterations in metabolism and appetite modulation. This stands in contrast to fasting during sedentary wakefulness where subjects have progressive hypoglycemia over 12 h [4]. NI represents a break in the nighttime fast when a patient awakens from sleep to eat prior to the final morning awakening. It is likely that a variety of underlying pathological processes lead to NI. However, recent evidence suggests that many episodes of NI are best characterized as restlessness, with eating being necessary to fall back asleep. This pattern of eating in order to return to sleep bears a striking similarity to the motor restlessness of RLS. Importantly, both NI and motor restlessness frequently arise and subside in parallel, suggesting that many cases of NI represent a nonmotor manifestation of RLS.

Some cases of NI may progress to SRED, which is dysfunctional NI often with features similar to sleepwalking, whereby patients incompletely arouse from sleep and ambulate to the kitchen. SRED episodes are described as occurring in an amnestic, and inappropriate manner. Most cases of amnestic SRED are drug-induced, especially with a sedative from the benzodiazepine receptor agonist (BRA) class, such as zolpidem. Since RLS is frequently difficult to diagnose, with symptoms that are easily mistaken for insomnia, this disorder is often misdiagnosed and mistreated with BRAs. As these agents suppress memory and executive function, it is not surprising that when given to patients with overwhelming urges to ambulate and eat, they lead to amnestic sleepwalking and eating episodes.

Clinical Presentation

SREDs episodes are described as occurring in an involuntary, compulsive, or "out of control manner". When SRED patients are at least partially aware of their amnestic behavior, hunger is notably absent and patients instead describe a compulsion to eat so that sleep may be reinitiated [43]. At night, patients with SRED consume foods higher in carbohydrates and fats than typical daytime ingestion [43], and thus not unexpectedly weight gain is commonly reported [43, 52]. The majority of patients report nightly symptoms that may persist for decades prior to pursuing treatment [43, 52]. Studies have reported a 4–5 % lifetime prevalence of SRED, with higher frequency among patients with other sleep disorders [30, 44]. Nearly a quarter of patients with SRED experience more than five eating episodes per night [64]. It is

important to note that SRED and RLS are disorders where both eating and motor symptoms frequently coexist and fluctuate in parallel.

As previously mentioned, amnestic SRED is often related to sedative hypnotic medication use, most commonly zolpidem. This phenomenon is similar to amnestic arousals in slow-wave sleep (SWS). In cases of BRA-induced SWS arousals, the mechanism of action of these agents suppresses memory along with executive function, unleashing prolonged amnestic ambulation events by disinhibiting hippocampal and frontal lobe functioning [13, 65]. BRAs enhance Gamma-Amino Butyric Acid (GABA) activity at central GABA A receptors, resulting in hypnotic phenomena [66]. In the setting of patients with RLS who also have NI, the administration of a BRA would then be expected to induce the combination of SWS arousals and amnestic NI.

These cases are often characterized by prolonged episodes with elaborate food preparation [67, 68]. Not unexpectedly, there has been an increase in sleep-associated amnestic complex behavior in parallel to the contemporary rise in use of sedative hypnotic medication [66]. These complex amnestic behaviors frequently occur in the setting of Central Nervous Systems (CNS) polypharmacy or with supratherapeutic doses [68].

Unconscious SRED episodes may include nonfood ingestions, such as cigarettes, coffee grounds, or eggshells. Other patients will ingest substances that they would otherwise avoid during the daytime. This is a particular problem for diabetics or patients with food allergies [30, 43]. Furthermore, food preparation can sometimes include hazardous use of the stove or oven, with associated fire risk [30, 43]. Patients may also fall asleep with an oral bolus of food which, combined with the circadian decline in salivation, can lead to dental caries [69].

Pathophysiology

The Relation Between Sleep-Related Eating Disorder and Parasomnia

In the normal transition from light non-rapid eye movement (NREM) sleep to wakefulness, consciousness emerges quickly, typically within seconds. Alerting phenomena lead to the suppression of SWS, and more predominant fast cortical activity appears, compatible with wakefulness [70]. SRED and other related parasomnias occur when there is an incomplete dissociation of NREM sleep into wakefulness. Impaired arousal mechanisms and the persistence of sleep drive result in a failure of the brain to fully transition into wakefulness. Phenomena that deepen sleep and enhance sleep inertia promote NREM parasomnias by increasing this homeostatic sleep drive and impairing otherwise normal arousal mechanisms. The most common parasomnia-inducing conditions are sedative-hypnotic medications, sleep deprivation, and untreated sleep disordered breathing. Predisposing characteristics, such as a subconscious desire to ambulate and eat during the normal nocturnal fast, can further exacerbate these phenomena, resulting in the activation of the patient's functional motor neurons during an arousal with a relative paucity of activity in brain regions that control executive function and memory.

Amnesia and Sleep-Related Eating Disorder

Impaired consciousness has often been the defining criterion for SRED. In the original series of 32 SRED patients, 84 % claimed an impaired recall [52]. In another case series of 23 patients, 91 % had incomplete consciousness and/or amnesia for the behavior [43]. Conversely, a subsequent report noted full awareness in 26 patients after episodes of nocturnal eating in a sleep laboratory. All 26 patients had previously been given a diagnosis of SRED for dysfunctional NI [64]. Currently, reduced awareness and subsequent amnesia is again being considered as a required diagnostic criterion for SRED in the ICSD-3rd version; however, it is not required for ICSD-2 [31].

Medication-Induced Amnesia

The discrepancy in consciousness in SRED among these reports may be best explained by whether sedating agents were used [64, 71]. The first reports of amnestic nocturnal eating were associated with sedative psychotropic medications as well as other parasomnias [72]. Moreover, the majority of patients in the original series was taking hypnotic medication or had a previous history of SWS [52]. Conversely, all 26 patients tested in a sleep laboratory and found to have full consciousness during NI episodes were drug-free, and only one had a history of SW [64].

Certainly, the vast majority of patients who are prescribed sedative hypnotic medications do not demonstrate SRED, and SRED among psychophysiological insomnia (INS) patients is rare. In fact, large clinical trials have demonstrated the efficacy and safety of BRA among patients with insomnia. Among 25 INS patients treated with either a benzodiazepine or BRA, only two reported amnestic behavior, and in neither case did the events persist [13]. These findings are consistent with previous reports where SRED and SW are found to be rare (1 % or less) in zolpidem-treated insomnia patients when RLS has been carefully excluded [65]. Thus, the rise of BRA-induced SRED suggests that some patients may resemble insomniacs, but are subconsciously predisposed to nocturnal ambulation and eating. It appears that these patients are likely to have RLS, which is a condition distinct from insomnia.

The Relation Between Sleep-Related Eating Disorder and Benzodiazepine Receptor Agonists

Several early reports noted that amnestic nocturnal eating was associated with sedating psychotropic medications. A case of amnestic nocturnal eating reported in 1981 was associated with a combination of chlorpromazine, amitriptyline, and methyprylon [72]. Subsequently, SRED has been reportedly induced with triazolam, lithium, olanzapine, risperidone, zopiclone, and zaleplon [30].

As already noted, the majority of reported drug cases are associated with zolpidem. The first reported case of amnestic nocturnal eating related to zolpidem use was described in a member of the armed services in 1999 [73]. A series of zolpidem-induced SRED followed in 2002 with five middle-aged patients, two of whom already had intermittent episodes of conscious NI prior to starting zolpidem. All five patients were taking various neuropsychiatric agents, and incidentally all had a history of RLS. Soon after initiating zolpidem, each patient described amnestic NI that stopped with discontinuation [67].

Further reports have strengthened the relationship between zolpidem and SRED. In a series of 1235 patients at an outpatient psychiatry clinic, the combination of zolpidem and antidepressants posed the greatest risk for SRED [74]. In another report of 29 sleepwalkers with frequent BRA use, approximately two-thirds of the patients described SRED [75]. More recently, eight patients reported that SRED began soon after starting zolpidem [76]. The vast majority of reports note improvement, if not outright resolution, of amnestic events once the agents are discontinued [67, 73, 74, 77, 78]. A typical case report described a 51-year-old female with RLS who noted empty food packages in the mornings after she started taking zolpidem. She later discerned that she had been eating sandwiches on several occasions [78]. However, the eating behavior in drug-induced SRED may be prolonged and elaborate. An alarming example was a 45-year-old male who was noted missing on two occasions after going to bed. Subsequently, it was discovered that he had driven his car 2 km and climbed through a window into his workplace in order to eat chocolate and other snacks [79].

The Relationship Between Sleep-Related Eating Disorder and Restless Legs Syndrome

RLS, characterized by Ekbom in 1960, is a disorder affecting approximately 8–10 % of the population and is thus a common cause of sleep initiation and maintenance failure [80]. RLS, like SRED, has a higher prevalence in women [81].

RLS is a difficult condition to diagnose, as the criteria are subjective and patients can describe the symptoms in a seemingly infinite number of ways. Some examples include: restless, tingling, cramping, painful, numbing, burning, aching, creepy-crawly, itching, and so on. Often patients are unable to describe the sensations with words, but instead state that there is something wrong in regard to the lower extremities that compel them to move during sleep. Movement will transiently relieve the sensation, only to return within moments to further impede sleep.

Translating RLS criteria across languages and cultures is particularly challenging. Furthermore, many patients actively resist a diagnosis despite meeting the clinical criteria, as they claim that the name *restless legs syndrome* fails to characterize their suffering and is frequently derided as a trivial condition. Adding to the confusion are medications that partially alleviate motor restlessness and thus mask the clinical symptoms. These include widely prescribed classes of analgesic agents, such as

opioids and GABA agonists. Considering these confounding factors, it is reasonable to suspect that many cases of RLS are not properly diagnosed and that links to associated conditions, such as NI, go unrecognized.

Similarities in subjective phenomena, epidemiology, polysomnographic findings, clinical course, and treatment response suggest that NI is frequently a nonmotor manifestation of RLS. The evidence is particularly compelling in cases of medication-induced SRED, where the mistreatment of RLS as hypervigilant, INS is plausible and amnestic eating would be the expected result. Thus, it is not a surprise that 80 % of RLS patients exposed to sedative-hypnotics had subsequent amnestic SRED or sleepwalking behavior [13]. Other reports have noted that BRAs induce SRED among RLS patients [12, 67, 77]. Indeed, RLS appears to be ubiquitous in the setting of zolpidem-induced SRED [82], and there are no documented cases of zolpidem-induced SRED where RLS was explicitly considered and subsequently not discovered [67, 78, 82].

Conceptually, as RLS patients are predisposed to ambulation and Night Eating (NE) [12], amnestic sleepwalking and eating (i.e., SRED) is the expected result when these patients are treated with agents that suppress memory and executive function. Ekbom noted the relationship between NE and RLS in the original description of RLS patients in 1960: "They often have to get up and walk, 'like a caged bear,' to quote one of my patients, or they go into the kitchen and get something to eat" [80]. Patients frequently describe the eating as restless and claim that, like the motor symptoms of RLS, it is performed in order to facilitate sleep [30]. In both NI and SRED, patients state that after waking-up, they have a compulsion to eat, even without hunger, which interferes with sleep maintenance. Subsequently, once food is ingested, the feeling abates and sleep may be reinitiated [12, 30, 83]. Furthermore, as already noted, RLS and SRED symptoms and behaviors frequently coexist and fluctuate in parallel. In a survey of 88 RLS patients who presented to a sleep disorder center, 61 % had frequent NI and 36 % had SRED [13].

A recent case helps to illustrate the strong relationship between SRED and RLS. A 74-year-old female had presented 20 years prior with a history of uncontrollable RLS and SRED. Both the NI and RLS had been well controlled with various combinations of opioids and dopaminergics. Then with a right lower extremity zoster eruption, the patient had a relapse of both RLS (bilateral symptoms) and dysfunctional nocturnal eating. Compellingly, the RLS and SRED resolved in parallel with resolution of the skin lesions. Medications were not adjusted in the period immediately prior to, during or after the zoster event [84]. While a unifying mechanism in this case is unknown, iron-related proteins (iron is a catalyst in dopamine metabolism) are noted to change in the setting of herpetic infections [85].

Similar to RLS [86], several features of SRED suggest an underlying dopamine pathology. First, dopamine mediates impulsive behaviors, such as motor restlessness, smoking, and binge eating [86]. Second, polysomnography (PSG) evidence from 35 SRED patients demonstrated that 77 % had wakeful RLS and periodic limb movement (PLM) during sleep [64]. Third, rhythmic masticatory muscle activity (RMMA) and bruxism, both dopaminergic phenomena [64, 87] associated with RLS [88], are commonly seen in SRED [30, 64].

Two recent studies have investigated SRED and nondysfunctional NI in patients with RLS. In the first study, a community survey of 100 RLS patients revealed a high prevalence of SRED in the RLS patients (33 %) as compared to normal population controls (1 %) [12]. The authors pondered whether the compulsive nocturnal eating was a manifestation of RLS brain pathology or merely a way of "killing time," as previously suggested [28]. This question was addressed in a subsequent study of 130 patients with either RLS or insomnia who presented to a sleep disorders center. This report noted that 61 % of the RLS patients described either nondysfunctional NI (25 %) or SRED (36 %). In contrast, only 12 % of the patients with INS described NI, and none met the criteria for SRED. This study suggests that NI found in the patients with RLS was not merely a function of "killing time," as the INS patients were more likely to have prolonged (> 5 min) nightly awakenings (93 %) than the RLS patients (64 %) [13]. Patients with other causes of fragmented sleep rarely break the nocturnal fast.

Restless NI is not unexpected, given that RLS patients often describe the presence of other nonmotor nocturnal urges, such as smoking [83]. RLS patients demonstrate an increased prevalence of nocturnal smoking (12 %) as compared to matched controls (2 %). Interestingly, SRED was common among RLS patients with nocturnal smoking (83 %), and both phenomena often began simultaneously [83]. Like individuals with NI, nocturnal smokers report that they are unable to return to sleep without smoking.

In the past, it has been debated whether SRED in RLS patients may be caused by dopamine receptor agonists because dopaminergic agents can trigger impulsive behaviors, such as gambling. [89, 90]. At present, however, the preponderance of evidence suggests that dopamine agents are not the cause of SRED. First, dopamine agents suppress feeding behavior in animal models [91]. Second, a review of the original SRED series noted that dopaminergic therapy resolved dysfunctional eating in seven of eight patients [30]. Later, two cases of SRED were found to resolve with levodopa [92]. Third, in a survey of patients with both SRED and RLS, ten patients reported that NI emerged prior to or concomitant with motor restlessness and none reported that nocturnal eating emerged after the start of dopaminergic therapy. In addition, RLS patients with SRED were not significantly more likely to use dopaminergic drugs than RLS patients without SRED. In fact, RLS subjects whose nocturnal eating symptoms were under control were more likely to be on these agents than subjects who continued to have nocturnal eating [12]. Fourth, a double-blind treatment trial of pramipexole for SRED demonstrated improved sleep and reduced nighttime activity, with no increase in nocturnal eating [93]. Fifth, another clinical series monitored therapy outcome in 44 RLS patients previously unexposed to dopaminergics. In this population, the frequency of both NE and SRED diminished by half with dopaminergics. Furthermore, only one patient reported an exacerbation of NE after dopamine agents were initiated, and there were no cases of dopaminergics inducing de novo NE. Consistent with other reports, NE and SRED symptoms responded in parallel to motor RLS symptoms [13]. Finally, treatment with dopaminergic agents appears to improve other nonmotor manifestations of RLS that frequently

coexist with SRED. In particular, all patients who reported a remission of nocturnal smoking had been treated with dopaminergic agonists [83]. Thus, dopaminergic treatments for RLS are found to improve, rather than exacerbate, nocturnal eating and SRED-related phenomena.

Clinical Management

SRED management should include a severity assessment, identifying comorbid sleep disorders, in particular RLS, as well as inducing agents. Clinicians should first obtain a detailed history of the sleep–wake complaints, followed by a neuropsychiatric examination. A report from a bed partner is particularly helpful, as many patients are unable to properly recall the nocturnal events by the time they are discussed with a clinician.

Eliminating implicated medications and correcting comorbid sleep disorders often resolve the problem. The majority of patients with drug-induced SRED notice improvement after the inducing agents are discontinued [67, 68, 73, 76, 94, 95]. When SRED is associated with sedative-hypnotics, it is of particular importance to reconsider the diagnosis for which the medication was originally prescribed [13, 30, 66, 96].

It is pertinent to note that as with mild RLS symptoms, relatively benign, nondistressing NI episodes are common. In these cases, patients may be followed conservatively and given reassurance that treatment is not necessary. It may be helpful to obtain a serum ferritin level in SRED cases, as RLS may be caused by iron deficiency. Iron is a co-factor in tyrosine hydroxylase, a rate-limiting step in the metabolism of dopamine. Cases with levels less than 75 μg/L may benefit from oral iron replacement.

Polysomnography

PSG is used to characterize SRED with commonly consumed nocturnal food available at the bedside in order to facilitate eating behavior. If a patient eats during the study, the preceding sleep–wake state may be identified and the technologist can assess the patient's mentation as well as level of awareness. Similar to SWS, SRED most commonly arises out of NREM sleep. One study documented that 44 of 45 eating episodes in 26 patients arose from NREM sleep [64]. While REM sleep behavior disorder symptoms may resemble SRED, the presence of rapid eye movement (REM) sleep atonia, combined with the absence of dream mentation during eating episodes, can help rule out this condition [31].

PSG with video monitoring is often helpful in the evaluation of SRED, even if abnormal behaviors do not arise during the sleep study. Frequently, patients with SRED

do not demonstrate any nocturnal eating in the laboratory setting due to the intermittent nature of the behavior as well as the laboratory effect (foreign environment) of decreased N3 sleep as compared to the home. However, even without abnormal behaviors, PSG facilitates management in that patients may have reversible NREM sleep instability from sleep disordered breathing. In cases of SRED associated with obstructive sleep apnea, continuous positive airway pressure may eliminate both the sleep disordered breathing and the parasomnia [30]. Finally, as noted above, elevated PLMs and RMMA associated with the arousal from NREM sleep have been reported in the majority of SRED cases studied with PSG [30, 64].

Pharmacotherapy

In cases without comorbid sleep disorders (or at least unrecognized co-morbid sleep disorders), two classes of pharmacotherapies have been studied and appear to be potentially effective: dopaminergics and the anti-seizure medication topiramate. It is important to recognize that the evidence for these therapies is currently based on a small number of studies, typically case reports, noncontrolled case series, or small controlled clinical trials.

The original SRED case series noted that either bedtime levodopa or bromocriptine was effective in eliminating nocturnal eating in eight patients [51]. Subsequently, pramipexole, a dopamine agonist, was investigated in a small double-blind, placebo-controlled crossover trial. Pramipexole was found to be well tolerated, with subjects noting improved sleep, and reduced nighttime activity was documented with actigraphy [93].

An open label trial of topiramate demonstrated positive results in four patients with nocturnal eating. The agent was well tolerated, reports of nocturnal eating were diminished, and weight loss (mean of 11.1 kg) was noted in all four individuals over 8.5 months [97]. Subsequently, a 28-year-old obese male had a 10-year history of nocturnal eating that was halted with topiramate [98]. In another case series, 12 of 17 SRED patients treated with topiramate were responsive to treatment. The agent was well tolerated, and there was a mean weight loss of 9.2 kg among the treatment responders over 1.8 years [69]. Finally, a study of 25 SRED patients taking topiramate reported that 17 (68 %) of the patients were responsive to treatment. However, adverse events were high and 41 % of the patients discontinued the medication over 12 months [97].

Conclusion

NI is a common symptom of two clinical conditions. The first, NES-NI is considered an ED due to an abnormality in the circadian rhythm of mealtime, with a normal circadian timing of sleep onset [10]. The second, SRED, is considered to be

a parasomnia and closely linked to RLS and the mistreatment of RLS with sedative hypnotic medication.

As described above recent evidence suggested that SRED is, in many cases, a nonmotor manifestation of RLS and amnestic SRED is frequently due to the mistreatment of RLS as insomnia. First, NI is pervasive among patients with RLS and noted in Ekbom's original 1960 description [80]. Second, NI in RLS is not merely "killing time" as patients with other causes of fragmented sleep rarely break the nocturnal fast. Third, SRED is common in patients with RLS. Fourth, RLS is nearly ubiquitous, when searched for, in cases of SRED. In fact, every SRED report in which RLS was explicitly considered, RLS was found. Fifth, in most cases of BRA induced SRED the underlying disorder for which the sedative was originally prescribed was not INS, but instead RLS, a condition that is easily confused with INS. Sixth, as NE is common in RLS, BRA, which suppresses memory and executive function, would be expected to disinhibit amnestic SRED. Further, the rise of amnestic SRED reports parallels the widespread use of BRAs. Seventh, amnestic SRED is rarely noted when patients with underlying motor restlessness are carefully excluded from BRA treatment. Eighth, the compulsive nature of NE is similar in character to the motor manifestations of RLS, as they frequently arise, intensify, and subside in parallel. Ninth, polysomnographic studies demonstrate PLMs, RMMA, and bruxism in SRED. These phenomena are frequently noted in RLS and like RLS are associated with dopaminergic dysfunction. Tenth, dopaminergic treatments for RLS improve, rather than exacerbate NI and SRED.

The level of awareness during the nocturnal eating episodes represents the main differentiating feature between NES-NI and SRED, with SRED characterized by a lack of awareness during eating episodes and NES-NI characterized by full awareness [11]. However, at this point the only nocturnal eating which is undisputably characterized as SRED is unconscious nocturnal eating, which as noted above rarely occurs outside of the setting of sedative hypnotic medications. In review, patients with RLS have an urge to ambulate as well as eat and can be frequently misdiagnosed and treated for insomnia. In these cases amnestic nocturnal eating is then the expected manifestation of treatment with sedative hypnotic agents, which inhibit executive function and impair memory. Thus it is plausible that the only "*pure SRED*" cases are in fact adverse events related to medication misapplications.

In addition to the dysfunctional nighttime feeding, there are some notable similarities between NES and SRED. Both share a chronic course, familial associations, comorbid neuropsychiatric disease, and are frequently associated with weight gain and obesity. Further, it is of note that, in comparison to the extensive investigations of the NES, SRED research is still in its infancy. For example, many SRED reports fail to comment on the presence or absence of EH suggesting that many of these patients may be better characterized as having the NES.

Mechanistically, the NIs of NES has been attributed to an abnormality in the circadian timing of caloric intake relative to sleep while the NI of SRED has been characterized as a breakdown in nocturnal fasting mechanisms. These explanations are not mutually exclusive. In this regard, the RLS findings in SRED cases noted above may infact be complimentary to the circadian delay hypothesis of

NES. RLS symptoms, both motor and nonmotor, have circadian fluctuations which reach a symptomatic crescendo during the late evening in parallel with the abnormal nighttime feeding in NES and SRED [99].

The patient's primary presenting symptoms may explain the divergence of these similar conditions into different clinical fields; for it would be expected that patients who are predominantly affected by sleep initiation and maintenance difficulty (with nocturnal eating) would present to a sleep clinician. Conversely, patients whose predominant concern is excessive eating prior to sleep (with some sleep disruption) would more likely arrive at an eating disorder clinic. This range of clinical presentation suggests that NES and SRED may in fact be situated on opposite poles of a potentially unifying disorder.

Ultimately, integration between sleep and ED medicine is of paramount importance to better unravel pathophysiological mechanisms and reverse the contribution of nighttime eating to weight gain. Specifically, it should be investigated whether patients with SRED have EH and morning anorexia, or whether NES pateints have motor restlessness of RLS. Collaboration will either unify these currently disparate disorders or with greater insight demonstrate fundamentally distinct pathologies. Regardless, collaboration between investigators will help us reach the ultimate goal of identifying effective therapy for all patients.

In addition, NES and SRED were diagnosed following the criteria of Allison et al. [11] for NES and those suggested by the third edition of the ICSD [31] can be considered two distinct pathologies that sometimes coexist in the same patients. It remains an open question regarding the nosological position of patients affected by symptoms of both pathologies such as those who eat edible food but with not complete awareness of their nocturnal behavior or those who in the same night eat edible and nonedible food.

Practical Points

1. NI is a common symptom of two clinical conditions, NES-NI is considered an ED, and SRED is considered to be a parasomnia, linked to RLS and the mistreatment of RLS with sedative hypnotic medication.
2. NI, a break in the sleep-related fast, is common among patients with RLS
3. Patients with RLS describe nocturnal eating as restless, meaning performed in order to help reinitiate sleep.
4. RLS is easily mistaken for psychophysiological insomnia, a condition of cognitive hypervigilance, which is often effectively treated with sedative medication such as BRAs.
5. By suppressing memory and executive function, BRAs release amnestic primitive behaviors that in the case of RLS include ambulation and nocturnal eating. These, often out-of-control episodes are the hallmark of SRED.
6. The level of awareness during the nocturnal eating episodes represents the main differentiating feature between NES-NI and SRED, with SRED characterized by a lack of awareness during eating episodes and NES-NI characterized by full awareness.

7. There are some notable similarities between NES and SRED, both shares a chronic course, familial associations, comorbid neuropsychiatric disease, and are frequently associated with weight gain and obesity.
8. It remains an open question regarding the nosological position of patients affected by symptoms of both pathologies such as those who eat edible food but with not complete awareness of their nocturnal behavior or those who in the same night eat edible and nonedible food with complete awareness.

Case Example #1

Case Study of Night Ingestion Among Patient with Sleep-Related Eating Disorders

A 32-year-old male presented with difficulty maintaining sleep. He stated that for the last several years he had awoken in the middle of the night with an overwhelming compulsion to eat. He specifically stated that he was not hungry but instead felt an urge to eat in order to facilitate sleep.

In addition, the patient also noted other compulsions in parallel to his nocturnal eating. These include motor restlessness and nocturnal tobacco smoking. He had previously attempted to quit smoking only to relapse at 2 a.m. after being unable to initiate sleep.

Serum ferritin level was 120 (normal). Patient was diagnosed with RLS in combination with nocturnal eating and smoking. He was started on low-dose pramipexole that nicely resolved his difficulty with sleep initiation as well as nocturnal eating and smoking. At 6-month follow-up his sleep was much improved and had successfully quit smoking.

Case Example #2

Case Study of Night Ingestion Among Patient with Binge Eating Disorder

Suzy is a 56-year-old divorced woman living alone. She has three children who are all married and independent. Suzy was born in Russia and immigrated to Israel in her adolescence. She has a high school education and is currently working as a coordinator in a large factory in northern Israel. She is fully active and competent.

Suzy's weight is 85 kg and her height is 165 cm, making her BMI calculation 31.4. She decided to come to the Eating Disorder clinic after encouragement from her daughter. She complained to have been suffering from BED for the past 7 years. The first 2 years included binge eating episodes only during the daytime, which

eventually led to binge eating episodes during the night (after sleep onset) as well. These have been present for the past 5 years. She described the night ingestion as occurring three times every night. She is aware of her awakening most of the times, describing loss of control over eating, and consuming mainly carbohydrate and fat nutrients without any sense of hunger. She feels that she will not be able to fall back to sleep unless she eats. In the morning, she describes morning anorexia, tiredness during the day, and a bad mood that gets worse as the day progresses and evening sets. She feels embarrassed about her night eating problem, and is worried about it, and has difficulty functioning during the day. She tried to treat her problem in a variety of ways, e.g., sleep medication, hiding the food and closing the kitchen before sleep onset, as well as going to sleep in a house other than her own. All these attempts were unsuccessful. She has gained approximately 10 kg in the past 5 years.

The illness process: the problems started 7 years before her referral (age 49 years), soon after her divorce. She was slightly overweight all her life, and had tried several diets, but never had binge episodes. She described waking up to the smell of smoke every hour during her marriage because she had been afraid of her husband. This habit changed to night ingestion after the divorce.

References

1. Delvenne V, Kerkhofs M, Appelboom-Fondu J, Lucas F, Mendlewicz J. Sleep polygraphic variables in anorexia nervosa and depression: a comparative study in adolescents. J Affect Disord. 1992 Jul;25(3):167–72.
2. Lauer CJ, Krieg JC, Riemann D, Zulley J, Berger M. A polysomnographic study in young psychiatric inpatients: major depression, anorexia nervosa, bulimia nervosa. J Affect Disord. 1990 Apr;18(4):235–45.
3. American Sleep Disorders Association, Thorpy MJ. International classification of sleep disorders: diagnostic and coding manual. Rochester: Diagnostic Classification Steering Committee; 1990.
4. Van Cauter E, Polonsky KS, Scheen AJ. Roles of circadian rhythmicity and sleep in human glucose regulation. Endocr Rev. 1997 Oct;18(5):716–38.
5. Dzaja A, Dalal MA, Himmerich H, Uhr M, Pollmacher T, Schuld A. Sleep enhances nocturnal plasma ghrelin levels in healthy subjects. Am J Physiol Endocrinol Metab. 2004 Jun;286(6):E963–7.
6. Holl RW, Hartman ML, Veldhuis JD, Taylor WM, Thorner MO. Thirty-second sampling of plasma growth hormone in man: correlation with sleep stages. J Clin Endocrinol Metab. 1991 Apr;72(4):854–61.
7. Van Cauter E, Blackman JD, Roland D, Spire JP, Refetoff S, Polonsky KS. Modulation of glucose regulation and insulin secretion by circadian rhythmicity and sleep. J Clin Invest. 1991 Sep;88(3):934–42.
8. Boyle PJ, Nagy RJ, O'Connor AM, Kempers SF, Yeo RA, Qualls C. Adaptation in brain glucose uptake following recurrent hypoglycemia. Proc Natl Acad Sci U S A. 1994 Sep 27;91(20): 9352–6.
9. Maquet P, Hirsch E, Dive D, Salmon E, Marescaux C, Franck G. Cerebral glucose utilization during sleep in Landau-Kleffner syndrome: a PET study. Epilepsia. 1990 Nov–Dec;31(6): 778–83.
10. Allison KC, Lundgren JD, O'Reardon JP, Geliebter A, Gluck ME, Vinai P, et al. Proposed diagnostic criteria for night eating syndrome. Int J Eat Disord. 2010 Apr;43(3):241–7.

11. Vinai P, Ferri R, Ferini-Strambi L, Cardetti S, Anelli M, Vallauri P, et al. Defining the borders between sleep-related eating disorder and night eating syndrome. Sleep Med. 2012 Jun;13(6):686–90.
12. Provini F, Antelmi E, Vignatelli L, Zaniboni A, Naldi G, Calandra-Buonaura G, et al. Association of restless legs syndrome with nocturnal eating: a case-control study. Mov Disord. 2009 Apr 30;24(6):871–7.
13. Howell MJ, Schenck CH. Restless nocturnal eating: a common feature of Willis-Ekbom Syndrome (RLS). J Clin Sleep Med. 2012 Aug 15;8(4):413–9.
14. Stunkard AJ, Grace WJ, Wolff HG. The night-eating syndrome: a pattern of food intake among certain obese patients. AmJMed. 1955;19:78–86.
15. Kuldau JM, Rand CSW. The night eating syndrome and bulimia in the morbidly obese. Int J Eat Disord. 1986;5:143–8.
16. Stunkard A, Berkowitz R, Wadden T, Tanrikut C, Reiss E, Young L. Binge eating disorder and the night-eating syndrome. Int J Obes Relat Metab Disord. 1996 Jan;20(1):1–6.
17. Rand CS, Macgregor AM, Stunkard AJ. The night eating syndrome in the general population and among postoperative obesity surgery patients. Int J Eat Disord. 1997 Jul;22(1):65–9.
18. Birketvedt GS, Florholmen J, Sundsfjord J, Osterud B, Dinges D, Bilker W, et al. Behavioral and neuroendocrine characteristics of the night-eating syndrome. JAMA. 1999 Aug 18;282(7):657–63.
19. Gluck ME, Geliebter A, Satov T. Night eating syndrome is associated with depression, low self-esteem, reduced daytime hunger, and less weight loss in obese outpatients. Obes Res. 2001 Apr;9(4):264–7.
20. Napolitano MA, Head S, Babyak MA, Blumenthal JA. Binge eating disorder and night eating syndrome: psychological and behavioral characteristics. Int J Eat Disord. 2001 Sep;30(2):193–203.
21. Allison KC, Grilo CM, Masheb RM, Stunkard AJ. Binge eating disorder and night eating syndrome: a comparative study of disordered eating. J Consult Clin Psychol. 2005 Dec;73(6):1107–15.
22. O'Reardon JP, Ringel BL, Dinges DF, Allison KC, Rogers NL, Martino NS, et al. Circadian eating and sleeping patterns in the night eating syndrome. Obes Res. 2004Nov;12(11):1789–96.
23. Adami GE, Meneghelli A, Scopinaro N. Night eating syndrome in individuals with Mediterranean eating-style. Eat Weight Disord. 1997 Dec;2(4):203–6.
24. Ceru-Bjork C, Andersson I, Rossner S. Night eating and nocturnal eating-two different or similar syndromes among obese patients? Int J Obes Relat Metab Disord. 2001 Mar;25(3):365–72.
25. Allison KC, Wadden TA, Sarwer DB, Fabricatore AN, Crerand CE, Gibbons LM, et al. Night eating syndrome and binge eating disorder among persons seeking bariatric surgery: prevalence and related features. Obesity (Silver Spring). 2006 Mar;14(Suppl 2):77–82.
26. Thorpy MJ. Classification of sleep disorders. J Clin Neurophysiol. 1990 Jan;7(1):67–81.
27. Greeno CG, Wing RR, Marcus MD. Nocturnal eating in binge eating disorder and matched-weight controls. Int J Eat Disord. 1995 Dec;18(4):343–9.
28. Manni R, Ratti MT, Tartara A. Nocturnal eating: prevalence and features in 120 insomniac referrals. Sleep. 1997 Sep;20(9):734–8.
29. Spaggiari MC, Granella F, Parrino L, Marchesi C, Melli I, Terzano MG. Nocturnal eating syndrome in adults. Sleep. 1994 Jun;17(4):339–44.
30. Schenck CH, Mahowald MW. Review of nocturnal sleep-related eating disorders. Int J Eat Disord. 1994 May;15(4):343–56.
31. American Academy of Sleep Medicine. The international classification of sleep disorders: Diagnostic and coding manual. 2nd ed. West-chester; 2005.
32. Tzischinsky O, Latzer Y. Nocturnal eating prevalence, features and night sleep among Binge Eating Disorders and Bulimia Nervosa patients in Israel. Eur Eat Disord Rev. 2004;12:101–9.
33. Lundgren JD, Newberg AB, Allison KC, Wintering NA, Ploessl K, Stunkard AJ.^{123}I-ADAM SPECT imaging of serotonin transporter binding in patients with night eating syndrome: a preliminary report. Psychiatry Res. 2008 Apr 15;162(3):214–20.

34. Hoek HW. Incidence, prevalence and mortality of anorexia nervosa and other eating disorders. Curr Opin Psychiatry. 2006;19(4):389.
35. Hudson JI, Hiripi E, Pope HG Jr, Kessler RC. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. Biol Psychiatry. 2007 Feb 1;61(3):348–58.
36. Shisslak CM, Crago M, Estes LS. The spectrum of eating disturbances. Int J Eat Disord. 1995 Nov;18(3):209–19.
37. Keel PK, Klump KL. Are eating disorders culture-bound syndromes? Implications for conceptualizing their etiology. Psychol Bull. 2003;129(5):747–69.
38. Steinhausen HC. The outcome of anorexia nervosa in the 20th century. Am J Psychiatry. 2002 Aug;159(8):1284–93.
39. Keel PK, Mitchell JE, Miller KB, Davis TL, Crow SJ. Long-term outcome of bulimia nervosa. Arch Gen Psychiatry. 1999 Jan;56(1):63–9.
40. American Psychiatric Association. Task Force on DSM-IV. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. American Psychiatric Publishing Inc.; 2000.
41. Latzer Y, Tzischinsky O. Night eating syndrome and other eating disorders. In: Lundgren JD, Allison KC, Stunkard AJ, Mitchell JE, editors. Night eating syndrome: research, assessment, and treatment. New York: Guilford; 2012:108–26.
42. Gupta MA. Sleep related eating in bulimia nervosa—an under-reported parasomnia disorder. Sleep Research. 1991;20:182.
43. Winkelman JW. Clinical and polysomnographic features of sleep-related eating disorder. J Clin Psychiatry. 1998 Jan;59(1):14–9.
44. Winkelman J, Herzog D, Fava M. The prevalence of sleep-related eating disorder in psychiatric and non-psychiatric populations. Psychol Med. 1999;29(06):1461–6.
45. Lundgren JD, Rempfer MV, Brown CE, Goetz J, Hamera E. The prevalence of night eating syndrome and binge eating disorder among overweight and obese individuals with serious mental illness. Psychiatry Res. 2010;175(3):233–6.
46. Williamson DA, Lawson OD, Bennett SM, Hinz L. Behavioral treatment of night bingeing and rumination in an adult case of bulimia nervosa. J Behav Ther Exp Psychiatry. 1989;20(1):73–7.
47. Lundgren JD, McCune A, Spresser C, Harkins P, Zolton L, Mandal K. Night eating patterns of individuals with eating disorders: Implications for conceptualizing the night eating syndrome. Psychiatry Res. 2011 Mar 30;186(1):103–8.
48. Gupta M. Sleep-related eating in bulimia nervosa. An under-reported parasomnia disorder. Sleep Res. 1991;20:182.
49. Guirguis WR. Sleepwalking as a symptom of bulimia. Br Med J (Clin Res Ed). 1986 Sep 6;293(6547):587–8.
50. Roper P. Bulimia while sleepwalking, a rebuttal for sane automatism? Lancet. 1989 Sep 30;2(8666):796.
51. Schenck CH, Hurwitz TD, O'Connor KA, Mahowald MW. Additional categories of sleep-related eating disorders and the current status of treatment. Sleep. 1993 Aug;16(5):457–66.
52. Schenck CH, Hurwitz TD, Bundlie SR, Mahowald MW. Sleep-related eating disorders: polysomnographic correlates of a heterogeneous syndrome distinct from daytime eating disorders. Sleep. 1991 Oct;14(5):419–31.
53. Stunkard AJ, Allison KC. Two forms of disordered eating in obesity: binge eating and night eating. Int J Obes Relat Metab Disord. 2003 Jan;27(1):1–12.
54. Grilo CM, Masheb RM. Night-time eating in men and women with binge eating disorder. Behav Res Ther. 2004 Apr;42(4):397–407.
55. Adami GF, Campostano A, Marinari GM, Ravera G, Scopinaro N. Night eating in obesity: a descriptive study. Nutrition. 2002 Jul–Aug;18(7–8):587–9.
56. Colles SL, Dixon JB, O'Brien PE. Night eating syndrome and nocturnal snacking: association with obesity, binge eating and psychological distress. Int J Obes (Lond). 2007 Nov;31(11):1722–30.
57. Allison KC, Grilo CM, Masheb RM, Stunkard AJ. High self-reported rates of neglect and emotional abuse, by persons with binge eating disorder and night eating syndrome. Behav Res Ther. 2007 Dec;45(12):2874–83.

58. Sassaroli S, Ruggiero GM, Vinai P, Cardetti S, Carpegna G, Ferrato N, et al. Daily and nightly anxiety among patients affected by night eating syndrome and binge eating disorder. Eat Disord. 2009 Mar–Apr;17(2):140–5.
59. Mancini MC, Aloe F. Nocturnal eating syndrome: a case report with therapeutic response to dexfenfluramine. Sao Paulo Med J. 1994 Apr–Jun;112(2):569–71.
60. de Zwaan M, Burgard MA, Schenck CH, Mitchell JE. Night time eating: a review of the literature. Eur Eat Disord Rev. 2003;11(1):7–24.
61. Stunkard AJ, Allison KC, Lundgren JD, O'Reardon JP. A biobehavioural model of the night eating syndrome. Obes Rev. 2009 Nov;10(Suppl 2):69–77.
62. Lundgren JD, Shapiro JR, Bulik CM. Night eating patterns of patients with bulimia nervosa: a preliminary report. Eat Weight Disord. 2008 Dec;13(4):171–5.
63. Smyth JM, Wonderlich SA, Sliwinski MJ, Crosby RD, Engel SG, Mitchell JE, et al. Ecological momentary assessment of affect, stress, and binge-purge behaviors: day of week and time of day effects in the natural environment. Int J Eat Disord. 2009 Jul;42(5):429–36.
64. Vetrugno R, Manconi M, Ferini-Strambi L, Provini F, Plazzi G, Montagna P. Nocturnal eating: sleep-related eating disorder or night eating syndrome? A videopolysomnographic study. Sleep. 2006 Jul 1;29(7):949–54.
65. Holm KJ, Goa KL. Zolpidem: an update of its pharmacology, therapeutic efficacy and tolerability in the treatment of insomnia. Drugs. 2000 Apr;59(4):865–89.
66. Dolder CR, Nelson MH. Hypnosedative-induced complex behaviours: incidence, mechanisms and management. CNS Drugs. 2008;22(12):1021–36.
67. Morgenthaler TI, Silber MH. Amnestic sleep-related eating disorder associated with zolpidem. Sleep Med. 2002 Jul;3(4):323–7.
68. Schenck CH, Connoy DA, Castellanos M, Johnson B, Wills L, Cramer-Bornemann MA, et al. Zolpidem-induced sleep-related eating disorder (SRED) in 19 patients. Sleep. 2005;28 (supplement):a259.
69. Schenck CH. A study of circadian eating and sleeping patterns in night eating syndrome (NES) points the way to future studies on NES and sleep-related eating disorder. Sleep Med. 2006 Dec;7(8):653–6.
70. Steriade M, Llinas RR. The functional states of the thalamus and the associated neuronal interplay. Physiol Rev. 1988 Jul;68(3):649–742.
71. de Zwaan M, Roerig DB, Crosby RD, Karaz S, Mitchell JE. Nighttime eating: a descriptive study. Int J Eat Disord. 2006 Apr;39(3):224–32.
72. Nadel C. Somnambulism, bed-time medication and over-ating. Br J Psychiatry. 1981 Jul;139:79.
73. Harazin J, Berigan TR. Zolpidem tartrate and somnambulism. Mil Med. 1999 Sep;164(9): 669–70.
74. Lam SP, Fong SY, Ho CK, Yu MW, Wing YK. Parasomnia among psychiatric outpatients: a clinical, epidemiologic, cross-sectional study. J Clin Psychiatry. 2008 Sep;69(9):1374–82.
75. Lam SP, Fong SYY, Yu MWM, Li SX, Wing YK. Sleepwalking in psychiatric patients: comparison of childhood and adult onset. Aust N Z J Psychiatry. 2009;43(5):426–30.
76. Valiensi SM, Cristiano E, Martinez OA, Reisin RC, Alvarez F. Sleep related eating disorders as a side effect of zolpidem. Medicina (B Aires). 2010;70(3):223–6.
77. Najjar M. Zolpidem and amnestic sleep related eating disorder. J Clin Sleep Med. 2007 Oct 15;3(6):637–8.
78. Sansone RA, Sansone LA. Zolpidem, somnambulism, and nocturnal eating. Gen Hosp Psychiatry. 2008 Jan–Feb;30(1):90–1.
79. Dang A, Garg G, Rataboli PV. Zolpidem induced nocturnal sleep†related eating disorder (NSRED) in a male patient. Int J Eat Disord. 2009;42(4):385–86.
80. Ekbom KA, Restless legs syndrome. Neurology. 1960;10:868–73
81. Ohayon MM, Guilleminault C, Priest RG. Night terrors, sleepwalking, and confusional arousals in the general population: their frequency and relationship to other sleep and mental disorders. J Clin Psychiatry. 1999 Apr;60(4):268–76; quiz 277.

82. Yun CH, Ji KH. Zolpidem-induced sleep-related eating disorder. J Neurol Sci. 2010;288(1): 200–01.
83. Provini F, Antelmi E, Vignatelli L, Zaniboni A, Naldi G, Calandra-Buonaura G, et al. Increased prevalence of nocturnal smoking in restless legs syndrome (RLS). Sleep Med. 2010 Feb;11(2):218–20.
84. Mahowald MW, Cramer Bornemann MA, Schenck CH. A case of reversible restless legs syndrome (RLS) and sleep-related eating disorder relapse triggered by acute right leg herpes zoster infection: literature review of spinal cord and peripheral nervous system contributions to RLS. Sleep Med. 2010 Jun;11(6):583–85.
85. Maffettone C, De Martino L, Irace C, Santamaria R, Pagnini U, Iovane G, et al. Expression of iron-related proteins during infection by bovine herpes virus type-1. J Cell Biochem. 2008 May 1;104(1):213–23.
86. Paulus W, Dowling P, Rijsman R, Stiasny-Kolster K, Trenkwalder C. Update of the pathophysiology of the restless-legs-syndrome. Mov Disord. 2007;22(Suppl 18):431–9.
87. Lavigne GJ, Kato T, Kolta A, Sessle BJ. Neurobiological mechanisms involved in sleep bruxism. Crit Rev Oral Biol Med. 2003;14(1):30–46.
88. Lavigne GJ, Montplaisir JY. Restless legs syndrome and sleep bruxism: prevalence and association among Canadians. Sleep. 1994 Dec;17(8):739–43.
89. Nirenberg MJ, Waters C. Compulsive eating and weight gain related to dopamine agonist use. Mov Disord. 2006 Apr;21(4):524–29.
90. Tippmann-Peikert M, Park JG, Boeve BF, Shepard JW, Silber MH. Pathologic gambling in patients with restless legs syndrome treated with dopaminergic agonists. Neurology. 2007 Jan 23;68(4):301–03.
91. Martin-Iverson MT, Dourish CT. Role of dopamine D-1 and D-2 receptor subtypes in mediating dopamine agonist effects on food consumption in rats. Psychopharmacology (Berl). 1988;96(3):370–74.
92. Schenck CH, Mahowald MW. Combined bupropion-levodopa-trazodone therapy of sleep-related eating and sleep disruption in two adults with chemical dependency. Sleep. 2000 Aug 1;23(5):587–88.
93. Provini F, Albani F, Vetrugno R, Vignatelli L, Lombardi C, Plazzi G, et al. A pilot double-blind placebo-controlled trial of low-dose pramipexole in sleep-related eating disorder. Eur J Neurol. 2005 Jun;12(6):432–36.
94. Wing YK, Lam SP, Li SX, Zhang J, Yu MW. Sleep-related eating disorder and zolpidem: an open interventional cohort study. J Clin Psychiatry. 2010 May;71(5):653–56.
95. Tsai MJ, Tsai YH, Huang YB. Compulsive activity and anterograde amnesia after zolpidem use. Clin Toxicol (Phila). 2007;45(2):179–81.
96. Chiang A, Krystal A. Report of two cases where sleep related eating behavior occurred with the extended-release formulation but not the immediate-release formulation of a sedative-hypnotic agent. J Clin Sleep Med. 2008 Apr 15;4(2):155–56.
97. Winkelman JW. Sleep-related eating disorder and night eating syndrome: sleep disorders, eating disorders, or both? Sleep. 2006 Jul 1;29(7):876–77.
98. Martinez-Salio A, Soler-Algarra S, Calvo-Garcia I, Sanchez-Martin M. Nocturnal sleep-related eating disorder that responds to topiramate. Rev Neurol. 2007 Sep 1–15;45(5):276–9.
99. Allen RP. Controversies and challenges in defining the etiology and pathophysiology of restless legs syndrome. Am J Med. 2007 Jan;120(1 Suppl 1):13–21.

Chapter 22
Parasomnia Overlap Disorder

Thomas Freedom

Introduction

One may think of three states of being, wake (W), non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep [1]. Under normal circumstances, these states appear to be distinct, although state boundaries are somewhat flexible. It may be possible for features of different states to occur simultaneously [2]. For example, in transitions from W to sleep, it is possible to feel partially aroused but with level of consciousness diminished from full awareness, and sleep paralysis can occur occasionally in people with normal sleep. In some circumstances, the state boundaries break down leading to dissociation of these states with features of more than one state occurring simultaneously [3]. Parasomnias are undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousals from sleep [4]. As sleep is not a "whole brain process", but involves many interacting neurotransmitter systems in the brain stem, hypothalamus, and basal forebrain that converge onto common systems in the thalamus and cortex [5, 6], it is conceivable that breakdown may occur when these systems are not synchronized or are not operating in concert. When there is a breakdown in these state boundaries, parasomnias may occur [7].

Disorders of arousal include somnambulism, confusional arousals, and night terrors [8]. They occur when there is an incomplete dissociation from non-rapid eye movement sleep into wakefulness. There is a partial arousal, predominantly from slow wave sleep. The activation of central pattern generators occurring during this partial arousal results in the abnormal behaviors without volition or awareness [9].

Parasomnias usually associated with rapid eye movement sleep include rapid eye movement sleep behavior disorder (RBD), recurrent isolated sleep paralysis, and

T. Freedom (✉)
Department of Neurology, NorthShore University Health System, Glenview 60026, IL, USA
e-mail: TFreedom@northshore.org

Pritzker School of Medicine, University of Chicago, Chicago, IL, USA

S.V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_22, © Springer Science+Business Media New York 2013

nightmare disorder [10]. Brainstem dysfunction is implicated in the pathology of these disorders [11]. RBD, first reported in 1986, involves the loss of atonia during REM sleep resulting in enactment of dreams [12, 13]. It is hypothesized that that disinhibition of selective brainstem motor generators may produce both behavior and dream content. The generator for motor behaviors may become disinhibited. This could allow activation of an ascending output to forebrain dream-synthesizing centers and inactivation of a descending inhibitory output to the spinal motor neurons, producing dreaming and enactment behavior [14].

Parasomnia Overlap

Parasomnia overlap syndrome includes features of both REM parasomnias and disorders of arousal [15]. It is considered a variant of RBD [16]. Patients may show features of dream enactment and nocturnal ambulation or confusional arousals. The differential diagnoses include RBD, nocturnal frontal lobe seizures, confusional arousals, sleepwalking, sleep terrors, posttraumatic stress disorder, and nightmares [17, 18]. Parasomnia overlap syndrome, linking RBD with disorders of arousal may serve to expand the concept of state-dependent motor dyscontrol. Having clinical and polysomnographic evidence of both disorders of arousal and RBD suggests the possibility that motor dyscontrol during sleep is the primary abnormality. If this motor dyscontrol occurs during NREM, the result is disorders of arousal: if during REM, the result is RBD [3]. The natural history of parasomnia overlap disorder, as yet, is not known.

A case report described patients with frequent movements in sleep arising from both REM and NREM sleep [19]. In a patient with conversion disorder, previously diagnosed nocturnal "psuedoseizures" were found to be due to severe mixed parasomnia comprising RBD and a non-REM parasomnia [20]. In another report, a 51-year-old man with Machado–Joseph disease presented with a 3-year history of prolonged confusion following nocturnal wandering and violent behavior. Polysomnography with videotape recording demonstrated sleepwalking episodes emerging from NREM sleep and occasionally from rapid eye movement (REM) sleep, up to 120 min in duration. This was followed by confusional episodes lasting as long as 47 min. Periodic limb movements and obstructive sleep apnea were also found. There was no epileptiform activity. The patient improved with a combination of temazepam and carbidopa–levodopa [21].

In a different study, 33 patients with combined sleepwalking, sleep terrors, and RBD were observed over an 8-year period. The behaviors involved injury to self. All patients underwent clinical and polysomnographic evaluations. In 67 % of patients, no underlying cause determined. They had a significantly earlier age for onset of parasomnia than the symptomatic patients. Symptomatic patients had neurological, cardiac, psychiatric, or a mixed etiology. In 20 patients, 90 % ($n = 18$) had complete or substantial control with bedtime clonazepam, alprazolam, and/or carbamazepine. Self-hypnosis was effective in 1 patient [22].

Other patients with features of overlap parasomnias have been subsequently reported. A 40-year-old woman with an inflammatory brainstem lesion had features of somnambulism and RBD [23]. Two cases of overlap syndrome were reported in Harlequin syndrome (unilateral autonomic dysfunction) [24]. Sexual parasomnia behavior has been reported in two patients with symptoms of REM and NREM parasomnias [25]. More recently, a case of confusional arousal arising from REM was reported [26].

Status Dissociatus

Status dissociatus can also be considered a variation of RBD [15]. There is a mixture of W, NREM sleep, and REM sleep. There is complete breakdown of state boundaries and simultaneous appearance of these three states results in nearly continuous motor and/or verbal behavior in the absence of polysomnographically defined conventional REM and NREM sleep stages [27].

This was initially reported in 6 patients. This began in 3 patients with alcohol withdrawal, olivopontocerebellar degeneration, and after cardiac surgery. The sleep polysomnograms showed generalized low voltage fast activity (1 patient with a small amount of slow wave sleep). Patients had muscular twitches and eye movements (slow and rapid). All 3 patients reported sleep with dream mentation. Two of them responded to clonazepam. Three other patients with narcolepsy/cataplexy had complaints of abnormal sleep-related motor and/or verbal activity with polysomnograms showing simultaneous or rapidly oscillating W, NREM sleep, and REM sleep. Patients responded to clonazepam [28].

Subsequent reports have described similar breakdown of states after surgery for a tegmental pontomesencephalic cavernoma [29], in Guillain–Barre syndrome [30], and recently also in anti-NMDA receptor encephalitis [31].

Agrypnia Excitata

Agrypnia excitata is a state in which sleep and W cannot be clearly distinguished. Severe insomnia and mental confusion with dream enactment occur, associated with motor and autonomic activation. On polysomnograms, there is a loss of slow wave sleep, unresponsiveness associated with dream-like mentation, and congruent motor behavior arising in the context of a completely disorganized sleep structure. This was initially reported in patients with fatal familial insomnia, Morvan's chorea, and delirium tremens [32, 33]. Other reports also included these three disorders [34–36]. In addition, this was also reported in a case of adult onset Mulvihill-Smith syndrome. This is a genetic condition (suspected autosomal recessive) characterized by premature aging, multiple pigmented nevi, decreased facial subcutaneous fat, microcephaly, short stature, mental retardation, and recurrent infections [37]. It has

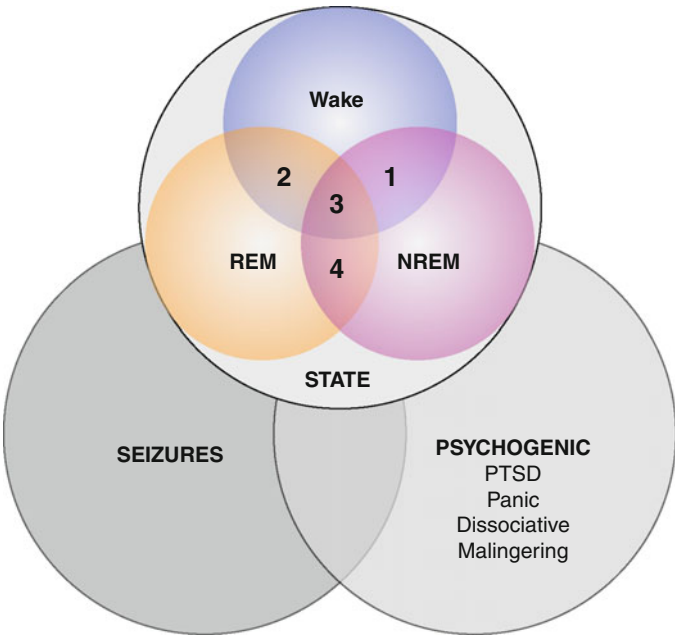
Table 22.1 Clinical, neurophysiological, and pathological comparison of DT, MC, and FFI. (Reprinted from Montagna [33] with permission from Elsevier)

Behavior	DT	MC	FFI
Insomnia	Present	Persistent for months	Present early (subwakefulness)
Hallucinations/oneirism	Severe	Present	Present in fully developed disease, with enacted dreams
Motor hyperactivity	Present	Neuromyotonia	Persistent through the 24 h
Autonomic hyperactivity	Severe	Present	Present early
Cortisolemia	Increased	Increased	Increased
Plasma catecholamines	Increased	Increased	Increased
Polysomnography			
Spindles/K complexes	Reduced/absent	Reduced/absent	Reduced/absent
SWS	Severely reduced/absent	Absent	Reduced/absent
REM sleep	Increased, abnormal without atonia	Without atonia	Without atonia
Pet/Pathology	Atrophy of the thalamus, mammillary bodies, temporal and orbitomesial cortex	Antibodies in thalamus and striatum (?)	Atrophy of anterior and dorsomedian thalamus and cingulate cortex

also been reported in Creutzfeldt–Jakob disease [38]. Two patients with bilateral paramedian thalamic dysfunction also shared similar symptoms [39].

Fatal familial insomnia (FFI) is a hereditary disease caused by a point mutation of the prion protein gene. The average age of onset is 50 years. It has a clinical course ranging from 7 months to 7 years. The major features are apathy, drowsiness and stupor, and dream enactment. There is increased autonomic activity, including: hyperhydrosis, sialhorrhoea, tachycardia, hypertension, and low grade fever. Motor signs include dysarthria, ataxia, evoked and spontaneous myoclonus [32, 40]. Morvan's fibrillary chorea is a rare disorder with severe insomnia associated with intense anxiety, delirium, and hallucinations. These symptoms are accompanied by autonomic overactivity: hyperhydrosis, tachycardia, hypertension and fever; and by cramps, fasciculations, myotonia, and motor agitation [41]. Delirium tremens is characterized by confusion, delusions, vivid hallucinations, tremor and motor agitation, sleeplessness and autonomic hyperactivity arising some days after abrupt alcohol withdrawal. All three of these are associated with thalamic dysfunction [42] (See Table 22.1 for comparison).

During dream enactment, patients appear to perform movements consistent with the contents of their dreams. They are able to recall the dreams upon awakening. With the progression of the disease, in particular in FFI, there is more difficulty recalling the dreams, and patients become more and more confused, alternating between wakefulness and oneiric confusional states [32, 43].



1. Disorders of arousal (NREM)
Confusional arousals
Sleep-related abnormal sexual behaviors
Sleepwalking
Sleep terrors
Sleep-related eating disorders

2. Narcolepsy Triad
Hypnagogic Hallucinations
Sleep Paralysis, and Cataplexy

REM Sleep Behavior Disorder (RBD)
Lucid dreaming
Out-of-body experiences

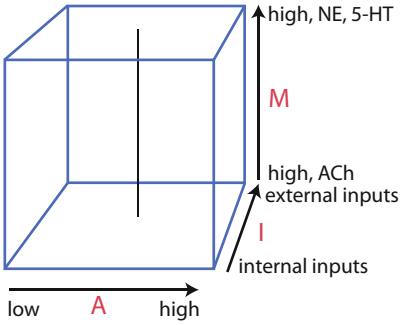
3. Status Dissociatus
Parasomnia overlap syndrome

4. Asymptomatic
(no conscious awareness)

Fig. 22.1 The overlapping nature of state and conditions associated with parasomnia. (Adapted from Mahowald [45], with permission from Elsevier.)

Discussion

The fact that different states of being, although usually distinct, can overlap with each other leads to the emergence of phenomena during sleep and wakefulness in which an exact state cannot be determined with subsequent unusual and pathological experiences and behaviors. A number of possibilities can exist with mixed states. Wake/REM combinations can lead to cataplexy, hypnagogic hallucinations, sleep paralysis, REM sleep behavior disorder, and lucid dreaming (in which the dreamer realizes he is dreaming) [44]. NREM/W combinations lead to sleepwalking, confusional arousals, and sleep terrors. Mixed REM/NREM states are associated with parasomnia overlap. Finally, in status dissociatus, W/NREM/REM combinations occur. This is illustrated in Fig. 22.1, [45].



Model Factor	Psychological	Neurobiological
A - Activation: Level of energy processing capacity	• Word count • Cognitive complexity e.g., perceptual vividness emotional intensity, narrative	• EEG activation • Firing level and synchrony of reticular, thalamic and cortical neurons
I - Information Source internal or external	• Real world space, time and person referents and their stability • Real vs. imagined action	• Level of presynaptic and postsynaptic inhibition • Excitability of sensori-motor pattern generators
M - Mode Organization of data	• Internal consistency? • Physical possibility? • Linear logic?	• Activity level of aminergic neurons

Fig. 22.2 The Activation-Input Source-Neuromodulation model (AIM). Illustration of three dimensional state space and the psychological neurobiological correlates of each dimension. (Reprinted with permission from Hobson [2], Copyright ©Cambridge University Press.)

The existence of three stages occurring in combination has been characterized in a model known as AIM. In this model (Fig. 22.2), there are three factors that determine states. The first is activation. This is the level of energy leading to arousal and alertness. The next is input, either external as during wakefulness, or internally generated as in dreaming. The third factor is neuromodulation, the level of catecholaminergic vs. cholinergic input to the brainstem. The different states are determined by the levels of these three inputs (Fig. 22.3), [2]. The breakdown of state boundaries can be explained by this model. Weaknesses of the model include the lack of accounting for other neurotransmitter systems involved in state generation [5, 6].

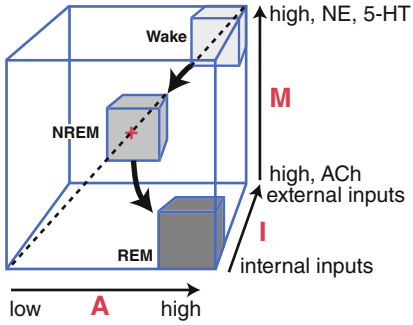


Fig. 22.3 Normal transitioning within the AIM state space from wake to NREM and then to REM. (Reprinted with permission from Hobson [2], Copyright ©Cambridge University Press)

Conclusion

Parasomnia overlap represents a condition in which a disorder of arousal coexists with RBD. The features of both REM and NREM parasomnias suggest a possibility of a common mechanism between these two types of parasomnias. Parasomnia overlap has been described as existing within the spectrum of sleep motor dyscontrol disorders and dissociated states of being. The existence of an NREM–REM sleep disorder suggests that the basic abnormality of the motor parasomnias may consist of motor dyscontrol during sleep, with the affected sleep stage and the type of parasomnia, being influenced by developmental factors (encompassing the entire life cycle) and by various other biological and clinical factors [22]. Status dissociatus represents extreme breakdown of state boundaries in which there is a mixture or rapid cycling of NREM, REM, and W. In agrypnia excitata, the distinction between sleep and wake cannot be made easily and there is insomnia, delirium, dream enactment, and autonomic and motor overactivity.

Practical Points

1. Under normal conditions the three states of being, W, NREM, and REM are stable.
2. State boundaries are not absolute and mixed states can occur.
3. Mixed states can lead to parasomnias.
4. Parasomnia overlap syndrome occurs when features of NREM and REM sleep mixed with W occur.
5. Status dissociatus results in a breakdown of state boundaries with features of all state intermingled.
6. In agrypnia excitata, insomnia, dream enactment, and autonomic and motor hyperactivity are seen.
7. In some cases, especially agrypnia, there is irreversible and/or progressive neurological deterioration.

Case Example

A 38-year-old female presented with a history of abnormal sleep behaviors since childhood. She reported episodes of wandering in her sleep and had found herself awakening in rooms other than her bedroom, with no memory as to how she got there. She had been observed walking in her sleep, and during these episodes was difficult to arouse. These episodes could occur three or four times a week.

She also had episodes for the past 9 years of shouting, punching, and kicking in her sleep. When awakened from these episodes, she was aware of having had dreams with threatening content, consistent with her behaviors. These episodes had been occurring once or twice a week. Mild injury had occurred. Some of the "wandering" behaviors had also been associated with violent activity.

Physical and neurological examinations were normal. EEG was normal. Polysomnography demonstrated excessive periodic limb movements in REM sleep, but no REM without atonia. No significant sleep disordered breathing was observed.

Clonazepam was started with a decrease in episodes to once or twice a month. Further increases in clonazepam were not tolerated.

References

1. Mahowald MW, Schenck CH. Dissociated states of wakefulness and sleep. Neurology. 1992;42 Suppl 6:s44–51.
2. Hobson JA, Pace-Schott EF, Stickgold R. Dreaming and the brain: toward a cognitive neuroscience of conscious states. Behav brain sci. 2000;23:793–842.
3. Mahowald MW, Cramer Bornemann MA, Schenck CH. State dissociation, human behavior, and consciousness. Curr top med chem. 2011;11(19):2392–402.
4. American Academy of Sleep Medicine. International classification of sleep disorder. Second edition. Diagnostic and coding manual. 2005;137.
5. Brown RE, Basheer R, McKenna JT, Strecker RE, McCarley RW. Control of sleep and wakefulness. Physiol Rev. 2012;92:1087–187.
6. Moszczynski A, Murray BJ. Neurobiological aspects of sleep physiology. Neurol Clin. 2012;30:963–85.
7. Howell MJ. Parasomnias: an updated review. Neurotherapeutics. 2012;9:753–75.
8. American Academy of Sleep Medicine. International classification of sleep disorder. Second edition. Diagnostic and coding manual. 2005:139–47.
9. Derry CP, Harvey AS, Walker MC, Duncan JS, Berkovic SF. NREM arousal parasomnias and their distinction from nocturnal frontal lobe epilepsy: a video EEG analysis. Sleep. 2009;32:1637–44.
10. American Academy of Sleep Medicine. International classification of sleep disorder. Second edition. Diagnostic and coding manual. 2005:148–58.
11. Montplaisir J, Gagnon JF, Postuma RB, Vendette M. REM sleep parasomnias. In: Vinken PJ, Bruyn GW, editors. Handbook of clinical neurology, vol. 99. Edinburgh: Elsevier; 2011. pp. 869–82.
12. Salva M, Guilleminault C. Olivopontocerebellar degeneration, abnormal sleep, and REM sleep without atonia. Neurology. 1986;36:576–7.
13. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep. 1986;9:293–308.

14. Abad VC, Guilleminault C. Review of rapid eye movement behavior sleep disorders. Curr Neurol Neurosci Rep. 2004;4(2):157–63.
15. American Academy of Sleep Medicine. International classification of sleep disorder. Second edition. Diagnostic and coding manual. 2005:150.
16. Mahowald MW, Schenck CH. REM Sleep Parasomnias. In: Kryger MH, Dement W, Roth T, editors. Principles and practice of sleep medicine, 5th ed. Philadelphia: Saunders; 2011. pp. 1090–1.
17. Malhotra RK, Avidan AY. Parasomnias and their mimics. Neurol Clin. 2012;30:1067–94.
18. Plazzi G, Vetrugno R, Provini F, Montagna P. Sleepwalking and other ambulatory behaviours during sleep. Neurol Sci. 2005;26 Suppl 3:s193–8.
19. Ohayon MM, Schenck CH. Violent behavior during sleep: prevalence, comorbidity and consequences. Sleep Med. 2011;11(9):941–6.
20. Bokey K. Conversion disorder revisited: severe parasomnia discovered. Aust NZ J Psychiat. 1993;27:694–8.
21. Kushida CA, Clerk AA, Kirsch CM, Hotson JR Guilleminault C. Prolonged confusion with nocturnal wandering arising from NREM and REM sleep: a case report. Sleep. 1995;18:757–64.
22. Schenck CH, Boyd JL, Mahowald W. Parasomnias: a parasomnia overlap disorder involving sleepwalking, sleep terrors, and REM sleep behavior disorder in 33 polysomnographically confirmed cases. Sleep. 1997;20:972–81.
23. Limousin N, Dehais C, Gout O, et al. A brainstem inflammatory lesion causing REM sleep behavior disorder and sleepwalking (parasomnia overlap disorder). Sleep Med. 2009;10:1059–62.
24. Lombardi C, Vetrugno R, Provini F, Plazzi G, Pierangeli G, Coccagna G, Lugaresi E, et al. Harlequin syndrome: an association with overlap parasomnia. J Neurol Neurosurg Psych. 2004;75:341–5.
25. Cicolin A, Tribolo A, Giordano A, Chiarot E, Peila E, Terreni A, Bucca C, et al. Sexual behaviors during sleep associated polysomnographically confirmed parasomnia overlap disorder. Sleep Med. 2011;12:523–8.
26. Bhat S, Patel D, Rosen D, Chokroverty S. A case of a confusional arousal arising from REM sleep. Sleep Med. 2012;13:317–8.
27. Vetrugno R, Montagna P. From REM sleep behaviour disorder to status dissociatus: insights into the maze of states of being. Sleep Med. 2011;12 Suppl 2:s68–71.
28. Mahowald MW, Schenck CH. Status dissociatus—a perspective on states of being. Sleep. 1991;14:69–79.
29. Provini F, Vetrugno R, Pastorelli F, Lombardi C, Plazzi G, Marliani AF, Lugaresi E, et al. Status dissociatus after surgery for tegmental ponto-mesencephalic cavernoma: a state-dependent disorder of motor control during sleep. Mov disord. 2004;19:719–23.
30. Cochen V, Arnulf I, Demeret S, Neulat ML, Gourlet V, Drouot X, Moutereau S, et al. Vivid dreams, hallucinations, psychosis and REM sleep in Guillain-Barre syndrome. Brain. 2005;128 (Pt 11):2535–45.
31. Stamelou M, Plazzi G, Lugaresi E, Edwards MJ, Bhatia KP. The distinct movement disorder in anti-NMDA receptor encephalitis may be related to status dissociatus: A hypothesis. Mov disord. 2012;27:1360–3.
32. Lugaresi E, Provini F. Agrypnia excitata: clinical features and pathophysiological implications. Sleep Med Rev. 2001;5:313–22.
33. Montagna P, Lugaresi E. Agrypnia excitata: a generalized overactivity syndrome and a useful concept in the neurophysiopathology of sleep. Clin neurophysiol. 2002;113:552–60.
34. Iriarte J, Ayuso T, Echavarri C, Alegre M, Urrestarazu E, Lacruz F, Gállego J, et al. Agrypnia excitata in fatal familial insomnia. A video-polygraphic study. Neurology. 2007;69:607–8.
35. Provini F, Cortelli P, Montagna P, Gambetti P, Lugaresi E. Fatal insomnia and agrypnia excitata: sleep and the limbic system. Rev Neurol (Paris). 2008;164:692–700.
36. Donadio V, Montagna P, Pennisi M, Rinaldi R, Di Stasi V, Avoni P, Bugiardini E, et al. Agrypnia Excitata: a microneurographic study of muscle sympathetic nerve activity. Clin neurophysiol. 2009;120:1139–42.

37. Yagihashi T, Kato M, Izumi K, Kosaki R, Yago K, Tsubota K, Sato Y, et al. Case report: adult phenotype of Mulvihill-Smith syndrome. Am J Med Genet. 2009;Part A 149A:496–500.
38. La Morgia C, Parchi P, Capellari S, Lodi R, Tonon C, et al. "Agrypnia excitata" in a case of sporadic Creutzfeldt-Jakob disease VV2. J Neurol Neurosurg Psych. 2009;80:244–6.
39. Montagna P, Provini F, Plazzi G, Vetrugno R, Gallassi R, Pierangeli G, Ragno M et al. Bilateral paramedian thalamic syndrome: abnormal circadian wake-sleep and autonomic functions. J Neurol Neurosurg Psych. 2002;73:772–4.
40. Lugaresi E, Medori R, Montagna P et al. Fatal familial insomnia and dysautonomia with selective de-generation of thalamic nuclei. New Engl J Med. 1986;315:997–1003.
41. Lee EK, Maselli RA, Ellis WG, Agius MA. Morvan's fibrillary chorea: a paraneoplastic manifestation of thymoma. J Neurol Neurosurg Psych. 1998;65:857–62.
42. Ropper AH, Brown RHM, Adams RD. Alcohol and alcoholism. In: Principles of neurology, 8th ed. New York: McGraw-Hill; 2005. pp. 275–84.
43. Guaraldi P, Calandra-Buonaura G, Terlizzi R, Montagna P, Lugaresi E, Tinuper P, Cortelli P, et al. Oneiric stupor: the peculiar behaviour of agrypnia excitata. Sleep medicine. 2011;12 Suppl 2:S64–7.
44. Kahn D, Gover T. Consciousness in dreams. Int Rev Neurobiol. 2010;92:181–95.
45. Mahowald MW, Schenck CH. Non-rapid eye movement sleep parasomnias. Neurol Clin. 2005;23:1077–106.

Part VI
Neurological, Psychiatric, and Medical Disorders Presenting as Parasomnias

Chapter 23
Neurological Conditions Associated with Parasomnias

Kiran Maski and Smit S. Chauhan

Introduction

Parasomnias have long captured the interest of neurologists and sleep specialists as these physical and behavioral phenomena are not reliably localized to specific neural substrates and cannot be easily explained by conventional models of consciousness. Activation of locomotor centers coupled with dissociative states result in complex neurobehaviors that can be difficult to distinguish from epileptic events or movement disorders. Non-rapid eye movement (NREM) and rapid eye movement (REM) parasomnias are associated with a number of neurological conditions including attention deficit hyperactivity disorder (ADHD), epilepsy (discussed in Chap. 17), autism spectrum disorders (ASDs), Tourette's syndrome, stroke, traumatic brain injury (TBI), and various dementias (Table 23.1). In this chapter, we discuss various neurological conditions that have been associated with specific types of parasomnias. In most cases, the neurological conditions are associated with indirect and direct alterations of sleep quantity and quality which in turn can increase opportunities for disorders of arousal. Furthermore, some medications aimed at treating the symptoms of neurological conditions may contribute to the development of parasomnias (Table 23.2). In contrast, REM behavior disorder (discussed in Chap. 15) localizes to specific neuroanatomical structures on neuropathological and neuroimaging studies in patients with Parkinson's disease which provides critical insight into the pathophysiology of both the disease state and the parasomnia itself.

K. Maski (✉)
Department of Neurology, Boston Children's Hospital, Harvard Medical School,
333 Longwood Avenue, 4th Floor, Boston, MA 02115, USA
e-mail: kiran.maski@childrens.harvard.edu

S. S. Chauhan
Department of Pediatric Sleep Medicine, Boston Children's Hospital, 300 Longwood Avenue,
Fegan 9, Boston, MA 02115, USA
e-mail: drsmitchauhan@gmail.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_23, © Springer Science+Business Media New York 2013

Table 23.1 Parasomnias associated with neurological disorders

Neurological disorder	Parasomnia(s)
Migraines	Sleepwalking [51]
Seizures	Sleep enuresis, bruxism, sleep talking, confusional arousals [82, 83]
Stroke	REM behavior disorder (RBD) [56, 57]
Parkinson's disease	RBD and sleepwalking [74, 77]
Dementia with Lewy body disease	RBD, sleep related hallucinations [73]
Tourette's syndrome	RBD [67]
Traumatic brain injury	Sleep walking, night terrors, RBD [63]
Autistic spectrum disorders	Nocturnal enuresis, night terrors, nightmares [34]
Attention deficit hyperactivity disorders	Sleep talking, night terrors, confusional arousals [13, 23, 84]

In understanding the association of parasomnias with neurological diseases, it is important to review the theoretical etiologies of parasomnias. Parasomnias are thought to be disorders of arousal and can arise when sleep is excessively fragmented through the night. Sleep fragmentation can occur with increase in the number of electroencephalographic arousals secondary to conditions such as sleep disordered breathing (SDB) and periodic limb movements of sleep (PLMS). Associations between PLMS and SDB and neurological disorders such as ADHD and Parkinson's disease are discussed within this chapter and warrant investigation with a polysomnogram (PSG) if characteristic symptoms are clinically reported [1]. In addition, the stress, pain, environmental changes, immobility associated with more severe disease burden can further degrade sleep quality. This may explain why the presentation of parasomnias can be more common with increased disease severity or in hospital settings [2]. There is some evidence as well that sleep is inherently altered in neurological conditions. In these cases, parasomnias may occur more frequently during more easily disturbed NREM slow wave sleep [3, 4]. Lastly, increased sleepiness can contribute to sleep inertia and thus more difficulty achieving full cortical arousals during sleep–wake transitions [5]. This condition contributes to feeling of sleep drunkiness which results in impaired vigilance and performance.

Attention Deficit Hyperactivity Disorder (ADHD)

ADHD is one of the most prevalent neurodevelopmental disorders in childhood with estimated worldwide prevalence of 5–12 % in school age children [6, 7] with symptoms frequently persistent into adulthood. Symptoms are characterized by persistent and significant inattention and/or hyperactivity/impulsivity and often result in academic struggles, difficulties with peer relations, and problematic behaviors. Sleep problems are a common comorbidity in ADHD with parents reporting sleep problems

Table 23.2 List of medications/substances associated with parasomnias

Medication/substance category	Medications	Parasomnia(s)
Antidepressants	TCAs, MAO inhibitors, SSRIs, SNRIs, bupropion, mirtazapine, trazodone	Nightmares, sleepwalking, REM sleep behavior disorder
Hypnotics	Zolpidem, triazolam, eszopiclone, ramelteon, zaleplon	Sleep related eating disorder, sleep walking, sleep related hallucinations
Mood stabilizers	Lithium	Sleep enuresis, sleep walking
Psychotropics	Phenothiazines, anticholinergics	NREM parasomnias, sleep related eating disorder
Migraine prophylactics	Metoprolol, topiramate	Nightmares, sleep walking, sleep related hallucinations
Typical antipsychotics	Perphenazine, fluphenazine, thioridazine, chlorprothixene	Sleep walking
Atypical antipsychotics	Risperidone, olanzapine	Sleep walking, sleep related eating disorder
Alpha adrenergic agonists	Clonidine, guanfacine	Sleep walking, confusional arousals, sleep related hallucinations
Diuretics		Sleep enuresis
Drugs of abuse	Cocaine, amphetamines, cannabis, PCP, MDMA, LSD	Confusional arousals, sleep related hallucinations, sleep related eating disorder
Alcohol		Disorders of arousal, sleep related eating disorder
Past alcohol use		Sleep related hallucinations
Alcohol cessation		Sleep related eating disorder
Caffeine		Sleep enuresis
Smoking cessation		Sleep related eating disorder

TCA tricyclic antidepressant, *MAO* monoamine oxidase, *SSRI* selective serotonin reuptake inhibitors, *SNRI* serotonin norepinephrine reuptake inhibitors, *LSD* phencyclidine, *MDMA* methylenedioxymethamphetamine, *LSD* lysergic acid diethylamide

in 25–50 % of children with this diagnosis, even in the absence of stimulant medication use [8]. Parents report increased motor activity in sleep [9, 10] and more restless sleep [11, 12] among children with ADHD compared to controls. Parasomnias were reported to be higher in frequency in an ADHD population compared to controls with reports of sleep walking, sleep talking, night terrors, confusional arousals occurring most commonly [8–11, 13].

Parasomnias in children with ADHD may be attributed to poor overall sleep quality compared to controls. Bedtime resistance, sleep onset delays, nocturnal wakings, sleep disordered breathing, and periodic limb movements of sleep have all been reported to be higher in the ADHD population [10, 14–16]. Such disturbances fragment sleep with increased arousal periods and tendency for parasomnia behavior to occur. Furthermore, the stability of NREM sleep in children with ADHD has been analyzed with evaluation of the cyclic alternating pattern (CAP) produced in sleep.

CAP is defined as an endogenous rhythm recurring in intervals up to 2 min, present in NREM sleep and characterized by periodic EEG activity with sequences of electrocortical activations (phase A of the cycle) that are distinct from the background EEG activity (phase B of the cycle) [17, 18]. Children with ADHD show overall a lower CAP rate and number of sequences [19]. Such NREM instability could also allow for the tendency toward disordered arousal by increasing sleep inertia and/or subcortical arousals. Lastly, stimulant medications affect sleep latency, sleep quality, and total sleep time [20–22] suggesting that medications may contribute to parasomnias; however, studies have shown similar sleep disturbances in children with ADHD off medications [23] and improved sleep disturbances when children with ADHD receive stimulants [24]. This suggests that it is insufficient to withdraw stimulant medications to treat parasomnias in children with ADHD, though no formal clinical trials have been performed as of yet.

Autism Spectrum Disorders (ASDs)

ASDs encompass the diagnosis of autism, Asperger syndrome (AS), and pervasive developmental disorder-not otherwise specified (PDD-NOS). According to the Diagnostic and Statistical Manual IV, ASDs are neurodevelopmental disorders with core impairments in social interactions and communications in association with restricted, repetitive, stereotyped behaviors and interests. The most recent estimated incidence of ASDs in the United States is 1 in 88 children and is five times more common in boys than girls [25].

Sleep problems are endemic to children with ASDs with a prevalence ranging from 40–86 % [26–29]. The prevalence of sleep disorders among children with ASD is higher than children with other development delays [30, 31] and is unrelated to intellectual quotient (IQ) [32] or age [33]. The range of sleep problems includes bedtime resistance, circadian abnormalities, sleep disordered breathing, periodic limb movements of sleep, and parasomnias but the most common reported problem is sleep onset and sleep maintenance insomnia [34, 35]. Parents frequently report their children with ASDs have nightmares, wake screaming and have nocturnal enuresis, behaviors strongly suggestive of parasomnias [34]. Liu et al. [29] reported that 53 % of children with ASDs have parasomnias in a parental survey. Younger age, cosleeping, epilepsy, attention deficit hyperactivity disorder (ADHD), asthma, bedtime ritual, medication use, and family history of sleep problems were related to sleep problems in this population. REM behavior disorder (RBD) seems relatively rare in children with ASDs; only one child with RBD had PDD in a recent retrospective review of polysomnography data [36]. In terms of differentiating the subtypes of ASDs by sleep disorder, only Polimeni et al. [27] reported that parasomnias are more prevalent in AS than in autism. However, lower functioning children may not be able to communicate well at baseline leaving it up to parental determination if nocturnal wakings are purposeful or child is in dissociative state.

Understanding the etiology of parasomnias in children with ASDs is complex because medication use and associated psychiatric and neurodevelopmental comor-

bidities such as anxiety, depression, and ADHD can all increase presentation of parasomnias. It is also worth mentioning that epilepsy is common in children with ASDs with prevalence rates ranging between 7 and 46 % [37, 38] and nocturnal seizures may also mimic parasomnia-like behavior. It is not clear if the inherent abnormalities of sleep architecture in patients with ASDs that make them more vulnerable to parasomnias. Data characterizing the macroarchitecture of sleep using polysomnography in this population has shown that children have shorter sleep time, lower sleep efficiency, and lower rapid eye movement (REM) sleep compared to children with typical development [39–41]; however, discrepancies in this literature do exist [42–44]. In terms of microarchitecture of sleep, only one PSG study on 20 young adults with ASDs showed a nonsignificant trend toward a decrease in delta power and increase theta power in slow wave sleep compared to controls [45]. Such findings may suggest less "deep" NREM sleep that could be more prone to fragmentation. Furthermore, CAP rates during slow wave sleep have been shown to be significantly lower than that of controls [46] reflecting NREM sleep instability. Interestingly, children with Asperger syndrome had increase in CAP parameters in slow wave sleep suggesting that the stability of slow wave activity (SWA) may correlate with severity of ASD presentation [47]. Further research is needed to understand the neurophysiology of sleep in children with ASDs and presentation of sleep disruptions including parasomnias.

Migraine

An association between migraine and sleep is well known to the clinical neurologist as many migraine sufferers report improvement in headache with a bout of sleep. However, patients also report sleep complaints with migraines suggesting a bidirectional relationship. The most common complaints of sleep disorders include restless leg syndrome, daytime sleepiness, insomnia, and parasomnia [48]. Among migraine patients who report parasomnias, bruxism, somnambulism, sleep talking and night terror seem most commonly reported compared to controls [49, 50]. Casez et al. [51] reported that 32.8 % of adult patients with migraine had a history of somnambulism during childhood, whereas only 5.1 % of patients without migraine had a similar history. Similarly, Barabas et al. reported 67 % of sleepwalkers had migraine. Given the strength of association between sleep walking and migraine headaches, somnambulism has been proposed as a minor diagnostic criterion in the clinical diagnosis of childhood migraine [51].

There are a few possible explanations for the relationship between migraine and parasomnias. For one, pain may contribute to increased number of arousals and opportunities for parasomnia. Furthermore, specific types of medications such as propranolol and tricyclic agents used to treat migraines have been reported to increase parasomnia behaviors and disrupt sleep [5]. Underlying sleep problems such as sleep disordered breathing associated with migraines and parasomnias require further clinical investigation. In this case, morning headaches would be expected on

clinical presentation as elevated end tidal carbon dioxide levels build through the night contributing to cerebral vasodilation [52]. Lastly, migraine and parasomnias may share a common intrinsic cause such as neurotransmitter changes. Luc et al. propose a hypothesis that alterations in serotonin levels could contribute to migraine and sleep disorders [53]. According to their theory, disruption of the cycle between REM and non-REM activity through serotonin imbalance cause sleep disorders and a decline in systemic serotonin levels can lead to migraine. Supporting this is positron emission tomography scans demonstrating serotonergic areas in the brain receiving more blood flow during a migraine and injection of serotonin analogues relieves migraine [54]. Given that selective serotonin reuptake inhibitors have shown to increase, not decrease, parasomnia behaviors [55], this theory may not be fully substantiated.

Traumatic Brain Injury and Stroke

Lesions within the brain whether acquired from traumatic brain injury or stroke have resulted in the development of parasomnias. For instance, pontine tegmental strokes can lead to REM behavior disorder [56, 57] due to the location of REM on/off neurons that regulate REM atonia. More typically, parasomnias may arise in stroke patients due to other underlying sleep disorders that fragment sleep. The prevalence of sleep disordered breathing in acute stroke patients is 50–70 % by some reports [58, 59]. Sleep disordered breathing is most commonly a preexisting condition in patients presenting with acute stroke [60] but poststroke ischemic lesions in medullary and pontine centers could result in respiratory disturbances as well. Up to 12 % of poststroke patients have been reported to have restless leg syndrome often with coexisting periodic limb movements of sleep [61]. RLS was attributed to ischemic lesions in the pons, thalamus, basal ganglia, and corona radiate in these cases. Traumatic brain injury is often associated with insomnia, fatigue, and sleepiness with narcolepsy (with or without cataplexy), sleep apnea (obstructive or central), periodic limb movement disorder, and parasomnias occurring less commonly [62]. Of the parasomnias, sleep walking, night terrors, RBD and dissociative states have been reported [63], though no clear pathophysiology is present. Of note, patients kept in ICU settings can present with parasomnias due to environmental changes contributing to poor sleep quality and shorter sleep duration, medication administration/withdrawal, unfamiliar setting, alcohol with withdrawal, and fever/infection [2].

Tourette's Syndrome

Gilles de la Tourette syndrome is considered a neuropsychiatric disorder characterized by at least one year history of motor and vocal tics. Often symptoms start in childhood and may still be present through adulthood with waxing/waning severity

and frequency. Comorbid conditions include attention deficit disorders, obsessive compulsive disorders, and learning disorders. Sleep disturbances have been reported in upto 60 % of patients with Tourette's syndrome with difficulty falling asleep and early morning awakening as common complaints [64, 65]. From polysomnographic data, there does not appear to be much difference in terms of REM and NREM cycling or stage amounts; however, Cohrs et al. [66] found that patients had increased motor activity in both REM and NREM sleep. The authors interpreted these results as evidence of a hyperarousal state during sleep in children with Tourette's syndrome due to reduced intracortical inhibition of motor pathways. Interestingly, there was reduced number of electroencephalographic arousals with movements compared to control subjects suggesting a subcortical mechanism resulting in increased movements.

While this study does not report increase in parasomnias in the Tourette's population, other studies have reported increase in prevalence in RBD in these patients [67]. While the pathophysiology of RBD in Tourette's syndrome is not clear, an increase in frequency of RBD in these patients suggests dysfunction of pontine motor inhibition similar to Parkinson disease patients. Likewise, sleepwalking has been reported in upto 19 % of children with Tourette's syndrome compared to 8 % of controls [68] but pathophysiology again is unclear. Further research is needed to clarify the relationship of RBD, sleep walking, and Tourette's syndrome as it may further insight into the etiology of this neurological condition. Lastly, iatrogenic causes of parasomnias in TS should be considered. Clonidine, which is a central alpha2 agonist that decreases adrenergic tone, is widely used in patients with tic disorders. Clonidine suppresses REM sleep and slow wave sleep and thus when rapidly discontinued or tapered, a rebound of REM and slow wave sleep can occur which might precipitate REM and NREM parasomnias [69].

The Alpha Synuceinopathies

Parkinson's disease (PD), Dementia with Lewy Bodies (DLB), pure autonomic failure (PAF), and multiple systems atrophy (MSA) are neurodegenerative disorders classified as alpha-synucleinopathies, characterized by the presence of abnormal accumulation of alpha-synuclein in neurons and glial cells on pathology. In PD, DLB, and PAF, this protein is accumulated in the shape of Lewy bodies in the cytoplasm of neurons, whereas MSA is characterized by the presence of alpha-synuclein in oligodendrocytes. RBD has been documented in patients with synucleinopathies years before the onset of their motor manifestations [70, 71]. This finding is indicative of the degeneration of the pedunculopontine nucleus and sublateral dorsal nucleus in the pontine tegmentum early in the disease process preventing inhibition of the spinal motor neurons normally quiescent in REM sleep [72].

The prevalence of RBD differs among alpha synucleinopathies, ranging from 100 % in MSA to sporadic observations in PAF [73]. The prevalence of RBD in PD was estimated at 15–47 % using a structured questionnaire and 33 % using polysomnographic recordings [74]. RBD seems to be more common in patients

with an akinetic-rigid subtype, longer disease history, orthostatic hypotension, and higher doses of dopaminergic drugs, and RBD has also been related to a higher risk of developing cognitive impairment [73]. However during the course of the disease, there is fluctuating expression of the clinical RBD syndrome. In a cohort of 61 patients with RBD, assessed by caregiver interview, the yearly incidence of RBD was 9 %, while clinical RBD symptoms disappeared yearly in another 14 % of patients [75]. Given the potential for injury to the patient and bed partner, treatment of RBD with clonazepam or melatonin is often recommended clinically.

Somnambulism has also been a reported parasomnia in patients with PD. Merello reported a 5 % incidence of sleep walking in a sample of 312 patients with PD [76]; more recently Poryazova et al. [77] reported the occurrence of adult-onset sleepwalking in a series of six patients with idiopathic Parkinson's disease confirmed by video electroencephalography. All patients had at least one concomitant sleep–wake disorder, including REM sleep behavior disorder. In this report, authors speculate that the neurodegenerative changes associated with Parkinson's disease at the brainstem level can affect the ascending control of state transition and the descending control of locomotion and muscle tone, giving rise to sleepwalking. PD is also associated with frequent sleep disruptions due to medication effects (i.e., levadopa can result in dyskinesias and nightmares during sleep), symptoms such as tremor, bradykinesia and rigidity that make it difficult to achieve comfortable positioning in sleep, and high rates of comorbid depression which can alter sleep quality. Furthermore, brainstem degeneration may impact respiratory centers resulting in sleep disordered breathing and sleep–wake disturbances. Such sleep disruptions and poorer quality of sleep can give rise to tendency for parasomnias such as sleep walking to be expressed.

Alzheimer's Disease

Patients with Alzheimer's disease (AD) have less reported sleep abnormalities compared to patients with dementias resulting from alpha synucleinopathies. This may suggest a preferential neurodegeneration of the brainstem with alpha synucleinopathies compared to taupathies and amyloidpathies typical of AD. Sleep disorders are more commonly reported in late stages of AD in contrast to early presentation in alpha synucleinopathies [78]. Patients with AD have increase in nighttime awakenings, increase in daytime sleep, and decrease in slow wave sleep and REM sleep [79]. The pathophysiology of sleep problems in patients with AD may involve direct and indirect mechanisms. Degeneration of cholinergic neurons in the basal of Meynert of the forebrain, pedunculo-pontine and lateral dorsal tegmental nuclei of the brainstem may result in less ability to maintain wakefulness during the day, and contributing to sleep fragmentation at night. Alternatively, there may be degeneration of neurons in suprachiasmatic nuclei contributing to circadian dysrhythmias and inversion of sleep rhythms [80]. Secondary sleep fragmentation may also be attributed to comorbid anxiety/depression, cholinergic medications and improper environmental cues for sleep which may be present in long term care facilities/nursing homes. Despite

increase in number of awakenings and arousals in sleep, parasomnias are rarely reported among the AD population. In one case report, an 88-year-old man with Alzheimer's developed sleep talking, sleep walking, and REM behavior disorder with rivostigmine use, an acetylcholinesterase inhibitor [81].

Conclusion

Development of parasomnias with neurological conditions is multifactorial and related to environmental changes, medications, comorbid psychiatric symptoms, and underlying sleep disorders. At this time, few neurological diseases first present with parasomnias with exception of RBD in alpha synucleinopathies. As research advances, investigations of sleep macroarchitecture and microarchitecture is needed to further investigate high rates of sleep problems in patients with neurological conditions to determine if intrinsic abnormalities contribute to sleep fragmentation and development of parasomnais. No data on how parasomnias effect daytime functioning of patients with neurological conditions is available, but at the least, an increase in daytime sleepiness could be anticipated. Whether this increase in daytime sleepiness could contribute to deterioration of neurological functioning is yet another area for research investigation.

Practical Points

a. Parasomnias are associated with specific neurologic conditions but are heterogeneous in presentation.
b. REM behavior disorders present early in alpha-synucleinopathies and may reflect ascending brainstem neurodegeneration.
c. Etiology of parasomnias is multifactorial and attributed to medications, environmental changes, stress, comorbid psychiatric conditions, and underlying sleep disorders.
d. Familiarity with medications that can contribute to parasomnias is needed before attributing sleep disruption to the neurological condition itself.

References

1. Kotagal S, Nichols CD, Grigg-Damberger MM, Marcus CL, Witmans MB, Kirk VG, et al. Non-respiratory indications for polysomnography and related procedures in children: an evidence-based review. Sleep. 2012;35(11):1451–66.
2. Schenck CH, Mahowald MW. Injurious sleep behavior disorders (parasomnias) affecting patients on intensive care units. Intensive care med. [Research Support, Non-U.S. Gov't]. 1991;17(4):219–24.

3. Guilleminault C, Kirisoglu C, da Rosa AC, Lopes C, Chan A. Sleepwalking, a disorder of. NREM sleep instability. Sleep med. 2006 Mar;7(2):163–70.
4. Bruni O, Ferri R, Novelli L, Finotti E, Miano S, Guilleminault C. NREM sleep instability in children with sleep terrors: the role of slow wave activity interruptions. Clin Neurophysiol. 2008 May;119(5):985–92.
5. Markov D, Jaffe F, Doghramji K. Update on parasomnias: a review for psychiatric practice. Psychiatry (Edgmont). 2006 Jul;3(7):69–76.
6. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry. 2007 Jun;164(6):942–8.
7. Faraone SV, Sergeant J. Gillberg C, Biederman J. The worldwide prevalence of ADHD: is it an American condition? World Psychiatry. 2003 Jun;2(2):104–13.
8. Corkum P, Tannock R, Moldofsky H. Sleep disturbances in children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 1998 Jun;37(6):637–46.
9. Corkum P, Moldofsky H, Hogg-Johnson S, Humphries T, Tannock R. Sleep problems in children with attention-deficit/hyperactivity disorder: impact of subtype, comorbidity, and stimulant medication. J Am Acad Child Adolesc Psychiatry [Research Support Non-US Gov't]. 1999 Oct;38(10):1285–93.
10. Konofal E, Lecendreux M, Bouvard MP, Mouren-Simeoni MC. High levels of nocturnal activity in children with attention-deficit hyperactivity disorder: a video analysis. Psychiatry Clin Neurosci. 2001 Apr;55(2):97–103.
11. Mayes SD, Calhoun SL, Bixler EO, Vgontzas AN, Mahr F, Hillwig-Garcia J, et al. ADHD subtypes and comorbid anxiety, depression, and oppositional-defiant disorder: differences in sleep problems. J Pediatr Psychol [Comparative Study Research Support NIH Extramural Research Support Non-US Gov't]. 2009 Apr;34(3):328–37.
12. Corkum P, Tannock R, Moldofsky H, Hogg-Johnson S, Humphries T. Actigraphy and parental ratings of sleep in children with attention-deficit/hyperactivity disorder (ADHD). Sleep. 2001 May 1;24(3):303–12.
13. Silvestri R, Gagliano A, Arico I, Calarese T, Cedro C, Bruni O, et al. Sleep disorders in children with Attention-Deficit/Hyperactivity Disorder (ADHD) recorded overnight by video-polysomnography. Sleep Med. 2009 Dec;10(10):1132–8.
14. Cortese S, Faraone SV, Konofal E, Lecendreux M. Sleep in children with attention-deficit/hyperactivity disorder: meta-analysis of subjective and objective studies. J Am Acad Child Adolesc Psychiatry [Meta-Analysis]. 2009 Sep;48(9):894–908.
15. Sadeh A, Pergamin L, Bar-Haim Y. Sleep in children with attention-deficit hyperactivity disorder: a meta-analysis of polysomnographic studies. Sleep Med Rev. 2006 Dec;10(6):381–98.
16. Picchietti DL, England SJ, Walters AS, Willis K, Verrico T. Periodic limb movement disorder and restless legs syndrome in children with attention-deficit hyperactivity disorder. J Child Neurol. [Research Support, U.S. Gov't, Non-P.H.S.]. 1998 Dec;13(12):588–94.
17. Parrino L, Ferri R, Bruni O, Terzano MG. Cyclic alternating pattern (CAP): the marker of sleep instability. Sleep Med Rev. 2012 Feb;16(1):27–45.
18. Terzano MG, Parrino L, Sherieri A, Chervin R, Chokroverty S, Guilleminault C, et al. Atlas, rules, and recording techniques for the scoring of cyclic alternating pattern (CAP) in human sleep. Sleep Med. 2001 Nov;2(6):537–53.
19. Miano S, Donfrancesco R, Bruni O, Ferri R, Galiffa S, Pagani J, et al. NREM sleep instability is reduced in children with attention-deficit/hyperactivity disorder. Sleep. 2006 Jun;29(6):797–803.
20. Efron D, Jarman F, Barker M. Side effects of methylphenidate and dexamphetamine in children with attention deficit hyperactivity disorder: a double-blind, crossover trial. Pediatrics [Clinical Trial Randomized Controlled Trial Research Support Non-US Gov't]. 1997 Oct;100(4):662–6.
21. Schwartz G, Amor LB, Grizenko N, Lageix P, Baron C, Boivin DB, et al. Actigraphic monitoring during sleep of children with ADHD on methylphenidate and placebo. J Am Acad Child Adolesc Psychiatry. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. 2004 Oct;43(10):1276–82.

22. Corkum P, Panton R, Ironside S, Macpherson M, Williams T. Acute impact of immediate release methylphenidate administered three times a day on sleep in children with attention-deficit/hyperactivity disorder. J Pediatr Psychol [Randomized Controlled Trial Research Support Non-US Gov't]. 2008 May;33(4):368–79.
23. Owens J, Sangal RB, Sutton VK, Bakken R, Allen AJ, Kelsey D. Subjective and objective measures of sleep in children with attention-deficit/hyperactivity disorder. Sleep Med [Research Support Non-US Gov't]. 2009 Apr;10(4):446–56.
24. Sobanski E, Schredl M, Kettler N, Alm B. Sleep in adults with attention deficit hyperactivity disorder (ADHD) before and during treatment with methylphenidate: a controlled polysomnographic study. Sleep [Controlled Clinical Trial]. 2008 Mar;31(3):375–81.
25. Data and Statistics-Autism Spectrum Disorders [Internet]. [Place unknown]. Center for Disease Control; 2012 [updated March 29, 2012; cited 11/25/2012]. http://www.cdc.gov/ncbddd/autism/data.html.
26. Patzold LM, Richdale AL, Tonge BJ. An investigation into sleep characteristics of children with autism and Asperger's Disorder. J Paediatr Child Health. 1998 Dec;34(6):528–33.
27. Polimeni MA, Richdale AL, Francis AJ. A survey of sleep problems in autism, Asperger's disorder and typically developing children. J Intellect Disabil Res. [Comparative Study]. 2005 Apr;49(Pt 4):260–8.
28. Wiggs L, Stores G. Sleep patterns and sleep disorders in children with autistic spectrum disorders: insights using parent report and actigraphy. Dev Med Child Neurol. 2004 Jun;46(6):372–80.
29. Liu X, Hubbard JA, Fabes RA, Adam JB. Sleep disturbances and correlates of children with autism spectrum disorders. Child Psychiatry Hum Dev. [Research Support, Non-U.S. Gov't]. 2006 Winter;37(2):179–91.
30. Krakowiak P, Goodlin-Jones B, Hertz-Picciotto I, Croen LA, Hansen RL. Sleep problems in children with autism spectrum disorders, developmental delays, and typical development: a population-based study. J Sleep Res. 2008 Jun;17(2):197–206.
31. Goodlin-Jones BL, Tang K, Liu J, Anders TF.Sleep patterns in preschool-age children with autism, developmental delay, typical development. J Am Acad Child Adolesc Psychiatry. 2008 Aug;47(8):930–8.
32. Richdale AL, Prior MR. The sleep/wake rhythm in children with autism. Eur Child Adolesc Psychiatry. 1995 Jul;4(3):175–86.
33. Goldman SE, Richdale AL, Clemons T, Malow BA. Parental Sleep concerns in autism spectrum disorders: variations from childhood to adolescence. J Autism Dev Disord. 2012 Apr;42(4):531–8.
34. Richdale AL, Schreck KA. Sleep problems in autism spectrum disorders: prevalence, nature, & possible biopsychosocial aetiologies. Sleep Med Rev [Review]. 2009 Dec;13(6):403–11.
35. Souders MC, Mason TB, Valladares O, Bucan M, Levy SE, Mandell DS, et al. Sleep behaviors and sleep quality in children with autism spectrum disorders. Sleep. 2009 Dec;32(12):1566–78.
36. Lloyd R, Tippmann-Peikert M, Slocumb N, Kotagal S. Characteristics of REM sleep behavior disorder in childhood. J Clin Sleep Med. 2012 Apr 15;8(2):127–31.
37. Bolton PF, Carcani-Rathwell I, Hutton J, Goode S, Howlin P, Rutter M. Epilepsy in autism: features and correlates. Br J Psychiatry [Research Support Non-US Gov't]. 2011 Apr;198(4):289–94.
38. Brooks-Kayal A. Epilepsy and autism spectrum disorders: are there common developmental mechanisms? Brain Dev. 2010 Oct;32(9):731–8.
39. Buckley AW, Rodriguez AJ, Jennison K, Buckley J, Thurm A, Sato S, et al. Rapid eye movement sleep percentage in children with autism compared with children with developmental delay and typical development. Arch Pediatr Adolesc Med. 2010 Nov;164(11):1032–7.
40. Johnson KP, Giannotti F, Cortesi F. Sleep patterns in autism spectrum disorders. Child Adolesc Psychiatr Clin N Am. 2009 Oct;18(4):917–28.
41. Tanguay PE, Ornitz EM, Forsythe AB, Ritvo ER. Rapid eye movement (REM) activity in normal and autistic children during REM sleep. J Autism Child Schizophr. 1976 Sep;6(3):275–88.

42. Malow BA, Marzec ML, McGrew SG, Wang L, Henderson LM, Stone WL. Characterizing sleep in children with autism spectrum disorders: a multidimensional approach. Sleep. 2006 Dec 1;29(12):1563–71.
43. Melke J, Goubran Botros H, Chaste P, Betancur C, Nygren G, Anckarsater H, et al. Abnormal melatonin synthesis in autism spectrum disorders. Mol Psychiatry. 2008 Jan;13(1):90–8.
44. Limoges E, Mottron L, Bolduc C, Berthiaume C, Godbout R. Atypical sleep architecture and the autism phenotype. Brain. 2005 May;128(Pt 5):1049–61.
45. Tani P, Lindberg N, Nieminen-von Wendt T, von Wendt L, Virkkala J, Appelberg B, et al. Sleep in young adults with Asperger syndrome. Neuropsychobiology. 2004;50(2):147–52.
46. Miano S, Bruni O, Elia M, Trovato A, Smerieri A, Verrillo E, et al. Sleep in children with autistic spectrum disorder: a questionnaire and polysomnographic study. Sleep Med. 2007 Dec;9(1):64–70.
47. Bruni O, Ferri R, Vittori E, Novelli L, Vignati M, Porfirio MC, et al. Sleep architecture and NREM alterations in children and adolescents with Asperger syndrome. Sleep. 2007 Nov;30(11):1577–85.
48. Cevoli S, Giannini G, Favoni V, Pierangeli G, Cortelli P. Migraine and sleep disorders. Neurol Sci. 2012 May;33(Suppl 1):S. 43–6.
49. Bruni O, Russo PM, Ferri R, Novelli L, Galli F, Guidetti V. Relationships between headache and sleep in a non-clinical population of children and adolescents. Sleep Med. 2008 Jul;9(5):542–8.
50. Miller VA, Palermo TM, Powers SW, Scher MS, Hershey AD. Migraine headaches and sleep disturbances in children. Headache. [Research Support, U.S. Gov't, P.H.S.]. 2003 Apr;43(4):362–8.
51. Casez O, Dananchet Y, Besson G. Migraine and somnambulism. Neurology. 2005 Oct 25;65(8):1334–5.
52. Poceta JS, Dalessio DJ. Identification and treatment of sleep apnea in patients with chronic headache. Headache. 1995 Nov–Dec;35(10):586–9.
53. Luc ME, Gupta A, Birnberg JM, Reddick D, Kohrman MH. Characterization of symptoms of sleep disorders in children with headache. Pediatr Neurol. 2006 Jan;34(1):7–12.
54. Weiller C, May A, Limmroth V, Juptner M, Kaube H, Schayck RV, et al. Brain stem activation in spontaneous human migraine attacks. Nat Med. [Research Support, Non-U.S. Gov't]. 1995 Jul;1(7):658–60.
55. Kierlin L, Littner MR. Parasomnias and antidepressant therapy: a review of the literature. Front Psychiatry. 2011;2:71.
56. Reynolds TQ, Roy A. Isolated cataplexy and REM sleep behavior disorder after pontine stroke. J Clin Sleep Med. [Case Reports]. 2011 Apr 15;7(2):211–3.
57. Xi Z, Luning W. REM sleep behavior disorder in a patient with pontine stroke. Sleep med. [Case Reports Research Support, Non-U.S. Gov't]. 2009 Jan;10(1):143–6.
58. Bassetti C, Aldrich MS, Chervin RD, Quint D. Sleep apnea in patients with transient ischemic attack and stroke: a prospective study of 59 patients. Neurology [Research Support Non-US Gov't Research Support US Gov't PHS]. 1996 Nov;47(5):1167–73.
59. Bassetti CL, Milanova M, Gugger M. Sleep-disordered breathing and acute ischemic stroke: diagnosis, risk factors, treatment, evolution, and long-term clinical outcome. Stroke. 2006 Apr;37(4):967–72.
60. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. N Engl J Med. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, Non-P.H.S. Research Support, U.S. Gov't, P.H.S.]. 2005 Nov 10;353(19):2034–41.
61. Lee SJ, Kim JS, Song IU, An JY, Kim YI, Lee KS. Poststroke restless legs syndrome and lesion location: anatomical considerations. Mov Disord. 2009 Jan 15;24(1):77–84.
62. Viola-Saltzman M, Watson NF. Traumatic brain injury and sleep disorders. Neurol Clin. 2012 Nov;30(4):1299–312.
63. Schenck CH, Boyd JL, Mahowald MW. A parasomnia overlap disorder involving sleepwalking, sleep terrors, REM sleep behavior disorder in 33 polysomnographically confirmed cases. Sleep. [Comparative Study Review]. 1997 Nov;20(11):972–81.

64. Jankovic J, Rohaidy H. Motor, behavioral and pharmacologic findings in Tourette's syndrome. Can J Neurol Sci. 1987 Aug;14(Suppl 3):541–6.
65. Glaze DG, Frost JD Jr., Jankovic J. Sleep in Gilles de la Tourette's syndrome: disorder of arousal. Neurology. 1983 May;33(5):586–92.
66. Cohrs S, Rasch T, Altmeyer S, Kinkelbur J, Kostanecka T, Rothenberger A, et al. Decreased sleep quality and increased sleep related movements in patients with Tourette's syndrome. J Neurol Neurosurg Psychiatry. 2001 Feb;70(2):192–7.
67. Trajanovic NN, Voloh I, Shapiro CM, Sandor P. REM sleep behaviour disorder in a child with Tourette's syndrome. Can J Neurol Sci. [Case Reports]. 2004 Nov;31(4):572–5.
68. Barabas G, Matthews WS, Ferrari M. Somnambulism in children with Tourette syndrome. Dev Med Child Neurol. 1984 Aug;26(4):457–60.
69. Stores G. Dramatic parasomnias. J R Soc Med. [Review]. 2001 Apr;94(4):173–6.
70. Schenck CH, Bundlie SR, Mahowald MW. Delayed emergence of a parkinsonian disorder in 38 % of 29 older men initially diagnosed with idiopathic rapid eye movement sleep behaviour disorder. Neurology [Research Support Non-US Gov't]. 1996 Feb;46(2):388–93.
71. Iranzo A, Molinuevo JL, Santamaria J, Serradell M, Marti MJ, Valldeoriola F, et al. Rapid-eye-movement sleep behaviour disorder as an early marker for a neurodegenerative disorder: a descriptive study. Lancet Neurol [Comparative Study Research Support Non-US Gov't]. 2006 Jul;5(7):572–7.
72. Boeve BF, Silber MH, Saper CB, Ferman TJ, Dickson DW, Parisi JE, et al. Pathophysiology of REM sleep behaviour disorder and relevance to neurodegenerative disease. Brain. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't Review]. 2007 Nov;130 (Pt 11):2770–88.
73. Zanigni S, Calandra-Buonaura G, Grimaldi D, Cortelli P. REM behaviour disorder and neurodegenerative diseases. Sleep Med. [Review Video-Audio Media]. 2011 Dec;12(Suppl 2):S 54–8.
74. Gagnon JF, Bedard MA, Fantini ML, Petit D, Panisset M, Rompre S, et al. REM sleep behavior disorder and REM sleep without atonia in Parkinson's disease. Neurology. [Clinical Trial Controlled Clinical Trial Research Support, Non-U.S. Gov't]. 2002 Aug 27;59(4):585–9.
75. Lavault S, Leu-Semenescu S, Tezenas du Montcel S, Cochen de Cock V, Vidailhet M, Arnulf I. Does clinical rapid eye movement behavior disorder predict worse outcomes in Parkinson's disease? J Neurol. [Research Support Non-US Gov't]. 2010 Jul;257(7):1154–9.
76. Merello M, Hughes A, Colosimo C, Hoffman M, Starkstein S, Leiguarda R. Sleep benefit in Parkinson's disease. Mov Disord. 1997 Jul;12(4):506–8.
77. Poryazova R, Waldvogel D, Bassetti CL. Sleepwalking in patients with Parkinson disease. Arch Neurol. [Case Reports]. 2007 Oct;64(10):1524–7.
78. Bliwise DL, Hughes M, McMahon PM, Kutner N. Observed sleep/wakefulness and severity of dementia in an Alzheimer's disease special care unit. J Gerontol A Biol Sci Med Sci [Research Support US Gov't PHS]. 1995 Nov;50(6):M303–6.
79. Vitiello MV, Borson S. Sleep disturbances in patients with Alzheimer's disease: epidemiology, pathophysiology and treatment. CNS Drugs [Research Support US Gov't Non-PHS Research Support US Gov't PHS Review]. 2001;15(10):777–96.
80. Witting W, Kwa IH, Eikelenboom P, Mirmiran M, Swaab DF. Alterations in the circadian rest-activity rhythm in aging and Alzheimer's disease. Biol Psychiatry. [Research Support, Non-U.S. Gov't]. 1990 Mar 15;27(6):563–72.
81. Yeh SB, Yeh PY, Schenck CH. Rivastigmine-induced REM sleep behavior disorder (RBD) in a 88-year-old man with Alzheimer's disease. J Clin Sleep Med [Case Reports]. 2010 Apr 15;6(2):192–5.
82. Bisulli F, Vignatelli L, Naldi I, Licchetta L, Provini F, Plazzi G, et al. Increased frequency of arousal parasomnias in families with nocturnal frontal lobe epilepsy: a common mechanism? Epilepsia. [Comparative Study Research Support Non-US Gov't]. 2010 Sep;51(9):1852–60.

83. Grigg-Damberger M, Ralls F. Primary sleep disorders and paroxysmal nocturnal nonepileptic events in adults with epilepsy from the perspective of sleep specialists. J Clin Neurophysiol. [Review]. 2011 Apr;28(2):120–40.
84. Owens JA, Maxim R, Nobile C, McGuinn M, Msall M. Parental and self-report of sleep in children with attention-deficit/hyperactivity disorder. Arch Pediatr Adolesc Med [Comparative Study]. 2000 Jun;154(6):549–55.

Chapter 24
Psychiatric Disorders Presenting with Parasomnias

Robert A. Kowatch

Introduction

There are three common psychiatric disorders that may include nocturnal symptoms as part of their clinical presentation: nocturnal panic attacks (PAs), posttraumatic stress disorder (PTSD), and dissociative disorders (DD). We will review the clinical characteristics, polysomnographic features, and treatment of these disorders. It is important to remember that patients with a psychiatric disorder spend one-third of their life asleep and parasomnias often occur as part of their clinical presentation.

Nocturnal Panic Attacks

Nocturnal PAs are abrupt awakenings from sleep in a state of panic without an obvious trigger. Nocturnal PAs are most often experienced by patients with panic disorder, an anxiety disorder characterized by repeated, unexpected PAs, and fear about their recurrence. In *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-IV there are two types of panic disorders, one with the fear of open spaces (agoraphobia), the second without agoraphobia [1].

Patients with panic disorder and nocturnal PAs typically wake-up from sleep with a rapid heartbeat, sweating, dizziness, shortness of breath, and a sense of impending doom. Other less typical symptoms include a sensation of choking, chest pain, numbness or tingling, weakness, and a sense of dissociation. Patients with nocturnal PAs often have a strong wish of escaping from the situation that provoked the attack and may try to avoid these situations in the future. This often leads to initial and middle insomnia.

R. A. Kowatch (✉)
Department of Psychiatry Ohio State Medical Center/Nationwide Children's Hospital,
700 Children's Drive,
J West 4th Floor, Room G4-4921, Columbus, OH 43023, USA
e-mail: robert.kowatch@nationwidechildrens.org

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_24,

The clinical characteristics of a panic disorder are the presence of recurrent, unexpected PAs associated with more than 1 month of subsequent persistent worry about (1) having another attack, (2) consequences of the attack, or (3) significant behavioral changes related to the attack [1]. PAs are a period of intense fear in which 4 of 13 defined symptoms develop abruptly and peak rapidly less than 10 min from symptom onset. To make the diagnosis of panic disorders, PAs cannot directly result from substance use, medical conditions, or other psychiatric disorders. The following are potential symptom manifestations of a PA:

- Palpitations, "pounding heart", or accelerated heart rate
- Sweating
- Trembling or shaking
- Sense of shortness of breath or smothering
- Feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded, or faint
- Derealization or depersonalization (feeling detached from oneself)
- Fear of losing control or going crazy
- Fear of dying
- Numbness or tingling sensations
- Chills or hot flashes.

Nocturnal PAs occur in approximately 30–70 % of patients with panic disorders [2]. In one large survey, 50 % of panic disorder patients reported having nocturnal PAs at least once and 30 % reported nocturnal PAs repeatedly [3]. The majority of patients with nocturnal PAs also experience PAs during the day [3]. There is a small group of patients whose PAs occurred mainly during the night. Nocturnal PAs may also occur in patients with PTSD [4]. Most patients with nocturnal PAs report that these attacks occur between 1 and 3 h after sleep onset, they typically occur once per night and last 5–10 min. Patients report waking up during the nocturnal PA and may vividly recall awakening with a PA when they awaken.

Hauri et al. studied 24 adult patients with panic disorders for three consecutive nights with polysomnography (PSG) [5]. They reported that the patients with PD had slightly longer sleep latency, lower sleep efficiency, and more body movements during stage 2 sleep compared to the healthy control subjects. Eight PAs were recorded arising out of sleep, with six occurring in the transition phase between stage 2 and stage 3 sleep.

Nocturnal PAs are usually non-REM events usually occurring in late stage 2 to early stage 3 sleep. In contrast, night terrors typically occur during stage 4 sleep and patients typically cannot recall these events. Nocturnal PAs may be triggered by apneic episodes and sleep apnea should be ruled out in patients with nocturnal PAs. There are no specific electroencephalographic (EEG) abnormalities during nocturnal PAs. Nocturnal PAs are non-REM events as opposed to nightmares that occur during REM sleep. Nocturnal PA may also be precipitated by benzodiazepine withdrawal [2]. Patients with PTSD and nocturnal PAs often connect their awakenings during a PA to specific trauma-related dreams and images. whereas patients with Nocturnal PAs do not.

The treatment of nocturnal PAs ideally includes both cognitive behavioral therapy (CBT) and pharmacotherapy. CBT is a psychotherapeutic approach that emphasizes distorted/dysfunctional thoughts, emotions, and behavior through a goal oriented, structured and time limited procedure. CBT has been demonstrated to treat both the daytime and nocturnal PAs with good success [3]. CBT focuses on education about the nature of panic, the physiologic signs of arousal preceding PAs, breathing techniques for relaxation, and "cognitive restructuring" of unrealistic beliefs about PAs, e.g., "No one has ever died from a night time PA." There are no large controlled trials about the efficacy of medications for nocturnal PAs. Case reports have indicated success in treating nocturnal PA with alprazolam, tricyclic antidepressants [6], and selective serotonin reuptake inhibitors (SSRIs) [7].

Posttraumatic Stress Disorder

PTSD is an anxiety disorder that can develop after exposure to a traumatic event or ordeal during which there was "the potential for or actual occurrence of grave physical harm" [8]. Examples of traumatic events that may trigger PTSD include violent personal assaults, tornadoes, floods, rape, motor vehicle accidents, and military combat. Patients with PTSD experience persistent frightening thoughts and memories of their ordeal, sleep problems, feel detached or numb, or are easily startled. PTSD is very common in adults, adolescents, and children. The National Comorbidity Survey Replication (NCS-R) assessed among 5,692 participants for PTSD using DSM-IV criteria and estimated the lifetime prevalence of PTSD among adult Americans was 6.8 % [9]. At initial screen, 41 % of soldiers who had been to Iraq or Afghanistan reported sleep problems and those who had initially reported any insomnia had significantly higher overall scores for PTSD severity at follow-up than any service members without such a complaint [10, 11].

Sleep disturbances, typically insomnia and/or nightmares, are extremely common in patients with PTSD and are frequently referred to as the "hallmark symptom" of PTSD [12]. Patients with PTSD will often have both initial and middle insomnia and some may have vivid emotional nightmares that they can recall or night terrors that occur during the first half of the night without a clear dream recall [11].

Depression and substance abuse are frequent comorbid disorders among patients with PTSD and parasomnias should be recognized and treated appropriately. There is some research that suggests that development of sleep disturbances after a traumatic event may predict the development of full PTSD [13, 14], Treatment of these sleep disorders may prevent the development of full PTSD.

A metaanalysis of sleep findings in PTSD by Kobayashi et al. reported that PTSD patients had more stage 1 sleep, less slow-wave sleep, and greater REM density compared to people without PTSD [15]. But, none of these findings on PSG are diagnostic for PTSD. The diagnosis of PTSD is based upon the patient's trauma history and clinical symptoms.

There has been a great deal of research into developing specific CBTs for PTSD. Imagery rehearsal therapy (IRT) is a brief, well-tolerated treatment that decreases

chronic nightmares, improves sleep quality, and decreases PTSD symptom severity [16]. During IRT a patient with PTSD is encouraged to recall their recurrent traumatic nightmare, write it down, change the, story line, ending or any part of the dream to a more positive one, and rehearse the rewritten dream scenario so that they can displace the unwanted ending when the dream recurs. IRT acts to inhibit the original nightmare, providing a "cognitive shift" that refutes the original premise of the nightmare. This technique is practiced for 10–20 min/day while awake. CBT is as effective as pharmacologic treatment in the short term and more enduring in beneficial effect [11].

A variety of medications have been found to be useful in the treatment of the sleep disturbances associated with PTSD. Tricyclic antidepressants such as amitriptyline imipramine, have been found to be useful in improving sleep in patients with PTSD [17]. But, the side effects of tricyclic antidepressants including urinary retention, dry mouth, blurred vision, and confusion limit their clinical use. In some patients, SSRIs, for example fluvoxamine, have been found to be useful in decreasing the insomnia and nightmares of PTSD patients [18]. However, in other patients, SSRIs led to complaints of sleep fragmentation and increases in daytime fatigue. Case reports have suggested that the benzodiazepines may be helpful in the short term for these patients, but ultimately tolerance and abuse are problems [19].

The atypical antipsychotics (AA), e.g., olanzapine, quetiapine, and risperidone, are used frequently in psychiatry because of the large effect sizes and lower rates of adverse events compared to first generation antipsychotics. One controlled trial in 19 adult patients with PTSD who were minimally responsive to 12 weeks of treatment with a SSRI, demonstrated that the addition of olanzapine for posttraumatic stress improved depressive and sleep disorder symptoms [20]. One open-label study of quetiapine suggested that it also improves sleep disturbances in combat veterans with PTSD [21]. Prazosin, a 1-α adrenoreceptor antagonist used for the treatment of hypertension has also been used to treat the nightmares associated with PTSD. Several small controlled trials proved that prazosin is useful in the reduction of posttraumatic nightmares in veterans with PTSD [22, 23].

The Standards of Practice Committee (SPC) of the American Academy of Sleep Medicine (AASM) commissioned a task force in 2007 to assess the literature on the treatment of nightmare disorders [24]. This task force included PTSD studies in which improvement in nightmares could be specifically identified as an evaluable outcome measure. Prazosin was the only pharmacologic agent recommended for treatment of PTSD associated nightmares (Level I evidence) with randomized clinical trials or high-quality cohort trials.

Sleep-Related Dissociative Disorders

Sleep-related DDs are a variant of psychiatric DDs that most often occur in people who have been physically, sexually, or verbally abused. Dissociation describes a psychological mechanism with the separation of discrete mental processes from the mainstream of mental activity and disruptions in consciousness, memory, identity,

or perception. Most patients with a sleep-related DD have corresponding daytime episodes of disturbed behavior, confusion, and associated amnesia. Sleep-related DD is more common in females than males and the age of onset varies from childhood through adulthood [25].

In the *DSM-IV text revision (TR)* there are five major types of dissociative categories diagnostic for DD: dissociative amnesia, dissociative identity disorder (multiple personality disorder), dissociative fugue, depersonalization disorder, and DD not otherwise specified (NOS) [8]. Of these five categories, three categories of DDs, dissociative identity disorder, dissociative fugue, and DD NOS, have been identified with sleep-related DDs.

Nocturnal behaviors in patients with DD may include yelling, walking, running, or in some cases more complex behaviors [26]. The frequency of these events is variable and they may occur several times per night or at weekly intervals. Often patients are amnestic for their nocturnal behaviors. Complications include injuries to the patient or their bed partner or self-mutilations—the patient may cut or burn themselves during a nocturnal DD. Sleep-related DD can emerge at any point during the sleep period and episodes are typically elaborate behaviors occurring at transitions from wakefulness to sleep or within minutes from an awakening from stage N1, stage N2, or REM sleep [25].

Patients with DD have complicated presentations, symptom complexes, and treatment courses [27]. A thorough psychiatric assessment by a psychiatrist or clinical psychologist with experience in DDs is essential for patients with nocturnal DD as well as referral to a sleep disorders center for a clinical assessment and overnight PSG. Sleep-related seizures may be ruled out by either an overnight PSG with an extended EEG montage, or long-term EEG monitoring.

Treatment for sleep-related DD should involve individual psychotherapy, group therapy, and pharmacotherapy. There are no controlled studies of medications for the treatment of sleep-related DD, but bedtime clonidine, periactin, or prazosin have been reported to be helpful in treating sleep-related DD [28].

Conclusion

The diagnoses and management of psychiatric parasomnias is complicated by the nocturnal nature of these disorders and their comorbid psychiatric disorders. The management of these disorders is best approached by a combination of psychotherapy and pharmacotherapy. Table 24.1 summarizes the clinical features and treatment approaches for each of these disorders.

Practical Points

A general approach to these disorders should include:

1. A thorough clinical assessment by a multidisciplinary team that includes a psychiatrist, psychologist, and a sleep specialist. This assessment should include:

Table 24.1 Summary of characteristics of psychiatric disorders with parasomnias

	Nocturnal PAs	PTSD	Sleep-related DD
Symptoms	Preexisting panic disorder	Exposure to a traumatic event	Preexisting DD
	Abrupt awakening from sleep with a rapid heartbeat, sweating, dizziness, shortness of breath and a sense of impending doom	Initial, middle, and terminal insomnia	
	1–3 h after sleep onset	Nightmares are more common, night terrors may also occur	Yelling, walking, running, or in some cases more complex behaviors
	Full recall of the attack		Amnesia for nocturnal events
Gender/age range	F > M > 18 (years)	F > M (all ages)	F > M > 18 (years)
PSG	Slightly longer sleep latency, lower sleep efficiency, more overall movement time and more body movements during stage 2 sleep	Increased stage 1 sleep, less slow-wave sleep, and greater REM density	Transitions from wakefulness to sleep or within minutes from an awakening from stage N1, stage N2, or REM sleep
Treatment	CBT	IRT	Psychiatric treatment with individual psychotherapy and group therapy
	Medications		
	Benzodiazepines or SSRIs	Prazosin, SSRIs	Clonidine, periactin or prazosin

CBT cognitive behavioral therapy, *DD* dissociative disorders, *IRT* imagery rehearsal training, *PAs* panic attacks, *PSG* polysomography, *PTSD* posttraumatic stress disorder, *REM* rapid eye movement, *SSRIs* selective serotonin reuptake inhibitors

(a) Clinical sleep–wake interview and examinations, ideally with the bed partner.
(b) Review of past and current medical records, along with questionnaires that covers: sleep–wake history [29], medical and psychiatric history, and caffeine/alcohol/substance use and abuse history; a review of any current physical and psychiatric symptoms; past or current history of abuse (physical, sexual, verbal–emotional); and family medical, sleep, and psychiatric history.
(c) Screening psychological tests for Axis I and II disorders, e.g., symptom checklist-90, patient health questionnaire (PHQ-9), dissociative experiences scale, etc.
(d) Neurologic and psychiatric review of systems and examination.
(e) Hospital-based, overnight polysomnographic monitoring, with continuous PSG time-synchronized, audio-visual recording and with a full conventional seizure montage, chin and four-limb electromyograms, electrocardiogram (ECG), and nasal–oral airflow with full respiratory effort monitoring.

Case Example

The patient was a 28-year-old White male who had recently returned from three tours of duty, two in Iraq, and one in Afghanistan, where he was a explosive ordnance disposal (EOD) E-7 specialist in the US Army. Prior to enlistment he was a star athlete in high school and had completed 2 years at a junior college. While enlisted he was exposed to high-velocity explosions on a weekly basis, of different strengths and varying proximities. While deployed he used Ambien CR on a nightly basis to fall asleep and drank heavily when on leave.

Since his honorable discharge from the military 3 months ago, he has had trouble falling asleep, and awakens in the middle of night short of breath, sweating, and fearful. He has these fearful awakenings 3–4 times/week. He continues to use Ambien CR every night and drinks 8–10 beers prior to passing out on the couch watching television. He is unemployed and living with his wife and two small children. He denies feeling depressed, but is afraid to go to large shopping malls and carries a loaded Glock 9 mm pistol everywhere he goes. He wife has noticed that he has become withdrawn and anxious since his return and is always "on edge." She stopped sleeping in the same bed with him shortly after he returned from overseas because of his frequent "nightmares."

During the clinical interview he appears as a slender, healthy White male with a body mass index (BMI) of 18 and a neck size of 16 in. His tonsils were 1+/4+ and his Mallampati class was one. The rest of his physical examination (PE) was unremarkable. He denied any depressive symptoms but did admit that "he has been on edge a lot and had a hard time sleeping" since his military discharge. He also reports that he does not like to go to the shopping malls for fear of having "an attack of nerves" that he describes as a sudden feeling of anxiety, sweating, and shortness of breath. These episodes last 5–10 min and are similar to what he experiences after he falls asleep. He denied excessive daytime somnolence but did say that he sometimes dozes off in the afternoon while watching television.

The patient reports that he was diagnosed with PTSD and was prescribed Ambien CR for his "nightmares" by his family doctor. You decide to do an overnight sleep study followed by a Mean Sleep Latency Test (MSLT). The results of his sleep study and MSLT are listed below:

Summary of Polysomnographic Findings The patient took his usual dose of Ambien CR 6.25 mg on the night of the study. Sleep architecture and EEG are summarized in Table 24.2.

There were a total of eight awakenings > 1 min during this study. There were 58 arousals for an arousal index of 8.

Respiratory Analysis Baseline respiratory rate of 20– 22 breaths/min. There are 0 central, 0 obstructive, and 0 mixed apneas recorded. There were 0 hypopneas observed during the course of this study. The apnea/hypopnea index was 0. The REM apnea/hypopnea index is 0. Abnormal thoracic abdominal asynchrony was not noted during the study.

Table 24.2 Case example of sleep architecture and EEG

Lights out	10:19:14 PM	Lights on	06:40:14 AM
Total record time (min)	501	# REM episodes	3
		# of awakenings*	8
TST (min)	463	100 % of TST	
Total stage N1 sleep (min)	18.5	4 % of TST	
Total stage N2 sleep (min)	270	58 % of TST	
Total stage N3 sleep (min)	85	18 % of TST	
Total REM sleep (min)	89.5	19 % of TST	
Total movement time (min)	0		
Total wake time (min)	38		
WASO (min)	34		
Latency to sleep onset (min)	5		
Latency to stage 2 (min)	5		
Latency to REM sleep (min)	173		
Sleep Efficiency	92 %		

REM rapid eye movement, *TST* total sleep time, *WASO* wake-time after sleep onset

Gas Exchange Oxygenation: Highest O_2 saturation was 100 %. Lowest O_2 saturation was 94 %. Mean saturation during NREM was 98 % and during REM sleep was 98 %. 0 % of the entire study time was spent with an oxygen saturation of less than 90 %. Of the total sleep time, 0 min was spent with an oxygen saturation of < 90 %.

Ventilation Range of end tidal CO_2 ($ETCO_2$) was 29–46 Torr, maximum $ETCO_2$ recorded during the course of the study was 46 Torr. About 0 % of the total sleep was associated with an $ETCO_2 > 50$ Torr. Capillary blood gas at the end of the night showed a pH of 7.35, PCO_2 38.0 with simultaneous $ETCO_2$ 36 PO_2 73, and serum bicarbonate 21.1.

Cardiovascular The baseline heart rate was 75 beats/min. The lowest heart rate recorded during sleep was 60 beats/min. The mean heart rate during sleep was 66 beats/min. There were no specific bradycardias or cardiac dysrhythmias noted during the course of this study.

Electroencephalography/Electromyography/Audio/Digital Video No abnormal paroxysmal or spike wave activity was noted in the limited montage utilized during this study. Leg EMG monitoring showed a periodic leg movements (PLM) index of 0 which is normal. Review of the audio/digital video demonstrated the patient spent about 61 % of the night in the supine position. The patient snored about 10 % of the night.

Mean Sleep Latency Study A urine drug screen was obtained the morning after this PSG and had a specific gravity of 1.02. It was negative for amphetamines/methamphetamines/negative for substance abuse.

A four-nap multiple sleep latency test was performed. Sleep was achieved in two of four naps with mean sleep latency of 12 min. He had zero sleep onset REM periods. The only qualification was that a sleep log was not turned in at the time of this study, so sleep deprivation should be ruled out by history (Fig. 24.1).

His PSG was notable for fragmented sleep, increased beta-activity, frequent arousals and decreased percentage of REM sleep—all nonspecific findings. There

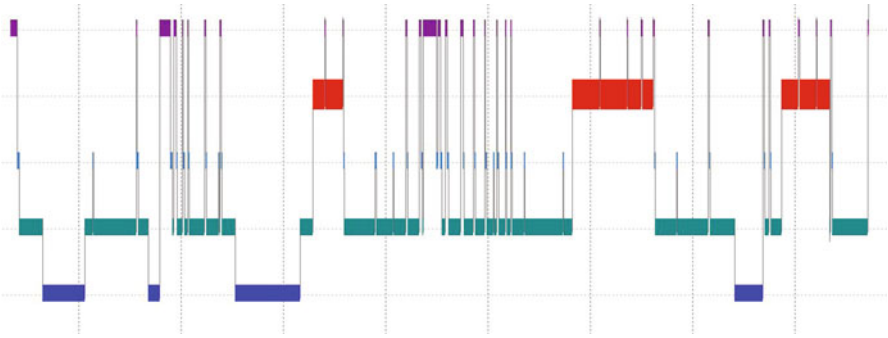


Fig. 24.1 Hypnogram of patient with PTSD

were no PAs during the single night recording, but based upon the patient's history you diagnose nocturnal PAs exacerbated by the patient's PTSD, substance abuse, and possible traumatic brain injury (TBI) based upon his EOD history. You recommend the following: (1) referral to a psychologist for CBT for his PTSD and panic disorder, (2) neuropsychological testing to determine if the patient has TBI from his EOD experiences [30], (3) assessment by a psychiatrist for potential treatment of his panic disorder with an SSRI, and (4) substance abuse counseling at the veterans affairs hospital (VAH).

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders-TR. Washington DC: American Psychiatric Association; 2000.
2. Sarisoy G, Boke O, Arik AC, Sahin AR. Panic disorder with nocturnal panic attacks: symptoms and comorbidities. Eur Psychiatry. 2008;23(3):195–200.
3. Craske MG, Tsao JC. Assessment and treatment of nocturnal panic attacks. Sleep Med Rev. 2005;9(3):173–84.
4. Sheikh JI, Woodward SH, Leskin GA. Sleep in post-traumatic stress disorder and panic: convergence and divergence. Depress Anxiety. 2003;18(4):187–97.
5. Hauri PJ, Friedman M, Ravaris CL. Sleep in patients with spontaneous panic attacks. Sleep. 1989;12(4):323–37.
6. Mellman TA, Uhde TW. Patients with frequent sleep panic: clinical findings and response to medication treatment. J Clin Psychiatry. 1990;51(12):513–6.
7. Andrisano C, Chiesa A, Serretti A. Newer antidepressants and panic disorder: a meta-analysis. Int Clin Psychopharmacol. 2013;28(1):33–45.
8. Association Psychiatric Association. Diagnostic and statistical manual of mental disorders, DSM-IV-TR. 4th ed. Arlington: American Psychiatric Association; 2000.
9. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6):593–602.
10. McLay RN, Klam WP, Volkert SL. Insomnia is the most commonly reported symptom and predicts other symptoms of post-traumatic stress disorder in U.S. service members returning from military deployments. Mil Med. 2010;175(10):759–62.

11. Lamarche LJ, De Koninck J. Sleep disturbance in adults with posttraumatic stress disorder: a review. J Clin Psychiatry. 2007;68(8):1257–70.
12. Ross RJ, Ball WA, Sullivan KA, Caroff SN. Sleep disturbance as the hallmark of posttraumatic stress disorder. Am J Psychiatry. 1989;146(6):697–707.
13. Harvey AG, Bryant RA. The relationship between acute stress disorder and posttraumatic stress disorder: a prospective evaluation of motor vehicle accident survivors. J Consult Clin Psychol. 1998;66(3):507–12.
14. Mellman TA, David D, Kulick-Bell R, Hebding J, Nolan B. Sleep disturbance and its relationship to psychiatric morbidity after Hurricane Andrew. Am J Psychiatry. 1995;152(11):1659–63.
15. Kobayashi I, Boarts JM, Delahanty DL. Polysomnographically measured sleep abnormalities in PTSD: a meta-analytic review. Psychophysiology. 2007;44(4):660–9.
16. Germain A, Richardson R, Moul DE, Mammen O, Haas G, Forman SD, et al. Placebo-controlled comparison of prazosin and cognitive-behavioral treatments for sleep disturbances in US Military veterans. J Psychosom Res. 2012;72(2):89–96.
17. van Liempt S, Vermetten E, Geuze E, Westenberg HG. Pharmacotherapy for disordered sleep in post-traumatic stress disorder: a systematic review. Int Clin Psychopharmacol. 2006;21(4):193–202.
18. Neylan TC, Metzler TJ, Schoenfeld FB, Weiss DS, Lenoci M, Best SR, et al. Fluvoxamine and sleep disturbances in posttraumatic stress disorder. J Trauma Stress. 2001;14(3):461–7.
19. Cates ME, Bishop MH, Davis LL, Lowe JS, Woolley TW. Clonazepam for treatment of sleep disturbances associated with combat-related posttraumatic stress disorder. Ann Pharmacother. 2004;38(9):1395–9.
20. Stein MB, Kline NA, Matloff JL. Adjunctive olanzapine for SSRI-resistant combat-related PTSD: a double-blind, placebo-controlled study. Am J Psychiatry. 2002;159(10):1777–9.
21. Robert S, Hamner MB, Kose S, Ulmer HG, Deitsch SE, Lorberbaum JP. Quetiapine improves sleep disturbances in combat veterans with PTSD: sleep data from a prospective, open-label study. J Clin Psychopharmacol. 2005;25(4):387–8.
22. Raskind MA, Peskind ER, Hoff DJ, Hart KL, Holmes HA, Warren D, et al. A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbance in combat veterans with post-traumatic stress disorder. Biol Psychiatry. 2007;61(8):928–34.
23. Raskind MA, Peskind ER, Kanter ED, Petrie EC, Radant A, Thompson CE, et al. Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: a placebo-controlled study. Am J Psychiatry. 2003;160(2):371–3.
24. Aurora RN, Zak RS, Auerbach SH, Casey KR, Chowdhuri S, Karippot A, et al. Best practice guide for the treatment of nightmare disorder in adults. J Clin Sleep Med. 2010;6(4):389–401.
25. Schenck CH, Arnulf I, Mahowald MW. Sleep and sex: what can go wrong? A review of the literature on sleep related disorders and abnormal sexual behaviors and experiences. Sleep. 2007;30(6):683–702.
26. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW. A polysomnographic and clinical report on sleep-related injury in 100 adult patients. Am J Psychiatry. 1989;146(9):1166–73.
27. Simeon D. Depersonalisation disorder: a contemporary overview. CNS Drugs. 2004;18(6):343–54.
28. Schenck CH, Mahowald MW. Parasomnias. Managing bizarre sleep-related behavior disorders. Postgrad Med. 2000;107(3):145–56.
29. Senthilvel E, Auckley D, Dasarathy J. Evaluation of sleep disorders in the primary care setting: history taking compared to questionnaires. J Clin Sleep Med. 2011;7(1):41–8.
30. Wallace DM, Shafazand S, Ramos AR, Carvalho DZ, Gardener H, Lorenzo D, et al. Insomnia characteristics and clinical correlates in Operation Enduring Freedom/Operation Iraqi Freedom veterans with post-traumatic stress disorder and mild traumatic brain injury: an exploratory study. Sleep Med. 2011;12(9):850–9.

Chapter 25
Medical Disorders Presenting with Parasomnias

Ramadevi Gourineni and Lisa Wolfe

Medical Disorders Presenting With Parasomnias

Medical causes of parasomnia are few and far between, but occasional reports are available in the literature. Mechanism is unclear given the rarity of these events, but a combination of arousal and sleep seems to be a gateway to the generation of parasomnia behavior. The specific pairing of medical conditions and their parasomnia counterparts lends some insight as to the role of sleep as a window to overall health.

This chapter will focus on parasomnias related to medical disorders and associated with drug use. Parasomnias related to neurological disorders will be discussed in a separate chapter.

Gastroesophageal Reflux

Gastroesophageal reflux disease (GERD) has been associated with the development of nocturnal rhythmic masticatory activity [1]. These episodes are similar to other parasomnias, in that they seem to be triggered by arousal due to the presence of acid in the esophagus [2]. In addition, the rhythmicity of the movements is suggestive of a sleep-related rhythmic movement disorder (RMD). There is currently no data supporting the use of antacid therapy to reduce these movements. There is however

R. Gourineni (✉)
710 North Lake Shore Drive suite 525, 60611 Chicago, IL, USA
e-mail: rgourineni@nmff.org

Department of Neurology, Northwestern Feinberg Hospital, Chicago, IL, USA
e-mail: r-gourineni@northwestern.edu

L. Wolfe
Department of Medicine, Northwestern Memorial Hospital, 675 North St. Claire St., Suite 18-250, 60611 Chicago, IL, USA
e-mail: lwolfe@northwestern.edu

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_25, © Springer Science+Business Media New York 2013

data supporting that avoiding the supine posture during sleep may be of benefit in reducing these movements [3].

Obstructive Sleep Apnea

Obstructive Sleep Apnea (OSA) has been associated with RMD, rapid eye movement (REM) behavior disorder (RBD), and sleep-related eating disorder (SRED). The association of OSA with parasomnias is likely bidirectional. At times, the respiratory-effort-related arousal is what triggers the parasomnia. At other times, the patient's difficulty tolerating continuous positive airway pressure (CPAP) during the initiation of therapy is associated with arousals, which then trigger parasomnia episodes. RMD is a primary example of this phenomenon. There are reports that RMD can be caused by CPAP therapy, but it may also be effectively resolved when PAP therapy for the OSA is instituted [4, 5]. SRED also has a unique bidirectionality with OSA. While SRED events can be triggered by respiratory-event-related arousals, there is also data suggesting that SRED-related weight gain may contribute to the development of OSA [6, 7].

As with the examples above, careful attention should be paid to the impact of arousal on the generation of parasomnia, and there is a need to correctly identify the source of the arousal, to fully understand the nature of any parasomnia. In adults, this may require full video polysomnography (PSG). RBD is the classic example of the need for this testing. Many patients have been misdiagnosed with RBD when severe OSA was the true underlying condition. In this setting, the severe OSA is responsible for violent arousals that can be mistaken for RBD events. Full in-lab PSG allows for both the appropriate diagnosis and PAP therapy intervention. Effective PAP therapy should completely resolve these "pseudo-RBD" events [8].

Infection

Although infections are more commonly associated with hypersomnia, parasomnias are also seen, though less commonly. Due to the associated inflammation, prominent sleepiness and consolidated sleep are more likely to be seen with infection. There are however, some notable exceptions, in which arousals during sleep are seen, in turn precipitating parasomnia. There is one report of SRED that occurred in association with herpes zoster infection [9]. The patient had a prominent involvement of the legs and developed both, new onset restless legs syndrome (RLS) and SRED. As the herpetic neuralgia resolved so did the SRED. In this case, it is likely that the neuropathy and nerve involvement rather than the acute infection triggered the arousals and SRED. Lung injury due to infection or acute respiratory distress syndrome (ARDS) is another condition with reports of parasomnia [10]. These patients report significant sleep disruption associated with trauma of their critical illness,

which in turn is associated with night terrors and prominent nightmares with vocalizations and movements. As the sleep quality improved so did the parasomnia. In the pediatric literature, acute Pertussis infection has been reported to be associated with sleepwalking and choking [11]. Initial evaluation for possible seizure as the cause of these events was investigated but the studies were not forthcoming and the symptoms resolved in all the children when the Pertusis infection was resolved.

Antibiotic therapy for infection may also be associated with parasomnias. A 10-year-old girl is reported to have developed acute agitated sleepwalking episodes associated with bizarre behavior and minor injuries, after initiation of ciprofloxacin therapy for recurrent urinary tract infections [12]. These events resolved after the therapy was discontinued.

Autonomic Dysfunction

RBD has been well described to occur in concert with neurodegenerative disorders such as Parkinson's disease, multiple system atrophy, Lewy body dementia, etc. These conditions are also frequently associated with autonomic dysfunction. There is a well-known long delay between development of RBD symptoms and the onset of symptoms of these neurologic disorders. Idiopathic RBD (iRBD), which is not related to the underlying neurodegenerative disorder and therefore, obvious causes of impaired autonomic function have still been noted to have autonomic instability. In one study of iRBD, sympathetic and parasympathetic activity was evaluated by investigating spectral analysis of both electrocardiogram (EKG) and respiratory stability. REM-related cardiac and respiratory responses were absent in this study [13]. This model highlights the unique multisystem mechanism of RBD.

Hormonal Disorders

There are rare reports of hormonal conditions associated with parasomnia. While RBD has a strong proclivity for men, testosterone does not seem to play a role in this phenomenon. When measured directly, men with iRBD have normal serum levels of total testosterone, free testosterone, bioavailable testosterone, luteinizing hormone, follicle stimulating hormone, estradiol-17 beta, sex-hormone binding globulin, prolactin, aspartate aminotransferase, alanine aminotransferase, creatinine, free thyroxine, and thyroid-stimulating hormone [14].

As opposed to RBD, non-rapid eye movement (NREM) parasomnia such as sleepwalking, has been reported to occur in the setting of hormonal imbalance. Hyperthyroidism, specifically thyrotoxicosis due to Graves disease, has been shown to induce NREM parasomnia in adults and therapy for the underlying thyroid abnormality is sufficient to resolve the sleep disorder [15]. The mechanism is poorly

understood, but this may be due to an increase in the amount of slow-wave sleep associated with thyroid hormone levels.

The last model of hormonal influence is pregnancy. The total number of parasomnia events have been shown to fall during pregnancy, and this effect is most prominent in Primiparas as compared to Multiparas, especially in regard to episodes of sleepwalking and talking [16]. In the postpartum period these NREM events increase, and may even increase beyond that noted prior to pregnancy. The authors suspect that stress associated with the care of the new born impairs sleep, and may increase the frequency of parasomnia episodes [17].

Hospitalization

The stress of hospitalization and chronic illness may influence the expression of parasomnia. In one report, a mother of a hospitalized child experienced a violent sleepwalking episode which was apparently triggered by 7 days of significant sleep loss and intense anxiety in regard to her child's medical condition [18]. This adult had experienced sleepwalking in childhood but not as an adult but the recurrence of this parasomnia episode in adulthood appears to be linked to the stress of her child's hospitalization.

In elderly adults with cancer, RBD has been reported to develop during hospitalization and although the mechanisms are unclear, possibilities include medication side effect, sleep deprivation, or even unidentified paraneoplastic factors [19]. In the end, understanding the mechanism of this RBD is likely less important than raising awareness amongst medical staff that RBD can occur in the hospital setting. These patients were evaluated for sun-downing, delirium, and seizure before their RBD was correctly identified and treated.

Lastly, medication effects in hospitalized patients may have an under-recognized role. Notably, reports of an increased risk of "falls" for hospitalized patients given zolpidem as a hypnotic. These reports raise the specter, that medication-related parasomnia may be an underappreciated contributing factor to these hospitalization-related complications [20].

Parasomnias Due to Drug or Substance

There are multiple case reports in the literature of parasomnias, in particular sleepwalking and nocturnal eating occurring in association with medications including antipsychotics, antidepressants, and hypnotic medications. Many of these episodes are reported in individuals with childhood and/or strong family history of parasomnias, but there are also reports of parasomnias in individuals who have no such history. The parasomnias resolved when the potential offending agent was either discontinued or the dosage was reduced, suggesting a definite causal role of these

agents. In addition, most of the agents that increased sleepwalking have a tendency to increase slow-wave sleep.

There is also a lot of literature on pharmacologically induced RBD, but this topic is discussed in other chapters.

Antipsychotic and Antidepressant Medications

The earliest reports of medication induced parasomnias are reports of sleepwalking in patients on therapy with antipsychotic medications. Most of these patients were on combination drug therapy that usually included a sedative/hypnotic medication. Psychotropic medications which have been associated with sleepwalking include thioridazine, lithium, and more recently quetiapine [21–24]. When questionnaire data from 389 patients attending a lithium clinic was studied, 6.9 % of all patients on both lithium monotherapy and combination therapy with other medications reported sleepwalking [23]. Only 11.6 % of these patients reported childhood history of sleepwalking.

Most of these episodes occurred 2–3 h after sleep onset and in cases where electroencephalogram (EEG) was recorded, the spells were seen to arise from slow-wave or stage N2 sleep confirming that these episodes are most likely NREM parasomnias. Also, as mentioned previously the sleepwalking episodes resolved in all these cases when the offending agent was removed or the dose was reduced, again strongly suggesting a causative role.

There is a case report of a 44-year-old woman on therapy with thioridazine for schizophrenia and trichlorethinal for insomnia. One day after consuming double the dose of trichlorethinal, she woke up at 3 AM and stabbed her daughter [21]. She was found to be psychotic the next day. Although this patient had childhood history of sleepwalking and nonviolent sleepwalking episodes while ingesting these medications before and after this spell, it is still not clear if this case of filicide was secondary to sleepwalking or a psychotic episode.

There are also several case reports of sleepwalking associated with paroxetine and bupropion therapy which resolved when the agents were stopped [25–27].

For all of these reasons, it is important for physicians, in particular psychiatrists to educate and monitor their patients on therapy with psychotropic medications for possible sleepwalking, particularly if they are on combination therapy.

Hypnotic Medications

Zolpidem is the hypnotic medication that has most commonly been associated with sleepwalking and other complex behaviors. Zolpidem is an imidazopyridine compound that binds to the benzodiazepine 1 receptor of the GABA (A) complex with high affinity for the alpha 1/alpha 5 subunits. Mendelson reported the first case of

zolpidem-related sleepwalking in a 20-year-old man with remote history of sleepwalking [28]. After ingesting 10 mg of zolpidem an hour before bedtime, he got up and walked on top of the bed after being aroused by an auditory stimulus during slow-wave sleep. Since this report, there have been multiple other reports of sleepwalking with both zolpidem monotherapy and combination therapy with other psychotropic medications [29–32]. These reports also include cases with no previous personal or family history of parasomnias [24].

Morgenthaler reported the first series of five patients with sleep-related eating associated with zolpidem [33]. Although none of these patients had previous history of SRED, all five of them had RLS, three had OSA, two had sleep walking, and one of them had psychophysiologic insomnia. Treatment of the underlying sleep disorder and discontinuation of the zolpidem resulted in resolution of SRED in all of these cases. Therefore, zolpidem, at least in patients with underlying sleep disorders that may result in arousal may cause or augment sleep-related eating behavior.

There are several case reports of sleep-related driving associated with zolpidem ingestion. In these cases, sleep driving is an actual parasomnia, where the patient wakes up in the middle of the night and drives his/her vehicle at a time when driving is not required [34–36]. This needs to be differentiated from drug-impaired driving where the patient is impaired due to the effect of medication. Many times these two conditions may overlap. The sleep driving may be initiated as a parasomnia, but as the parasomnia resolves, the patient is now driving and impaired. This latter state is more of a complex automatic state rather than a parasomnia [36]. In these cases, patients were found to have a high level of zolpidem in their blood or were reported to take other sedative medications or alcohol [35].

Complex behaviors such as confusion, amnesia, poor motor control, hallucinations, and even writing emails have also been reported with zolpidem and zaleplon ingestion [35, 37]. These episodes are seen more common when the hypnotic agent is ingested during the daytime for naps or if the patient tries to stay awake after ingesting the drug [35, 37, 38]. Most of these cases have also been associated with taking a higher than therapeutic dose of zolpidem or combining zolpidem with alcohol or other sedating medications. Several of the cases have involved accidents or injuries such as automobile accidents, falls, and flooding of apartments.

The hypnotic agent sodium oxybate, an agent used for the treatment of cataplexy and excessive daytime sleepiness in patients with narcolepsy, has also been associated with sleepwalking, sleep driving and SRED. Sleepwalking has been reported to occur in 0.4–5.7 % of patients in a dose-dependent manner [39, 40]. There are also case reports of sleep eating and sleep driving with this agent [40, 41]. Complex behaviors resolved in one case when the dose of sodium oxybate was reduced [41].

These reports are important in helping us understand how to educate and alert the prescribing physicians of the potential risk factors for complex nocturnal behaviors. The potential risk factors of zolpidem induced automatisms and parasomnias are listed in Table 25.1.

Although there are definite risk factors for complex nocturnal behaviors associated with zolpidem ingestion, according to the clinical psychopharmacology database, 1 % of normal patients ingesting zolpidem may experience amnesia.

Table 25.1 Potential risk factors for zolpidem-associated automatisms and parasomnias. (Source: reprinted from Poceta [35]. Used with permission of the American Academy of Sleep Medicine, Dariel, IL, 2013)

Concomitant ingestion of alcohol or sedating medications
Concomitant sleep disorder such as OSA or PLMS
A history of parasomnia
Hypnotic sedative ingestion at times other than habitual bedtime
Hypnotic sedative ingestion during agitated state with decreased likelihood of sleep
Hypnotic sedative ingestion when sleep deprived
Poor management of pill bottles
Living alone

OSA obstructive sleep apnea, *PLMS* periodic limb movements of sleep

Although most of the case reports for sleepwalking and complex nocturnal behaviors have been reported with zolpidem, a black box warning has also been added to all of the hypnotic medications, with a warning about sleepwalking, sleep driving, and other complex nocturnal behaviors.

Conclusion

Medical causes of parasomnia are rare, but represent an intersection between the central nervous system and the many other organ systems throughout the body. The generation of parasomnia events is intimately linked to arousal and as such, any medical condition or medication that stimulates awakenings or prevents adequate sleep consolidation can be linked to parasomnia. Although many conditions such as GERD, OSA, and thyroid disease have been linked to parasomnia, clinicians should always remain alert as any change in medication or health status may establish an internal milieu suitable for the generation of parasomnia.

Case Example

A 60-year-old male with no significant past medical history was admitted to the hospital for monitoring after an upper gastrointestinal (GI) bleed. Routine endoscopy was performed at 9:00 AM and a possible mass was noted. While awaiting the pathology results, the patient developed significant anxiety and was unable to sleep. At 11 PM the patient informed his nurse of his condition and as per standing orders and hospital formulary, the patient was given a 5 mg dose of zolpidem. After 25 min he still was not drowsy. He requested and received a second dose. He did not call the nurse again, but at 12:30 AM she was alerted that he was injured and bleeding, sitting on the floor of his room. She found that he was responsive but lethargic and disoriented. He was bleeding from a large laceration to the forehead after hitting the corner bed-side stand. He did not recall how or why the accident occurred. His

laboratory studies we repeated and found to be normal. His mental status was normal by the time a neurology consultant evaluated him at 6 AM, but he still had no recall of the events preceding his fall. Appropriate testing was performed and no abnormalities were noted.

Practical Points

- OSA causes arousals and may trigger true REM or NREM parasomnia events.
- OSA-related arousals may be inappropriately mistaken for RBD (pseudo-RBD).
- Infectious agents are not often associated with parasomnia, but coincident sleep disruption due to pain, cough, or just being hospitalized may trigger parasomnia events.
- Autonomic instability may be a feature of RBD.
- Thyrotoxicosis may trigger parasomnia events.
- Pregnancy may reduce parasomnia events but having a newborn in the house may worsen these episodes.
- Medications that have been associated with the development of parasomnia include: lithium, thioridazine, quetiapine, trichlorethinal, paroxetine, bupropion, zolpidem, and sodium oxybate.

References

1. Miyawaki S, Tanimoto Y, Araki Y, Katayama A, Imai M, Takano-Yamamoto T. Relationships among nocturnal jaw muscle activities, decreased esophageal pH, and sleep positions. Am J Orthod Dentofacial Orthop. 2004 Nov;126(5):615–9.
2. Ohmure H, Oikawa K, Kanematsu K, Saito Y, Yamamoto T, Nagahama H, et al. Influence of experimental esophageal acidification on sleep bruxism: a randomized trial. J Dent Res. 2011 May;90(5):665–71.
3. Miyawaki S, Lavigne GJ, Pierre M, Guitard F, Montplaisir JY, Kato T. Association between sleep bruxism, swallowing-related laryngeal movement, and sleep positions. Sleep. 2003 Jun 15;26(4):461–5.
4. Gharagozlou P, Seyffert M, Santos R, Chokroverty S. Rhythmic movement disorder associated with respiratory arousals and improved by CPAP titration in a patient with restless legs syndrome and sleep apnea. Sleep Med. 2009 Apr;10(4):501–3.
5. Chirakalwasan N, Hassan F, Kaplish N, Fetterolf J, Chervin RD. Near resolution of sleep related rhythmic movement disorder after CPAP for OSA. Sleep Med. 2009 Apr;10(4):497–500.
6. Amchentsev A, Kurugundla N, Lombardo G. Obstructive sleep apnea as a cause of nocturnal eating. Sleep Med. 2010 Feb;11(2):225.
7. Olbrich K, Muhlhans B, Allison KC, Hahn EG, Schahin SP, de Zwaan M. Night eating, binge eating and related features in patients with obstructive sleep apnea syndrome. Eur Eat Disord Rev. 2009 Mar;17(2):120–7.
8. Iranzo A, Santamaria J. Severe obstructive sleep apnea/hypopnea mimicking REM sleep behavior disorder. Sleep. 2005 Feb;28(2):203–6.
9. Mahowald MW, Cramer Bornemann MA, Schenck CH. A case of reversible restless legs syndrome (RLS) and sleep-related eating disorder relapse triggered by acute right leg herpes

zoster infection: literature review of spinal cord and peripheral nervous system contributions to RLS. Sleep Med. 2010 Jun;11(6):583–5.
10. Lee CM, Herridge MS, Gabor JY, Tansey CM, Matte A, Hanly PJ. Chronic sleep disorders in survivors of the acute respiratory distress syndrome. Intensive Care Med. 2009 Feb;35(2):314–20.
11. Eidlitz-Markus T, Zeharia A. Adolescent pertussis-induced partial arousal parasomnia. Pediatr Neurol. 2006 Oct;35(4):264–7.
12. von Vigier RO, Vella S, Bianchetti MG. Agitated sleepwalking with fluoroquinolone therapy. Pediatr Infect Dis J. 1999 May;18(5):484–5.
13. Lanfranchi PA, Fradette L, Gagnon JF, Colombo R, Montplaisir J. Cardiac autonomic regulation during sleep in idiopathic REM sleep behavior disorder. Sleep. 2007 Aug;30(8):1019–25.
14. Iranzo A, Santamaria J, Vilaseca I, de Osaba MJ. Absence of alterations in serum sex hormone levels in idiopathic REM sleep behavior disorder. Sleep. 2007 Jun;30(6):803–6.
15. Ajlouni KM, Ahmad AT, El-Zaheri MM, Ammari FL, Jarrah NS, AbuJbara MA, et al. Sleepwalking associated with hyperthyroidism. Endocr Pract. 2005 Jan-Feb;11(1):5–10.
16. Hedman C, Pohjasvaara T, Tolonen U, Salmivaara A, Myllyla VV. Parasomnias decline during pregnancy. Acta Neurol Scand. 2002 Mar;105(3):209–14.
17. Nielsen T, Paquette T. Dream-associated behaviors affecting pregnant and postpartum women. Sleep. 2007 Sep;30(9):1162–9.
18. Viana Bde M, Bawden FC, Valladares Neto Dde C, Caramelli P. Violent sleepwalking in a general hospital ward: a case report. Rev Bras Psiquiatr. 2009 Sep;31(3):281–2.
19. Shinno H, Kamei M, Maegawa T, Satake A, Inami Y, Horiguchi J, et al. Three patients with cancer who developed rapid-eye-movement sleep behavior disorder. J Pain Symptom Manage. 2010 Sep;40(3):449–52.
20. Kolla BP, Lovely JK, Mansukhani MP, Morgenthaler TI. Zolpidem is independently associated with increased risk of inpatient falls. J Hosp Med. 2013 Jan;8(1):1–6.
21. Luchins DJ, Sherwood AM, Gillin JC, Mendelson WB, Wyatt RJ. Filicide during psychotropic-induced somnambulism: a case report. Am J Psychiatry. 1978 Nov;135(11):1404–5.
22. Glassman JN, Darko D, Gillin JC. Medication-induced somnambulism in a patient with schizoaffective disorder. J Clin Psychiatry. 1986 Oct;47(10):523–4.
23. Landry P, Warnes H, Nielsen T, Montplaisir J. Somnambulistic-like behaviour in patients attending a lithium clinic. Int Clin Psychopharmacol. 1999 May;14(3):173–5.
24. Hafeez ZH, Kalinowski CM. Two cases of somnambulism induced by quetiapine. Prim Care Companion J Clin Psychiatry. 2007;9(4):313.
25. Kawashima T, Yamada S. Paroxetine-induced somnambulism. J Clin Psychiatry. 2003 Apr;64(4):483.
26. Khazaal Y, Krenz S, Zullino DF. Bupropion-induced somnambulism. Addict Biol. 2003 Sep;8(3):359–62.
27. Oulis P, Kokras N, Papadimitriou GN, Masdrakis VG. Bupropion-induced sleepwalking. J Clin Psychopharmacol. 2010 Feb;30(1):83–4.
28. Mendelson WB. Sleepwalking associated with zolpidem. J Clin Psychopharmacol. 1994 Apr;14(2):150.
29. Sattar SP, Ramaswamy S, Bhatia SC, Petty F. Somnambulism due to probable interaction of valproic acid and zolpidem. Ann Pharmacother. 2003 Oct;37(10):1429–33.
30. Lange CL. Medication-associated somnambulism. J Am Acad Child Adolesc Psychiatry. 2005 Mar;44(3):211–2.
31. Sharma A, Dewan VK. A case report of zolpidem-induced somnambulism. Prim Care Companion J Clin Psychiatry. 2005;7(2):74.
32. Yang W, Dollear M, Muthukrishnan SR. One rare side effect of zolpidem-sleepwalking: a case report. Arch Phys Med Rehabil. 2005 Jun;86(6):1265–6.
33. Morgenthaler TI, Silber MH. Amnestic sleep-related eating disorder associated with zolpidem. Sleep Med. 2002 Jul;3(4):323–7.
34. Doane JA, Dalpiaz AS. Zolpidem-induced sleep-driving. Am J Med. 2008 Nov;121(11):e5.
35. Poceta JS. Zolpidem ingestion, automatisms, and sleep driving: a clinical and legal case series. J Clin Sleep Med. 2011 Dec 15;7(6):632–8.

36. Pressman MR. Sleep driving: sleepwalking variant or misuse of z-drugs? Sleep Med Rev. 2011 Oct;15(5):285–92.
37. Siddiqui F, Osuna E, Chokroverty S. Writing emails as part of sleepwalking after increase in Zolpidem. Sleep Med. 2009 Feb;10(2):262–4.
38. Sansone RA, Sansone LA. Zolpidem, somnambulism, and nocturnal eating. Gen Hosp Psychiatry. 2008 Jan-Feb;30(1):90–1.
39. Mamelak M, Black J, Montplaisir J, Ristanovic R. A pilot study on the effects of sodium oxybate on sleep architecture and daytime alertness in narcolepsy. Sleep. 2004 Nov 1;27(7):1327–34.
40. Wang YG, Swick TJ, Carter LP, Thorpy MJ, Benowitz NL. Safety overview of postmarketing and clinical experience of sodium oxybate (Xyrem): abuse, misuse, dependence, and diversion. J Clin Sleep Med. 2009 Aug 15;5(4):365–71.
41. Wallace DM, Maze T, Shafazand S. Sodium oxybate-induced sleep driving and sleep-related eating disorder. J Clin Sleep Med. 2011 Jun 15;7(3):310–1.

Chapter 26
Parasomnias Caused by Other Conditions

Harish Rao and Umakanth Khatwa

Parasomnias, described as disorders of arousal, are more common in children, partly due to immaturity of the nervous system, increased stage N3 sleep, and sleep drive. Parasomnias typically occur during transitions between the three primary states of being awake, rapid eye movement (REM) sleep, and nonrapid eye movement (NREM) sleep. Family studies, twin studies, and human leukocyte antigen (HLA)-typing genetic studies suggest that genetics may play a role in generation of parasomnias [1].

Though considered benign in young children, these events can at times be serious and may also occur in adolescents and adults in whom it may pose a challenge in their evaluation and management. Table 26.1 describes the list of conditions which may precipitate a parasomnia. Table 26.2 lists some salient features of secondary parasomnias in which one should get a detailed clinical history and order additional testing as indicated to diagnose underlying medical/neurological disorders which may be precipitating these parasomnias. Polysomnography is required in only a minority of cases when the clinical evaluation is inconclusive or where the child may have multiple comorbid disorders. Considering the range and diverse manifestations of these events during sleep, it is no surprise that parasomnias are often misinterpreted as a manifestation of other medical, neurological, or psychiatric conditions.

H. Rao (✉)
Sleep Medicine, Boston Children's Hospital,
Harvard Medical School, Boston, USA
e-mail: Harish.rao@childrens.harvard.edu

U. Khatwa
Sleep Laboratory, Division of Respiratory Diseases,
Boston Children's Hospital,
Harvard Medical School, 333 Longwood Ave.,
LO 486, 02115 Boston, MA, USA
e-mail: umakanth.khatwa@childrens.harvard.edu

S.V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_26, © Springer Science+Business Media New York 2013

Table 26.1 Common causes of secondary parasomnia

Sleep fragmentation
SDB
Periodic limb movements of sleep
Sleep deprivation
Delayed sleep phase
Irregular sleep–wake cycle
Narcolepsy
Head trauma
REM sleep disorder
Seizure disorder
Medical conditions
Gastro esophageal reflux disease
Thyrotoxicosis
Urticaria
Psychiatric conditions
Medications
Malingering

REM rapid eye movement, *SDB* sleep disordered breathing

Table 26.2 Clinical indicators of secondary parasomnias

1	Age of onset > 6–7 years
2	Abnormal stereotypical movement
3	Snoring, enlarged tonsils
4	Restless legs symptoms and restless sleeper
5	Abnormal stereotypical movements during sleep
6	Changing and inconsistent history, secondary gain
7	Reflux symptoms, nighttime cough, pain
8	Cataplexy
9	Dream enactment
10	Migraine, headaches, neurological signs and symptoms
11	History of recent head trauma

Parasomnia Precipitated Due to Sleep Fragmentation

Obstructive Sleep Apnea (OSA)

Children with recurrent parasomnias are frequently noted to have sleep-disordered breathing (SDB). As both of these conditions are common in children, it may be challenging at times to differentiate if SDB is causing these parasomnias. Resolution of parasomnias after treatment of SDB lends credence to the hypothesis that parasomnias may be triggered by these conditions. Family members of children with parasomnias have also been noted to have higher incidence of SDB, thus providing additional evidence that sleep disorders that are known to trigger arousals could also precipitate parasomnias in some children [1]. Thus, genetic susceptibility to develop parasomnias, in any child with comorbid conditions which causes sleep fragmentation puts them at higher risk to develop these nocturnal events.

Table 26.3 Typical and atypical parasomnias in children

	Typical parasomnia	Atypical parasomnia
1	Arise out of specific sleep stage	No relation with sleep stage
2	Common in preschool age	More likely in older children
3	Otherwise healthy children	May have underlying medical problem
4	Description of events typical for the parasomnia	Description does not fit common parasomnia
5	Sleep study not essential for diagnosis	Sleep study/video EEG may be needed
6	Likely to outgrow with age	Resolves with treatment of the comorbid condition
7	Benign	Can be serious with deeper implications

EEG Electroencephalography

Parasomnias that occur as a result of SDB are more likely to occur in REM sleep as OSA and mostly tend to occur in REM sleep. As REM sleep is predominant in the later part of the night, parasomnias due to SDB tend to occur in the latter half of sleep. Increased upper airway resistance syndrome (UARS) can also predispose to parasomnias by causing sleep fragmentation. Poor sleep hygiene in the presence of OSA or UARS may increase the predilection for secondary parasomnias.

Typical childhood parasomnias are diagnosed clinically and do not need a polysomnogram. Moreover, an event may not occur during the study and hence may be missed. However children with atypical parasomnias (Table 26.3) may need a polysomnography to rule out other associated conditions like SDB if that is suspected. During the polysomnography, it is important to monitor their breathing with nasal cannula/pressure transducer system and/or esophageal manometry (if available), which are more sensitive than the thermistors in detecting milder obstructive events like respiratory effort related arousal (RERAs) and flow limitations. Treatment of SDB with adenotonsillectomy or positive airway pressure therapy will usually help in resolution of these events.

Before starting medications such as benzodiazepine, an anxiolytic and a myorelaxant to treat parasomnias, it is important to rule out secondary causes such as OSA, as these medications may potentially worsen the underlying OSA. When both OSA and parasomnias are diagnosed in children, it is important that OSA be treated first to see if this helps in resolution of these events.

Periodic Limb Movements of Sleep

Restless leg syndrome (RLS) and its nocturnal phenomenon, periodic limb movement during sleep (PLMS) are well known triggers for parasomnias by causing electrocortical (EEG) arousals particularly from N3 sleep. RLS can be primary or secondary

to pregnancy, renal disease, and iron deficiency. These symptoms may also manifest secondary to an underlying condition such as peripheral neuropathy. Though RLS can present itself at any age, it is relatively not suspected in children, while PLMS is a frequent cause of sleep fragmentation in children. Patients are usually unaware of the movements but may report frequent awakenings. Arousals associated with PLMS are the presumed mechanism for the triggering of parasomnias [2]. Sometimes these symptoms are considered as "growing pain". Patients presenting with PLMS should also be screened for symptoms of RLS.

However, in a recent study Manconi et al. [3] were able to demonstrate that with pharmacological approach it is possible to disconnect arousals from PLMS. This study raises important questions about the relationship between PLMS and arousals.

PLMS secondary to poor iron status is very common in children and responds well to oral iron therapy. Disappearance of parasomnias with treatment of PLMS and RLS with iron may help explain that these conditions may be causing secondary parasomnias. [1]. It is important to note that currently there are no FDA-approved treatments for periodic limb movement disorder (PLMD) in children. However in a recent small, double-blind, placebo-controlled study the benefit of dopaminergic treatment for PLMS in children has been shown. [4, 5].

Family members of children with parasomnias have also been noted to have higher incidence of RLS/PLMS providing additional evidence that sleep disorders that are known to trigger arousals could also precipitate parasomnias in some children [1]. Nocturnal eating disorders have been described elsewhere in this book, and will not be described here. However, it may be noted that recent literature is clearly showing a relationship of nocturnal eating disorders to RLS, especially in teenagers and adults.

Sleep Deprivation

Sleep deprivation increases the likelihood of parasomnias by increasing the sleep drive and N3 sleep as abrupt awakenings from N3 can then trigger parasomnias. Febrile illness and emotional stress, some medications, and alcohol consumption when combined with sleep deprivation increases the likelihood of parasomnias. This is usually seen in younger children and quickly resolves with avoiding sleep deprivation [6].

Following sleep deprivation, increase in delta power is consistently seen during recovery or 'catch up' sleep. Increased N3 sleep seen during recovery from sleep deprivation predisposes to parasomnias. Improving sleep hygiene and sleep duration is critical in management to prevent recurrence of parasomnias [7]. Parasomnias in narcolepsy and REM behavioral disorders are discussed elsewhere and will not be covered here.

Nocturnal Seizure Disorder

Nocturnal events such as parasomnias may be difficult to distinguish from seizures as both occur during sleep and a good description of the event may not be available. Parasomnias that are most likely to be confused with seizures are night terrors,

confusional arousals, sleepwalking, and REM behavior disorder (RBD). Often at times, parasomnias coexist with epilepsy, further complicating evaluation of nocturnal events. This has been described elsewhere in this book in Chap. 17. While epilepsy occurring at night can potentially disrupt sleep, sleep deprivation can also promote seizure activity in conditions such as juvenile mycoclonic epilepsy. Seizures occurring during sleep are most likely to happen during sleep–wake transitions. In general, seizure frequency is less in REM compared to NREM sleep; this relation is particularly stronger with focal seizures.

Head Trauma

There is a high prevalence of sleep disorders after traumatic brain injury (TBI) and these include OSA, excessive daytime sleepiness and increased total sleep time, insomnia, narcolepsy, and PLMS. Sleep deprivation and fragmentation or the TBI itself may predispose patients with TBI to develop parasomnias. Li et al. have reported that parasomnias were significantly greater in school-age children who had suffered head trauma than a comparison group [8]. But the literature is sparse regarding sleep disorders following head trauma. Though there are several case reports of narcolepsy following head trauma in adults, this association has not been robustly described in children. Night terrors can also be precipitated by TBI and at times difficult to treat. Treatment of associated sleep disorder is important and attention towards good sleep hygiene and treatment of anxiety is important. In some cases, a short course of benzodiazepine may be helpful [9].

Parasomnias Secondary to Medical Conditions

Parasomnias often emerge as a manifestation of an underlying neurological or medical condition. RBD is the parasomnia most frequently associated with an underlying neurological condition such as Parkinson's disease but can also occur with Lewy body dementia, Alzheimer's disease and progressive supranuclear palsy. RBD has been reported to occur after stroke in the tegmentum of the pons.

There have been case reports of sleepwalking and sleep-terrors occurring in pregnancy and postpartum women, possibly secondary to the influential role of hormones and sleep deprivation in inducing parasomnias [10–12]. Increased incidence of sleepwalking has been described with migraine and thyrotoxicosis [13, 14]. As mentioned previously, parasomnias tend to occur more frequently during febrile illnesses, especially in children. Several medical comorbid conditions that may cause insomnia or sleep disruption in children and adolescents such as obesity and metabolic syndrome, growth hormone deficiency, allergic conditions, various disorders accompanied by chronic pain, neoplasms and blood malignancies, and genetic and congenital disorders can potentially cause parasomnias [15].

While 'primary parasomnias' could be described as disorders of sleep-state per se, there are several organ-specific conditions which can precipitate parasomnias; these have been labeled as 'secondary parasomnias'. These could be from central nervous system (tinnitus, seizures), cardiopulmonary (arrhythmias, nocturnal asthma), gastrointestinal reflux disease (GERD), and others such as nocturnal cramps. Sandifer syndrome involves spasmodic torsional dystonia with arching of the back and rigid opisthotonic posturing, mainly involving the neck, back, and upper extremities, associated with symptomatic gastroesophageal reflux, esophagitis, or the presence of hiatal hernia. Such events occurring during sleep may be mistaken for seizures or parasomnias.

Another uncommon phenomenon which occurs at night is 'sleep-related laryngospasm'. This term refers to episodic, abrupt interruption of sleep accompanied by feelings of acute suffocation followed by stridor. Patients describe choking at the level of larynx. The attack resolves in few minutes with intense perspiration, breathing returning to normal, and the patient can go back to sleep. The attacks are very dramatic and are described by patients or relatives as traumatic and intense experiences. Patients live with the fear of recurrence which leads to severe anxiety, affecting quality of life of family members as well. The condition may be related to GERD. Treating underlying causes such as GERD may help resolve the condition but no specific therapy has been described. Though literature is sparse, this condition is included in the diagnostic and coding manual of the American Academy of Sleep Medicine [16].

Exploding Head Syndrome (EHS)

This is a rare condition characterized by a painless loud noise at the onset of sleep. The phenomenon was reported initially in 1920 by Armstrong-Jones when he referred to it as "snapping of the brain." The term *exploding head syndrome* was coined by Pearce in 1989 in a paper in which he described 40 patients with EHS. This syndrome is characterized by abrupt arousal, usually occurring in the transition from wake to sleep, with the sensation of a loud sound like an explosion or a sensation of bursting of the head. Most reported cases occur in the twilight state of sleep onset, but polysomnographic recording has documented their occurrence during both wakefulness and REM sleep. There is a single case report of exploding head syndrome followed by sleep paralysis as a migraine aura. As the condition is rare, no treatment studies are available. There is a case report of use of topiramate successfully reducing the intensity of events in a 39-year-old female with EHS [17].

Parasomnias Secondary to Psychiatric Conditions

Nightmares can occur following traumatic experiences. PTSD is the best described psychiatric condition associated with nightmares following the initial traumatic stressor. The highest risk for PTSD occurs following sexual assault and military combat.

Apart from nightmares, awakening in the fear of dream recall, vivid dreams, disrupted REM sleep, excessive motor activity, and dream enactment commonly occurs in PTSD [18].

The other condition where parasomnias are known to occur such as 'sleep panic arousals' is a panic disorder. Panic disorder is an anxiety disorder with recurrent spontaneous episodes of intense anxiety with a persistent worry about future panic attacks. Sleep panic attacks occur in 30–50 % of patients with panic disorder and can precede the appearance of diurnal panic episodes. It occurs in the initial part of sleep as abrupt and sudden arousals lasting few minutes. The arousal may be associated with sweating, tachycardia, shortness of breath, and other manifestations of sympathetic nervous system activation. Individuals suffering from sleep panic arousals can fully recall events and often have insomnia following the arousal.

Panic disorder can begin in childhood and adolescence and can masquerade as a wide variety of neurologic syndromes or parasomnias. Sleep complaints such as insomnia, or fear of going to bed, or falling asleep are common in patients with panic disorder. Sleep studies in these patients have not shown any abnormalities of sleep macrostructure or excessive arousability, but suggest that nocturnal panic is a NREM phenomenon. Nocturnal panic and other sleep disorders characterized by precipitous arousals (particularly sleep apnea or gastroesophageal reflux) may be easily confused. Similar presentations like dream anxiety attacks, sleep terrors, nocturnal seizures, sleep apnea, and nighttime panic attacks have the potential for misdiagnosis.

Malingering

Malingering and Munchausen syndrome by proxy, while they are not actually parasomnias, may masquerade as parasomnias. Careful clinical history and examination and sleep laboratory evaluation can usually provide an accurate diagnosis with effective therapeutic implications. Due to the potential forensic and medico-legal implications, sleep medicine specialists should be aware of these conditions as they may be asked to participate in legal proceedings resulting from sleep-related violence [19].

There have been many instances where crime has been committed but defendants have claimed immunity as the alleged crime has been purported to occur in relation to these events. Several parasomnias have the potential to result in violent or injurious behaviors arising from the sleep period. These parasomnias include the following: (1) disorders of arousal (DOA), (2) RBD, (3) nocturnal seizures, (4) psychogenic dissociative disorders, (5) malingering, and (6) Munchausen syndrome by proxy.

Medication Effect

A number of medications are known to trigger parasomnias. The difficulty lies in proving conclusively that the offending medication is responsible for these parasomnias, as many of these patients have underlying neurological or psychiatric conditions

Table 26.4 Medications predisposing to development of parasomnias

Sleepwalking	Thioridazine, chloral hydrate, lithium carbonate, perphenazine, desipramine, SSRIs, caffeine, and alcohol withdrawal
SRED	Triazolam, zolpidem
Sexsomnia	Zolpidem
RBD	Anti-depressants, MAOI, anxiolytics, beta-blockers, mirtazapine, flouxetine
Nightmares	Erythromycin, flouxetine, triazolam, verapamil, donepezil

MAOI monoamine oxidase inhibitors, *RBD* rapid eye movement behavior disorder, *SRED* sleep related eating disorder, *SSRIs* selective serotonin reuptake inhibitor

which could also cause parasomnias. Further, such patients are also on multiple medications which make it difficult to identify the responsible medication.

Much of early data about medications and parasomnias came from single case reports or case series, which led to more precise studies.

International classification of sleep disorders-revised (ICSD-R) and ICSD-2 has defined diagnostic criteria of parasomnias due to a drug or substance usage. They agree on three principles.

1. There must be a close relationship between exposure to a drug, medication or biological substance, and the onset of parasomnias signs and symptoms.
2. The emergent parasomnias must be a de novo parasomnias, the aggravation of a chronic intermittent parasomnias, or the reactivation of a previous parasomnia.
3. The parasomnias most predictably associated with medications or biological substances are the DOA, sleep-related eating disorder (SRED), and RBD.

NREM parasomnias such as sleepwalking has been associated with initiation or escalation of some medications used for treating psychiatric conditions such as bipolar disorder, schizoaffective patients, and patients with anxiety and insomnia. ICSD2 states that under predisposing conditions, drugs such as thioridazine, chloral hydrate, lithium carbonate, prolixin, perphenazine, and desipramine can exacerbate or induce sleepwalking. Selective serotonin reuptake inhibitor (SSRIs) generally decrease and tricyclics increase slow-wave sleep (SWS); therefore the latter may be expected to increase the frequency of sleepwalking (Table 26.4).

Triazolam, which is a benzodiazepine, was one of the first medications to be associated with sleep related eating disorder (SRED), followed by many reports linking zolpidem with SRED. Both are also described in association with several other NREM parasomnias. Zolpidem has been linked with initiation of SW, SRED, and sexsomnia.

Chronic alcohol and caffeine use reduce SWS and increase arousals from this sleep stage, thus predisposing individuals for parasomnias. Sleepwalking is the most common parasomnia linked with caffeine and alcohol.

Both acute and chronic RBD has been associated with use of many medications such as antidepressants, monoamine oxidase inhibitors (MAOI), antianxiety, and beta-blockers; though less likely to occur in the absence of significant neuropathology. RBD has also been described following abrupt withdrawal of imipramine, alcohol, and amphetamine abuse. ICSD-2 manual also implicates caffeine and chocolate abuse in causing or unmasking RBD. Prominent among other drugs implicated with RBD are use of Mirtazapine in Parkinsonism and Fluoxetine in depression and obsessive–compulsive disorder.

There has been an increase in the number of reports of these undesirable and even dangerous sleep-related events in the past years, particularly in the context of new medications being introduced every year. There is a need to study long-term effects of these medications as well as effects of their withdrawal and interaction with other medications [20].

Summary

The vast majority of parasomnias are due to either DOA or REM sleep behavioral disorder. Disruption or deprivation of sleep is a common underlying factor in induction of parasomnias, with SDB and PLMD being common causes. History should include information about sleep–wake schedules, ideally with sleep logs. Typical parasomnias occur in children of preschool age. Parasomnias occurring outside of this age-range should raise suspicion of atypical or secondary parasomnias. Treating the cause along with establishment of sleep hygiene is critical in management of the parasomnias.

Key Points

- Typical parasomnias occur in children of preschool age who outgrow the condition with establishment of sleep hygiene and changing sleep schedules.
- Though considered benign in children, these events can be serious with medicolegal implications in older adolescents and adults.
- Sleep study is not essential for diagnosis of typical parasomnias, but is usually requested to help differentiate an atypical parasomnia.
- Careful history with description of events and home video recording of events is extremely useful for diagnosis of the condition.
- Medication history with particular attention to temporal association is important in patients with psychiatric disorders.
- Recording sleep schedule with sleep logs and correcting sleep hygiene is important to prevent recurrence of parasomnias.

Case Example

An 11-year-old obese boy with a history of seasonal allergies presented with history of snoring, early morning headaches, recent onset nightmares and daytime sleepiness. His sleep schedules and duration were reasonably normal. His mother told that he has anxiety disorder and is unable to focus in his school. His nightmares started this spring when his allergies worsened and he had at least 4–5 episodes per week. On examination: body mass index (BMI) was 35, mild turbinate hypertrophy, no tonsillar hypertrophy, mild adenoids with crowded airways. A sleep study was ordered which revealed sleep fragmentation (EEG arousal index 18/h), severe OSA (apnea-hypopnea index (AHI 15/h)) and increased periodic limb movements of sleep (PLMS index 15/h). There was one instance of confusional arousal noted during sleep study. He was recommended continuous positive airway pressure(CPAP) titration and fitted with nasal mask and CPAP of 8 cw which helped resolve all the obstructive events. On follow-up, all his symptoms had resolved including nightmares and he felt much better.

References

1. Guilleminault C, et al. Sleepwalking and sleep terrors in prepubertal children: what triggers them? Pediatrics. 2003;111(1):e17–25.
2. Gingras JL, Gaultney JF, Picchietti DL. Pediatric periodic limb movement disorder: sleep symptom and polysomnographic correlates compared to obstructive sleep apnea. J Clin Sleep Med. 2011;7(6):A603–9.
3. Manconi M, et al. Dissociation of periodic leg movements from arousals in restless legs syndrome. Ann Neurol. 2012;71(6):834–44.
4. England SJ, et al. L-Dopa improves restless legs syndrome and periodic limb movements in sleep but not attention-deficit-hyperactivity disorder in a double-blind trial in children. Sleep Med. 2011;12(5):471–7.
5. Gozal D, Kheirandish-Gozal L. Iron deficiency and periodic leg movement disorder of sleep. Sleep Med. 2009;10(2):265–7.
6. Wills L, Garcia J. Parasomnias: epidemiology and management. CNS Drugs. 2002;16(12): 803–10.
7. Zadra A, Pilon M. NREM parasomnias. Handb Clin Neurol. 2011;99:851–68.
8. Li Y, et al. The association between sleep and injury among school-aged children in rural China: a case-control study. Sleep Med. 2008;9(2):142–8.
9. Kothare SV, Kotagal S. Sleep in childhood neurological disorders. New York: Demos Medical; 2011. xv, p.439.
10. Berlin RM. Sleepwalking disorder during pregnancy: a case report. Sleep. 1988;11(3):298–300.
11. Snyder S. Unusual case of sleep terror in a pregnant patient. Am J Psychiatry. 1986;143(3):391.
12. Nielsen T, Paquette T. Dream-associated behaviors affecting pregnant and postpartum women. Sleep. 2007;30(9):1162–9.
13. Casez O, Dananchet Y, Besson G. Migraine and somnambulism. Neurology. 2005;65(8): 1334–5.
14. Ajlouni KM, et al. Sleepwalking associated with hyperthyroidism. Endocr Pract. 2005;11(1): 5–10.
15. Lazaratou H, Soldatou A, Dikeos D. Medical comorbidity of sleep disorders in children and adolescents. Curr Opin Psychiatry. 2012;25(5):391–7.

16. Thurnheer R, Henz S, Knoblauch A. Sleep-related laryngospasm. Eur Respir J. 1997;10(9):2084–6.
17. Palikh GM, Vaughn BV. Topiramate responsive exploding head syndrome. J Clin Sleep Med. 2010;6(4):382–3.
18. Ohayon MM, Shapiro CM. Sleep disturbances and psychiatric disorders associated with posttraumatic stress disorder in the general population. Compr Psychiatry. 2000;41(6):469–78.
19. Bornemann MA, Mahowald MW, Schenck CH. Parasomnias: clinical features and forensic implications. Chest. 2006;130(2):605–10.
20. Thorpy MJ, Plazzi G. The parasomnias and other sleep-related movement disorders. Cambridge Medicine. Cambridge: Cambridge University Press; 2010. xiii, p. 341.

Part VII
Interventions for Parasomnias

Chapter 27
Cognitive and Behavioral Interventions for Parasomnias

Cynthia D. Nichols and Connie M. Bongiorno

The ultimate goal of cognitive and behavioral therapy is to improve mental and physical health by correcting maladaptive patterns of thought and behavior. This chapter describes cognitive and behavioral interventions for parasomnias, along with the evidence for the effectiveness of these therapies. Cognitive and behavioral interventions for parasomnias may be condition-specific, such as use of the urine alarm for sleep enuresis or imagery rehearsal training (IRT) for nightmares. Other interventions are more general, such as providing education about principles of good sleep-hygiene or use of cognitive reframing for sleep disruption associated with anxiety and depressive disorders.

Cognitive and behavioral interventions for parasomnias frequently occur in the context of treatment for psychiatric disorders such as depression, anxiety, and posttraumatic stress disorder (PTSD). The majority of cognitive and behavioral therapeutic techniques actively engage the patient in homework assignments and self-administered protocols. These interventions have the potential to improve a patient's sense of self-efficacy and may generalize to other aspects of mental health and behavior.

The evidence-based literature on cognitive and behavioral treatments included in this chapter is summarized for sleep enuresis, sleepwalking, sleep terrors, nightmares, nocturnal panic, rhythmic movement disorder, isolated sleep paralysis, exploding head syndrome, catathrenia, sleep-related eating disorder (SRED), and rapid eye movement (REM) sleep behavior disorder. Several case examples and a summary of practical points are also provided to demonstrate how the evidence is applied in clinical practice.

C. D. Nichols (✉)
Sleep Disorders Center, Munson Medical Center, 1105 Sixth Street,
Traverse City, MI 49684, USA
e-mail: cnichols@mhc.net

C. M. Bongiorno
Department of Library Services, Munson Medical Center, 1105 Sixth Street,
Traverse City, MI 49684, USA
e-mail: cbongiorno@mhc.net

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_27,

A literature search was conducted by a professional research librarian (CB) utilizing a search algorithm which encompassed medical subject headings defined by the National Library of Medicine, keyword and keyword placement, and related terms. Medline searches were performed using both the OVID and PubMed interfaces. Results were limited to human, English, therapy-based treatment, and the years 1990–2012. In addition, a universal search was obtained in ProQuest of over 140 databases, including PsychLit and PsychAbstracts, for added results. Selected citations were based on studies that were evidence-based and peer-reviewed when possible.

Adherence is crucial to the effectiveness of any therapy. While a comprehensive discussion of strategies to enhance adherence is beyond the scope of this chapter, the development of mutually agreed-upon goals and active problem-solving is critical to the success of all cognitive and behavioral interventions. The focus on overcoming obstacles to adherence is also an important part of most cognitive and behavioral treatment sessions. When discussion of goals and adherence is overlooked, the result is frequently an incorrect conclusion (by the patient, clinician, or both) that the therapy has not been effective. Achieving changes in maladaptive patterns of thinking and behavior is not always easy. A patient who has not followed through with "homework" may downplay the lack of adherence, hoping for something easier. A collaborative approach with the patient (and often the family as well) in overcoming obstacles to adherence clearly communicates the message that the recommended treatment is worth the effort.

Sleep Enuresis

Behavioral treatments for sleep enuresis utilize both operant and classical conditioning principles. These treatments include use of the urine alarm, exercises to improve pelvic floor muscle tone, relaxation techniques to achieve complete voiding of the bladder, planned sleep interruptions, reward systems, and biofeedback. Cognitive interventions including education, psychotherapy, and hypnosis are often combined with behavioral treatments but rarely used in isolation. Hypnosis and alternative treatments such as diet changes and acupuncture are covered chapter 29 by Robert DuMont in this book. Enuresis in children below the age of 5 years is considered normal, and therefore children under the age of 5 years are typically not included in studies of treatment effectiveness.

Urine Alarm Therapy

The urine alarm awakens a child with an audible alarm as soon as the sensor detects the first drops of urine. The sensor is connected to the child's pajamas or underwear, or to a bed-pad that is also used to keep the bed dry. The alarm disrupts the child's

sleep so that the child can go to the bathroom. The goal of the urine alarm is to teach the child to wake up as soon as the bladder is full, or to sleep through the night without urinating. Some alarms have wireless remote speakers that can be placed in a caregiver's room so that the caregiver can assist in getting the child up to the bathroom to finish urinating. The urine alarm was invented in 1938 by Orval and Molly Mowrer, two psychologists who developed the device when they were house parents in a residential cottage for children in New Haven, Connecticut [1]. A systematic review of the literature that compared psychological, pharmaceutical, and multicomponent interventions for primary nocturnal enuresis concluded that the urine alarm was the most effective long-term treatment [2].

The urine alarm is effective for children of age 5 years and older. A study evaluating the relationship between age of the child and effectiveness of alarm therapy demonstrated no differences in treatment response between younger (age 6–10 years) vs. older (age 11–17 years) children [3]. Children who have enuresis episodes earlier in the night and children who are unable to awaken in response to the alarm, however, are less likely to respond to use of the urine alarm [4].

Following an initial positive response to treatment, relapse is not uncommon when the alarm is withdrawn [5]. Even in children who relapse, however, the majority of children will respond to reinitiation of the alarm therapy [6]. Use of the enuresis alarm is associated with significantly less relapse than desmopressin (12 vs. 50 %) when treatment is stopped after 12 weeks [7].

Urine Alarm in Combination with Medication

Children who have either partial response, nonresponse, or relapse in response to desmopressin or combined desmopressin plus oxybutynin also demonstrate improvement with use of the enuresis alarm [8]. Adding desmopressin to alarm treatment did not improve either the functional bladder capacity or cure rate of children with monosymptomatic sleep enuresis [9].

Exercises to Increase Bladder Capacity

The most common exercise recommended for treatment of enuresis is to ask the patient to start and stop the flow of urine several times during each daytime voiding. Our literature review did not reveal any studies that evaluated this method of treatment in isolation. Holding exercises to increase functional bladder capacity have also been studied but did not demonstrate any incremental decrease in the frequency of enuresis episodes beyond treatment with an enuresis alarm alone [10]. The addition of diaphragmatic breathing exercises and pelvic floor retraining to desmopression and/or education about the importance of regular voiding, hydration, and appropriate posture during voiding, may result in decreased frequency of nocturnal enuresis [11].

Biofeedback

Biofeedback utilizes electronic instrumentation to display information about bodily function such as muscle activity. Biofeedback with either acoustic or visual signals has been demonstrated to train children to relax and void their bladder. This treatment has been utilized with mixed results primarily in children with discoordinated or incomplete voiding that is complicating the management of nocturnal enuresis [12].

Planned Sleep Interruption

A planned awakening to take the child to the bathroom is frequently used as a simple, practical parental intervention to decrease the frequency of enuresis episodes. A randomized control trial comparing several behavioral interventions with a control group demonstrated that waking and carrying the child to the toilet for an opportunity to urinate was more effective than use of a reward system (star chart for dry nights). This treatment resulted in 37 % dry nights as compared to 21 % in the control group and 32 % in the reward system group. Verifying the child was awake with use of a "password" did not increase dry nights [13].

Psychotherapy

Psychodynamic theory suggested that enuresis was the result of unconscious conflict, however, there is no evidence that psychodynamic therapy is effective for children with enuresis [14]. Cognitive therapy, in which the focus is on identifying and reframing dysfunctional thoughts regarding enuresis, is equally ineffective [15].

Combined Treatments

Dry bed training (DBT) is the most well-known form of combination treatment. DBT combines use of the urine alarm, night waking schedule, positive reinforcement for urinating in the toilet, cleanliness training, token reinforcement for dry nights, role playing, and imagery. Although one study suggested that DBT may be slightly more effective than use of the alarm system alone [16], a later study demonstrated that modified DBT without the urine alarm is no more effective when compared to the urine alarm alone [17]. A randomized study comparing desmopressin with another complex behavioral treatment that did not include the urine alarm demonstrated equal effectiveness of desmopressin and the cognitive-behavioral treatment [18].

Treatment Adherence

One study specifically addressed adherence to treatment for enuresis. Predictors of adherence included a positive perception of one's physical appearance and low levels of stress [19]. Adherence to treatment has been found to be higher for desmopressin vs. the alarm (95–98 % vs. 50–78 %) [20].

Case Example 1

A 13-year-old male with a longstanding history of enuresis during sleep experienced increased frequency in episodes over a 6-month period. Previously, he had a trial of desmopressin that was of minimal benefit. He discontinued the medication, stating that he does not like to take pills. He does not snore or have other symptoms of sleep-disordered breathing. His sleep schedule varies by 2 h on weekends as compared to school days, and he has some morning sleepiness particularly on Mondays. He mentioned that he fell asleep recently on the bus ride to school and awakened after a few minutes, immediately concerned that he might have enuresis when riding on the bus. He consumes an occasional caffeinated energy drink on the weekend. He tried to eliminate fluids in the evening, but this did not result in any decrease in his enuresis and he felt uncomfortably thirsty. He talks in his sleep several times per week. He had a recent episode of sleepwalking in which he went into his sister's room, opened her closet door, and urinated. He has also urinated in the laundry basket in the bathroom rather than in the toilet. In the past, he echoed his parents' opinion that his enuresis was "no big deal", but now he avoids camp and other "sleep-over" activities because of his enuresis.

The patient's parents purchased a urine alarm for him. He thought it was interesting that there were so many types to choose from, and this reassured him that there are many people who have the same problem. He selected a wireless device that also has a speaker in his parents' room so that his father would also awaken to steer him to the toilet in the bathroom. He liked the idea of the custom "ring tone" and had his father record the message "Dude, wake up! Go pee in the toilet". He was unwilling to improve his sleep-hygiene by getting up earlier on weekends but he began taking a 2-h nap on Sunday afternoons to "rest up" for school. He had four episodes during the first week of alarm use, in which the alarm awakened him and he was able to finish urinating in the toilet. He had one similar episode during the second week of treatment, and only very mild episodes during the next several weeks. He always awakened within a few seconds of hearing the alarm. After 3 months of using the alarm, he decided to stop using it "to find out what would happen" for 1 month prior to an overnight camping trip with the family of one of his friends. He had one episode during the second week without the alarm, but did not resume using it. He went on the camping trip as planned and did not have any enuresis, but he did bring his sleeping bag in a plastic bag "just in case", so that he could put the sleeping bag in the plastic bag in the morning if necessary. He went on several additional overnight trips during

the summer following treatment, and had no additional episodes of enuresis. He passed the alarm system down to his younger brother, who also has enuresis.

Sleepwalking and Sleep Terrors

Treatment for sleepwalking and sleep terrors often begins with the evaluation and treatment of comorbid sleep disorders, particularly inadequate sleep-hygiene, sleep-disordered breathing, and periodic limb movement disorder. Regardless of the underlying cause of the sleepwalking and/or sleep terrors, safety precautions to protect the patient from injury are very important. Although child gates may be helpful for preventing injury in some children, others may be seriously injured by falling or climbing over a gate during a sleepwalking episode. Use of door alarms should be considered to alert other members of the household to a sleepwalker's attempt to leave the safe environment.

Treatment of Comorbid Sleep Disorder

Treatment of sleep-disordered breathing and/or periodic limb movement disorder has been reported to resolve sleepwalking and sleep terrors in children [21] and adults [22].

Improvements in Sleep-Hygiene

Clinical observations of parents and health care professionals have described an association between insufficient and/or irregular sleep and sleepwalking in children, with decreases in sleepwalking episodes occurring after the sleep schedule has regularized [23].

Scheduled Awakenings

A scheduled awakening approximately 15–30 min prior to the usual time of a sleepwalking episode has been effective in decreasing or eliminating sleepwalking in children [24, 25]. In this intervention, parents are instructed to wake their child by shaking them lightly and asking them to wake up. When the child responds by opening the eyes or mumbling to parents, they are allowed to fall back to sleep. This routine is followed for approximately 1 month. The effects of this intervention may persist for 6 months or longer after the parent discontinues the awakenings.

Education and Reassurance

Sleep terrors in a child frequently disrupt the entire household. Providing education and reassurance to caregivers as well as siblings of the child with sleep terrors may prevent excessive focus on the symptom [26]. Patients and their families find it helpful when they are reassured that sleep terrors in children are unlikely to be of any psychological significance [27].

Case Example 2

A 3 ½-year-old female abruptly began having episodes of sleep terror almost every night, sometimes twice per night, after she began attending a daycare program 3 days per week. Her bedtime and rise time are regular. She does not resist bedtime, has a regular and positive evening routine, and does not cosleep or share her room with a sibling. She tends to be the first person in the household who is out of bed in the morning, and while she is awake and alert, she likes to have a slow start to her day. Her sleep environment is quiet, with a fan in the summer and a humidifier in the winter that improves the comfort of her room and adequately masks small sounds in the environment. She has a light on in the hallway outside of her room. She takes a 45–60 min nap daily (10:30 a.m. when she is at home, and 12:30 p.m. when she is in daycare).

Approximately 1 h after sleep onset, sometimes again 1–2 h later, her parents are awakened by her loud screaming. She typically says "mommy, daddy!" or "no, stop" repeatedly. She pushes her parents away when they attempt to soothe her. Her mother commented that she looks "possessed", with a strange stare that her parents perceive as "looking right through" them. Her mother also mentioned that she is afraid that the sleep terrors indicate that "something terrible" has happened to her daughter at daycare.

The patient's mother said that she "snores like a man" (particularly when her head is bent at an angle), breathes through her mouth at night, and has adenotonsillar hypertrophy but does not have recurrent episodes of otitis media, pharyngitis, tonsillitis, or observed apnea. A polysomnogram demonstrated mild to moderate obstructive sleep apnea (OSA) with an apnea–hypopnea index of 6 (21 during REM sleep) and oxygen desaturations to as low as 84 % during REM sleep. She had moderate to loud snoring and mild hypoventilation particularly during non-REM sleep with end-tidal CO_2 sustained into the low 50s for up to 20 min several times during the recording. She underwent an uncomplicated adenotonsillectomy. A postoperative polysomnogram demonstrated that her snoring resolved, her sleep-related respiratory disturbance index was < 1 during both REM and non-REM sleep, and she did not have any elevations in end-tidal CO_2 above 50 mmHg.

The patient had several episodes of confusional arousal during both polysomnograms and a brief sleep terror during her postoperative polysomnogram. There was no abnormal EEG activity other than some possibly hypersynchronous slow waves immediately preceding the sleep terror. During the sleep terror, she abruptly stood up

in bed and looked like she was going to run. The technologist and the patient's parent intervened immediately. Each stood on the opposite side of the bed to prevent the child from jumping or falling off the bed. The technologist held the wires loosely and prepared to disconnect the cable. The episode lasted approximately 110 s, followed by a big yawn and settling back into the bed.

The patient's parents reported that there was a reduction in frequency of the patient's sleep terrors following her adenotonsillectomy. They were reassured that sleep terrors frequently resolve spontaneously, and sleep-hygiene was again reviewed. The patient's mother said that the patient loves going to daycare, and the patient is cheerful and outgoing. The patient's mother attended the daycare program with the patient on several occasions and felt reassured that no one was mistreating her daughter.

The patient's mother was also encouraged to consider changing her nap time to coincide with the nap time in daycare. Within 2 weeks of changing the nap time, the patient's sleep terrors decreased to less than one per month. The duration and severity of the sleep terrors were also decreased.

Nightmares

The Standards of Practice Committee of the American Academy of Sleep Medicine (AASM) commissioned a task force in 2007 to perform a systematic review of the literature on treatment for nightmares in adults. The task force reviewed the literature through March 2009 and issued a best practice guideline in 2010 [28]. Treatments for nightmares in isolation and in the context of PTSD were evaluated. Cognitive and behavioral interventions for nightmares reviewed for the AASM guideline included exposure, relaxation, rescripting therapy (ERRT), hypnosis, sleep dynamic therapy, eye movement desensitization and reprocessing (EMDR) and the testimony method for PTSD-associated nightmares. For nightmares not associated specifically with PTSD, lucid dreaming and self-exposure therapy were also discussed.

Although there are both creative and theory-based interventions for nightmares that have face validity, the level of evidence for cognitive and behavioral interventions is low due to the small numbers of subjects, lack of control groups or other clinically appropriate comparison groups, varying operational definitions, and selection bias. It is also unclear as to whether different approaches are effective for PTSD-related nightmares vs. idiopathic nightmares. Selection of the intervention for nightmares still appears to be based primarily on the clinician's preference in the context of the patient's presenting symptoms.

Comparisons of Cognitive and Behavioral Treatments for Nightmares

A systematic review of cognitive-behavioral treatment for nightmares discussed nightmare recording, relaxation training, exposure and desensitization therapy,

imagery rehearsal therapy, and cognitive restructuring [29]. Exposure therapy had better treatment outcomes than relaxation training in the only study to compare two specific cognitive-behavioral interventions [30]. IRT has been studied more than other therapies but has not been compared to medication, placebo, or other cognitive-behavioral treatment. Both IRT and exposure therapy are adaptable to an internet-delivered self-help intervention in a stepped-care model [31].

Nightmares in the Context of Posttraumatic Stress Disorder (PTSD)

Treatment studies of nightmares and sleep in PTSD are potentially limited by selection bias, as patients who agree to participate in these studies may have symptoms that are less severe than those who do not agree to participate [32]. Improvement in either physiological sleep or in self-reported sleep quality does not always correlate with decreases in sleep nightmare frequency or severity. When sleep quality improves after treatment for nightmares, it may lag behind improvement in nightmare symptoms [33]. History of nightmares and other sleep disruption prior to a trauma is inconsistent in predicting PTSD-associated nightmares and other symptoms [34, 35]. Improvement in nightmares associated with PTSD may not result in improvement in overall PTSD symptoms [36].

Exposure Treatment

Exposure treatments for nightmares are based upon the technique of systematic desensitization via reciprocal inhibition, originated by Joseph Wolpe [37]. In this technique, patients are instructed in a relaxation procedure and visualization of neutral images. A fear hierarchy is then developed, followed by pairing the relaxation procedure with each step on the hierarchy until the fear response is no longer present. This technique has also been used in children. A case report applying Wolpe's approach to bedtime fears and recurrent nightmares described effective treatment for both symptoms [38]. Another application of this approach progresses through each scene in the dream using systematic desensitization and relaxation [39]. Exposure treatment may be less effective in individuals with personality disorders, who may have unfavorable outcomes including worsening of symptoms [40].

Patients utilizing exposure treatment are instructed to write down their nightmares in detail immediately upon awakening, using the present tense and first person, then read these descriptions either aloud or silently. In some exposure treatments, the patient is advised to read the description repeatedly during the day until their anxiety decreases. Exposure treatment has also shown to potentially decrease the frequency and severity of nightmares even without face-to-face contact with a therapist, when the patient follows a specific exposure protocol [30]. Another study with only one

face-to-face instruction session, demonstrated that use of self-administered exposure therapy reduced the frequency of nightmares [41]. Treatment also resulted in reduced symptoms of depression, anxiety, and somatic symptoms when compared to a waiting list control group, and patients remained improved at a 4-year follow-up.

Imagery Rehearsal Therapy (IRT)

IRT treatment assists the patient in learning to deliberately rewrite nightmares by mentally rehearsing images from the new scenario during wakefulness. IRT has been demonstrated to be effective in reducing the frequency and severity of nightmares in patients with PTSD [42], and has been adapted successfully for treatment of nightmares in sexual assault victims with PTSD [43, 44].

Evidence of effectiveness of IRT monotherapy (i.e., IRT without other interventions for daytime symptoms) in individuals with PTSD is controversial, possibly due to differences in the severity of PTSD symptoms between studies, and use in varied patient populations (combat veterans, adolescents, sexual assault victims). Combat veterans with severe symptoms may not have any improvement in nightmare symptoms with IRT monotherapy [45]. A three-session treatment of IRT monotherapy in adolescents demonstrated significant reduction in nightmares and other PTSD symptoms when compared to a wait-list control, with improvements that were sustained without further intervention or contact for at least 3 months [46]. Another study, however, suggested that IRT monotherapy was less effective than IRT as an adjunctive treatment in the context of a more comprehensive treatment program for veterans with PTSD [47]. In combat veterans with nightmares, IRT was demonstrated to be more effective when administered individually as compared to a group format [48].

IRT has been demonstrated to be an effective treatment for nightmares in children [49, 50] and adolescents [46]. Group instruction in IRT is also possible. In a single session group instruction comparing IRT with simply recording the nightmare, both treatment groups demonstrated a reduction in nightmares, but the IRT group also demonstrated improvement in anxiety, depression, somatization, hostility, and overall distress [51]. These improvements persisted 30 months after treatment [52].

Exposure, Relaxation, and Rescripting Therapy (ERRT)

ERRT combines psychoeducation, progressive muscle relaxation, and exposure (including writing out the nightmare, reading it aloud, and identifying common themes), then rescripting the nightmare (rewriting it and reading it aloud) [53, 54]. This treatment has been demonstrated to have some effectiveness in decreasing nightmares related to multiple types of trauma and to decrease PTSD symptoms other than nightmares even when these symptoms are not specifically targeted, possibly by reducing physiological reactivity to fear [55]. A study that compared the effectiveness of ERRT

with IRT for treatment of nightmares in individuals without severe PTSD symptoms demonstrated no difference in effectiveness between these treatments [56].

ERRT and IRT protocols both utilize education, maintenance of a nightmare diary, writing down the nightmares, progressive muscle relaxation, and exercising with nightmare imagery. The primary difference between these techniques is that IRT specifically instructs the patient to create and practice a new ending to the nightmare [31].

Eye Movement Desensitization Reprocessing (EMDR)

EMDR combines both cognitive techniques and a specific eye movement procedure. The eye movement procedure involves an eight-phase technique using bilateral eye movements, tones, and taps to identify and process disturbed memories, current triggers for anxiety and/or flashbacks, and focus on positive experiences. The goal is to increase insight and adaptive behaviors [57]. EMDR also utilizes numerous cognitive techniques in addition to the eye movement training. The added benefit of the eye movement training vs. the other treatment components is difficult to evaluate because EMDR has not been compared with other cognitive techniques for treatment of nightmares. The cognitive techniques applied in EMDR therapy include self-soothing strategies, deep breathing, encouraging a positive outlook by focusing on the patient's strengths rather than their perceived weaknesses, and reframing by discussing how the patient effectively handled stressful situations in the past [58].

Lucid Dreaming

Lucid dreaming as a treatment for nightmares involves instructing the patient to alter the nightmare storyline by becoming aware that one is actually dreaming. It also incorporates elements of exposure treatment. Lucid dreaming induction techniques for use in nightmare disorder include reflection during the day ("Am I dreaming or not?"), dream cueing (using an aspect of one's physical appearance such as a wrist watch, to focus on one's current experience), mnemonic induction (practice in visualization of lucid dreaming, e.g., "Next time I'm dreaming I want to remember that I am dreaming"), hypnagogic dream counting to force consciousness during the wake–sleep transition, and cued awakenings with a tape recorder [59]. In one pilot study of lucid dreaming for treatment of nightmares, the frequency of nightmares decreased even when patients were not able to achieve lucidity during dreaming [60]. Lucid dreaming may result in increased sleep fragmentation by encouraging and reinforcing hyperarousal, but individuals who benefit from the technique may feel that the sleep disruption is offset by the improvement in their symptoms.

Combined Treatments

Unique combinations of treatment strategies have been reported to be useful for patients with refractory nightmare symptoms [61], crime victims with nightmares, insomnia, PTSD, anxiety, and depression [62], and combat veterans with PTSD [63]. Use of exposure with or without imagining a different outcome for the dream has been effective in managing nightmares in patients with a combination of symptoms including phobias, anxiety, depression, and obsessive–compulsive disorder [64]. IRT may also provide additional benefit when nightmares persist after comprehensive inpatient treatment for PTSD [65]. Scheduled awakenings to practice IRT may be helpful in refractory nightmares associated with PTSD [66].

Cognitive-behavioral treatments for nightmares typically include the use of homework practice between sessions. This active engagement by the patient in treatment may reduce the patient's maladaptive beliefs about competence or helplessness, and is potentially an underlying mechanism of treatment effectiveness [67].

Case Example 3

A police officer disabled due to PTSD experienced recurrent nightmares and daytime flashbacks and vivid nightmares about accidents in which she was the first responder. The flashback episodes were often triggered when she heard a siren or smelled something burning. She is treated for OSA syndrome with an oral mandibular advancement appliance, but she does not always use the appliance. She frequently naps in the evening while watching television, then awakens (often after a disturbing dream). It was not unusual for her to consume caffeinated coffee as late as 2 a.m. while working at the computer, specifically to avoid returning to sleep. She is taking a selective serotonin re-uptake inhibitor (SSRI) antidepressant daily, and a short-acting benzodiazepine needed for flashbacks. She had previous insight-oriented psychotherapy for her PTSD that she felt was somewhat helpful.

The patient subsequently participated in four sessions of cognitive-behavioral therapy specifically focused on use of a systematic desensitization protocol, using a hierarchy that was developed from some of the accidents she investigated. She also used a "fast-forward" imagery technique to get through the flashback episodes more quickly. She began listening to music in her bedroom both during the day and at her preferred bedtime of 11 p.m., and felt that this was relaxing and distracted her from anticipatory anxiety about the possibility of a nightmare. She decreased her caffeine consumption to one mug of coffee in the morning at 8 a.m. and one with lunch.

Although the daytime flashback episodes were significantly improved and she no longer felt the need to take benzodiazepine medication during the day, the patient continued to have recurrent nightmares. She took her benzodiazepine medication about twice per week during the night, following an awakening with a nightmare and panic. She agreed to keep a log of her nightmares and their frequency, and wrote out in detail her memory of the two accidents that tended to recur most often

both as a dream and as a flashback. She added a comforting commentary at the end of each incident. For both incidents, she acknowledged that she did everything that she could for the accident victims and stayed with them so that they were not alone. When she awakened from a nightmare, she utilized the relaxation techniques and the comforting statement. She had significant decrease in both the frequency of her recurrent nightmares, and the distress associated with them, after utilizing this technique for 2 months. She also noticed that she was less likely to have a nightmare when she was more consistent in use of her oral appliance, and this served as a motivation to use it more consistently.

Nocturnal Panic

Although nocturnal panic is not a specific parasomnia in the current diagnostic nosology, nocturnal panic is frequently encountered clinically and managed effectively with cognitive and behavioral interventions. The majority of patients who suffer from panic attacks during wakefulness also experience nocturnal panic attacks. Treatment targets both the waking and nocturnal symptoms.

Cognitive and behavioral interventions for nocturnal panic include education, instruction in use of relaxation techniques to avoid hyperventilation, cognitive restructuring to change misappraisals of body sensations, and naturalistic exposure. Exposure therapy may include drinking coffee or exercising to increase heart rate, inducing and then managing the feared sensations in a more controlled environment. Cognitive-behavioral therapy for nocturnal panic has demonstrated to maintain effectiveness for at least 9 months after treatment [68].

Rhythmic Movement Disorder

Rhythmic movement disorder is distinguished from severe self-abusive daytime rhythmic movement in that it occurs only during the transition to sleep or during sleep. Our literature review revealed several case reports and case series of behavioral treatment for sleep-related rhythmic movement disorder.

Use of a metronome set to match the frequency of headbanging was one of the earliest reported treatments for both daytime rhythmic movement and sleep-related rhythmic movement disorder and may stop the activity by providing a salient distraction [69, 70].

Use of an aversive stimulus (a 100 W light that turned on automatically at the start of the movement and was on for 5 s, off for 15 s, and repeated if the movement persisted or recurred) was also effective in one case following 16 consecutive nights of treatment [71]. Another mildly aversive stimulus requiring the child to get out of bed and walk briskly up and down a hall several times as soon as the headbanging started was also effective in one case [72].

Changing the sleep environment (a mattress on the floor) was effective in two cases [73]. **Mild sleep restriction** (1–2 h less than habitual sleep time for 2 weeks) was effective treatment for rhythmic movement disorder in a case series of six children [74].

Treatment of OSA syndrome and restless legs syndrome (RLS) was associated with improvement of rhythmic movement disorder in one case [75]. Another patient who had previously been presumed to have RLS due to frequent rolling limb movements at night (and had failed to respond to a dopamine agonist) had near resolution of the rhythmic movements when diagnosed and treated with continuous positive airway pressure therapy (CPAP) for severe OSA syndrome [76].

Overcorrection methods have been described in several case reports. Overcorrection involves use of a behavior that is incompatible with the rocking movements. In one case, the rocking behavior resolved with a simple technique in which the patient was verbally informed of the rocking, then assisted to the prone or supine position and directed to lie still for 15 s. The verbal cue, followed by turning prone and holding was repeated 15 times for each episode of rocking [77]. Another overcorrection/negative practice technique used an alarm triggered by the rhythmic movement, which awakened a parent to implement the procedure. The child was instructed to get into her headbanging position, then say "Stop" out loud, lie back down on her back, and pull up her covers. This sequence was repeated 10 times following each headbanging episode, and was followed by a reward contingent on absence of headbanging for an increasing number of consecutive nights [78].

Case Example 4

A 9-year-old male developed a large callous on his forehead from his persistent body rocking. He demonstrated the movement, getting on his knees and rocking his body forward on the mattress. He has done this every night since he was about 2 years old. His mother believes that she may have caused this problem because she often rocked him to sleep as an infant. His movements were so vigorous that the bed hits the wall and disturbs the sleep of a sibling in an adjacent room. The patient described the rocking as completely under his control and grinned (with a slightly embarrassed look) as he stated that he likes to do it. If he awakened during the night, he rocked for 15–20 min.

A reward was promised to the patient that if he was able to learn to fall asleep without rocking (he was permitted to listen to the radio instead) for seven consecutive nights, his parents would purchase him a new game system. He was able to achieve this goal after 1 month. After he received his game system, he had a brief recurrence of rocking but when he was informed that he would have to give up his game for the day following a night with rocking, there was no further recurrence. He described no difference in his sleep-onset latency, with vs. without rocking.

Isolated Sleep Paralysis

Our literature search revealed only two articles that provided a recommended treatment for isolated sleep paralysis. A large survey of Japanese adolescents demonstrated a significant association between nightmares and sleep paralysis. This study also found that a regular sleep schedule was associated with a decrease in the frequency of isolated sleep paralysis [79]. The suspected cause of sleep paralysis is intrusion of REM sleep phenomena into wakefulness, and in some cases this may be related to instability of REM sleep patterns caused by irregular sleep schedules. Educating the patient about this relationship may be helpful in decreasing the anxiety associated with sleep paralysis [80].

Exploding Head Syndrome (EHS)

The diagnosis of EHS should be differentiated from other conditions with overlapping symptoms, with the primary differentiating factor in EHS being the absence of pain. Reassurance that this syndrome is benign is the most frequently cited behavioral intervention [81, 82]. A case series of 50 people with EHS also described the benign nature of this condition and recommended neither extensive investigation nor treatment [83]. Diseases and conditions with symptoms that overlap EHS include headache, aura with or without headache [84], primary thunderclap headache [85], and neoplasm [86]. A case series of nine patients with EHS reported no indication of an epileptic etiology to the condition [82]. There is a case report of EHS in a patient with OSA syndrome in which the EHS resolved after the OSA was effectively treated with an oral appliance [87].

Catathrenia (Sleep Groaning)

Similar to exploding head syndrome, catathrenia is usually considered to be a benign condition. Our literature search did not reveal any description of specific cognitive or behavioral interventions for catathrenia. Catathrenia has been described as a possible side effect of sodium oxybate [88]. It may also be misperceived as seizure [89]. Several reports describe catathrenia comorbid with OSA syndrome that resolved with CPAP therapy [90–92].

Other Parasomnias

Sleep Related Eating Disorder (SRED) our literature search did not reveal any references describing specific cognitive or behavioral treatments for SRED. Clinical observation has suggested, however, that consuming a light snack prior to bedtime and reducing easy accessibility to foods may decrease the frequency of SRED episodes.

REM sleep behavior disorder is typically managed with medication; however, safety measures are important not just for the patient but also for the bed partner. Bed partners (including pets) should sleep in a different area until the patient's symptoms are well-controlled [93].

Summary

In summary, there are both general and condition-specific cognitive-behavioral interventions for parasomnias (see Practical Points). Parasomnias may also occur in the context of other sleep disorders. Similar to current trends in the management of insomnia, a treatment approach that views parasomnias as comorbid with other physical conditions in the context of a patient's lifestyle is most likely to result in effective treatment.

Practical Points

- The urine alarm has more long-term effectiveness than desmopressin in the management of sleep enuresis.
- Scheduled awakenings may be helpful in treatment of sleep enuresis, nightmares, and sleepwalking.
- Treatment of sleep-disordered breathing and other comorbid sleep disorders may result in improvement or resolution of some parasomnias, including sleep enuresis, sleepwalking, rhythmic movement disorder, catathrenia, and exploding head syndrome.
- A sleep environment with safeguards to protect the patient (and others) from injury is particularly important for individuals who have episodes of sleepwalking and REM sleep behavior disorder.
- Regularization of the sleep schedule is helpful in management of sleepwalking and isolated sleep paralysis.
- Patients with rhythmic movement disorder may be effectively treated with mild sleep restriction, or with a combination of behavioral techniques that disrupt the rhythmic movement and reward the absence of movement.
- There are several specific techniques that have potential benefit in the treatment of nightmares, including IRT, ERRT, EMDR and the testimony method for PTSD-associated nightmares. For nightmares not associated specifically with PTSD, lucid dreaming and self-exposure therapy may also be effective.

References

1. Doroshow D. An alarming solution: bedwetting, medicine, and behavioral conditioning in mid-twentieth-century America. Isis. 2010;101:312–37.
2. Brown M, Pope A, Brown E. Treatment of primary nocturnal enuresis in children: a review. Child Care Health Dev. 2010;37(2):153–60.

3. Pereira R, Silvares E, Braga P. Behavioral alarm treatment for nocturnal enuresis. Int Braz J Urol. 2010;36(3):332–8.
4. Butler R, Gasson S. Enuresis alarm treatment. Scand J Urol Nephrol. 2005;39:349–57.
5. Ozgur B, Ozgur S, Dogan V, et al. The efficacy of an enuresis alarm in monosymptomatic nocturnal enuresis. Singapore Med J. 2009;50(9):879–80.
6. Gim C, Lillystone D, Caldwell P. Efficacy of the bell and pad alarm therapy for nocturnal enuresis. J Paediatr Child Health. 2009;45:405–8.
7. Kwak K, Lee Y, Park K, et al. Efficacy of desmopressin and enuresis alarm as first and second line treatment for primary monosymptomatic nocturnal enuresis: prospective randomized crossover study. J Urol. 2010;184:2521–6.
8. Kwak K, Park K, Baek M. The efficacy of enuresis alarm treatment in pharmacotherapy-resistant nocturnal enuresis. Urology. 2011;77:200–4.
9. Yucel S, Kol A, Guntekin E, et al. Anticholinergics do not improve cure rate of alarm treatment of monosymptomatic nocturnal enuresis. Urology. 2011;77:721–5.
10. Van Hoeck K, Bael A, Lax H, et al. Improving the cure rate of alarm treatment for monosymptomatic nocturnal enuresis by increasing bladder capacity—a randomized controlled trial in children. J Urol. 2008;179:1122–7.
11. Vesna Z, Milica L, Stankovic I, et al. The evaluation of combined standard urotherapy, abdominal and pelvic floor retraining in children with dysfunctional voiding. J Pediatr Urol. 2011;7:336–41.
12. Drzewiecki B, Kelly P, Marinaccio B, et al. Biofeedback training for lower urinary tract symptoms: factors affecting efficacy. J Urol. 2009;182:2050–5.
13. Van Dommelen P, Kamphuis M, van Leerdam F, et al. Nocturnal enuresis in young children: a randomized controlled trial. J Pediatr. 2009;154:662–6.
14. Friman P. Evidence-based therapies for enuresis and encopresis. In: Steele R, Elkin T, Roberts M, Eds. The handbook of evidence-based therapies for children and adolescents: bridging science and practice. New York: Springer; 2008.
15. Brown RA, Antonuccio D, DuPaul G, et al. Childhood mental health disorders: evidence base and contextual factors for psychosocial, psychopharmacological, and combined interventions. Washington DC: American Psychological Association; 2008.
16. Nawaz S, Griffiths P, Tappin D. Parent-administered modified dry-bed training for childhood nocturnal enuresis: evidence for superiority over urine alarm conditioning when delivery factors are controlled. Behav Intervent. 2002;17:247–60.
17. Glazener C, Evans J, Peto R. Complex behavioral and educational interventions for nocturnal enuresis in children. Cochrane Database Syst Rev. 2009;1:1–99.
18. Fera P, Lelis M, Glashan R, et al. Desmopressin versus behavioral modifications as initial treatment of primary nocturnal enuresis. Urol Nurs. 2011;31(5):286–9.
19. Baeyens D, Lierman A, Roeyers H, et al. Adherence in children with nocturnal enuresis. J Pediatr Urol. 2009;5:205–109.
20. Evans J, Malmsten B, Maddocks A, et al. Randomized comparison of long-term desmopressin and alarm treatment for bedwetting. J Pediatr Urol. 2011;7:21–9.
21. Guilleminault C, Palombini L, Pelayo R, et al. Sleepwalking and sleep terrors in prepubertal children: what triggers them? Pediatrics. 2003;111(1):e17–25.
22. Guilleminault C, Kirisoglu C, Bao G, et al. Adult chronic sleepwalking and its treatment based on polysomnography. Brain. 2005;128:1062–69.
23. Masand P, Popli A, Weilburg J. Sleepwalking. Am Family Physician. 1995;51(3):649–53.
24. Tobin J. Treatment of somnambulism with anticipatory awakening. Pediatrics. 1993;122:426–7.
25. Frank N, Spirito AN, Stark L, et al. The use of scheduled awakenings to eliminate childhood sleepwalking. J Pediatric Psychol. 1997;22:345–53.
26. Gates D, Morwessel N. Night terrors: strategies for family coping. J Pediatr Nurs. 1989;4(1):48–53.
27. Mahowald M, Schenck C. NREM sleep parasomnias. Neurol Clin. 1996;14(4):675–96.

28. Aurora R, Zak R, Auerbach S, et al. Best practice guide for the treatment of nightmare disorder in adults. J Clin Sleep Med. 2010;6(4):389–401.
29. Lancee J, Spoormaker V, Krakow B, van den Bout J. A systematic review of cognitive-behavioral treatment for nightmares: toward a well-established treatment. J Clin Sleep Med. 2008;4(5):475–80.
30. Burgess M, Gill M, Marks I. Postal self exposure treatment of recurrent nightmares: a randomized controlled trial. Br J Psychiatry. 1998;172:257–62.
31. Lancee J, Spoormaker V, van den Bout J. Long-term effectiveness of cognitive-behavioural self-help intervention for nightmares. J Sleep Res. 2011;20:454–9.
32. Woodward S, Stegman W, Pavao J, et al. Self-selection bias in sleep and psychophysiological studies of posttraumatic stress disorder. J Trauma Stress. 2007;20(4):619–23.
33. Germain A, Nielsen T. Impact of imagery rehearsal treatment on distressing dreams, psychological distress, and sleep parameters in nightmare patients. Behavior Sleep Med. 2003;1(3):140–54.
34. Davis J, Pruiksma K, Rhudy J, et al. A comparison of lifelong and posttrauma nightmares in a civilian trauma sample: nightmare characteristics, psychopathology, and treatment outcome. Dreaming. 2011;21(1):70–80.
35. Mellman T, David D, Kulick-Bell R, et al. Sleep disturbance and its relationship to psychiatric morbidity after Hurricane Andrew. Am J Psychiatr. 1995;152:1659–63.
36. Krakow B, Hollifield M, Johnston L, et al. Imagery rehearsal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder: a randomized controlled trial. J Am Med Assoc. 2001;286(5):537–45.
37. Wolpe J. Psychotherapy by reciprocal inhibition. California: Stanford University Press; 1958.
38. Palace E, Johnson C. Treatment of recurrent nightmares by the dream reorganization approach. J Behav Ther Exp Psychiat. 1989;20(3):219–26.
39. Geer J, Silverman I. Treatment of a recurrent nightmare by behavior-modification procedures: a case study. J Abnor Psychol. 1967;72:188–90.
40. Miller W, DiPilato M. Treatment of nightmares via relaxation and desensitization: a controlled evaluation. J Consult Clin Psychol. 1983;51(6):870–7.
41. Grandi S, Fabbri S, Panattoni N, et al. Self-exposure treatment of recurrent nightmares: waiting-list-controlled trial and 4-year follow-up. Psychother Psychosom. 2006;75:384–8.
42. Berlin K, Means M, Edinger J. Nightmare reduction in a Vietnam veteran using imagery rehearsal therapy. J Clin Sleep Med. 2010;6(5):487–8.
43. Krakow B, Hollifield M, Schrader R, et al. A controlled study of imagery rehearsal for chronic nightmares in sexual assault survivors with PTSD: a preliminary report. J Trauma Stress. 2000;13(4):589–609.
44. Germain A, Krakow B, Faucher B, et al. Increased mastery elements associated with imagery rehearsal treatment for nightmares in sexual assault survivors with PTSD. Dreaming. 2004;14:195–206.
45. Cook J, Harb G, Gehrman P, et al. Imagery rehearsal for posttraumatic nightmares: a randomized controlled trial. J Trauma Stress. 2010;23(5):553–63.
46. Krakow B, Sandoval D, Schrader R, et al. Treatment of chronic nightmares in adjudicated adolescent girls in a residential facility. J Adol Health. 2001;29(2):94–100.
47. Lu M, Wagner A, Van Male L, et al. Imagery rehearsal therapy for posttraumatic nightmares in U.S. veterans. J Trauma Stress. 2009;22:236–9.
48. Nappi C, Drummond S, Thorp S, et al. Effectiveness of imagery rehearsal therapy for the treatment of combat-related nightmares in veterans. Behav Ther. 2010;41:237–44.
49. St-Onge M, Mercier P, De Koninck J. Imagery rehearsal therapy for frequent nightmares in children. Behav Sleep Med. 2009;7:81–98.
50. Simard V, Nielsen T. Adaptation of imagery rehearsal therapy for nightmares in children: a brief report. Psychother Theor Res Prac Train. 2009;46(4):492–7.
51. Niedhardt E, Krakow B, Kellner R, et al. The beneficial effects of one treatment session and recording of nightmares on chronic nightmare sufferers. Sleep. 1992;15(5):470–3.

52. Krakow B, Kellner R, Niedhardt J, et al. Imagery rehearsal treatment of chronic nightmares: with a thirty month follow-up. J Behav Ther Exp Psychiatr. 1993;24(4):325–30.
53. Davis J, Wright D. Exposure, relaxation, and rescripting treatment for trauma-related nightmares. J Trauma Dissoc. 2006;7(1):5–18.
54. Davis J, Wright D. Randomized clinical trial for treatment of chronic nightmares in trauma-exposed adults. J Trauma Stress. 2007;20(3):123–33.
55. Rhudy J, Davis J, Williams A, et al. Cognitive-behavioral treatment for chronic nightmares in trauma-exposed persons: assessing physiological reactions to nightmare-related fear. J Clin Psychol. 2010;66(4):365–82.
56. Lancee J, Spoormaker V, van den Bout J. Cognitive-behavioral self-help treatment for nightmares: a randomized controlled trial. Psychother Psychosom. 2010;79:371–7.
57. Silver S, Brooks A, Obenchain J. Treatment of Vietnam War veterans with PTSD: a comparision of eye movement desensitization and reprocessing, biofeedback, and relaxation training. J Trauma Stress. 1995;8:337–42.
58. Shapiro F. Eye movement desensitization: a new treatment for post-traumatic stress disorder. J Behav Ther Exp Psy. 1989;20:211–7.
59. Abramovitch H. The nightmare of returning home: a case of acute onset nightmare disorder treated by lucid dreaming. Isr J Psychiatry Relat Sci. 1995;32(2):140–5.
60. Spoormaker V, van den Bout J. Lucid dreaming treatment for nightmares: a pilot study. Psychother Psychosom. 2006;75:389–94.
61. Tanner B. Multimodal behavioral treatment of nonrepetitive, treatment-resistant nightmares: a case report. Percept Motor Skill. 2004;99:1139–46.
62. Krakow B, Johnston M, Melendrez E, et al. An open-label trial of evidence-based cognitive behavior therapy for nightmares and insomnia in crime victims with PTSD. Am J Psychiat. 2001;158:2043–47.
63. Ulmer C, Edinger J, Calhoun P. A multi-component cognitive-behavioral intervention for sleep disturbance in veterans with PTSD: a pilot study. J Clin Sleep Med. 2011;7(1):57–68.
64. Bishay N. Therapeutic manipulation of nightmares and the management of neuroses. Brit J Psychiat. 1985;147:67–70.
65. Forbes D, Phelps A, McHugh A, et al. Imagery rehearsal in the treatment of posttraumatic nightmares in Australian veterans with chronic combat-related PTSD: 12-month follow-up data. J Trauma Stress. 2003;15(5):509–13.
66. Gehrman P, Harb G. Treatment of nightmares in the context of posttraumatic stress disorder. J Clin Psychol. 2010;66(11):1185–94.
67. Long M, Davis J, Springer J, et al. The role of cognitions in imagery rescripting for posttraumatic nightmares. J Clin Psychol. 2011;67(10):1008–16.
68. Craske M, Tsao J. Assessment and treatment of nocturnal panic attacks. Sleep Med Rev. 2005;9(3):173–84.
69. Lourie R. The role of rhythmic patterns in childhood. Am J Psychiat. 1949;103:653–60.
70. Evans J. Rocking at night. J Child Psychol Psychiat. 1961;2:71–85.
71. Martin R, Conway J. Aversive stimulation to eliminate infant nocturnal rocking. J Behav Ther Exp Psychiatr. 1976;7:200–1.
72. Golding K. Nocturnal headbanging as a settling habit: the behavioural treatment of a 4-year-old boy. Clin Child Psychol Psychiat. 1998;3:25–30.
73. Bramble D. Two cases of severe head-banging parasomnias in preipubertal males resulting from otitis media in toddlerhood. Child Care Health Dev. 1995;21(4):247–53.
74. Etzoni T, Katz N, Hering E, et al. Controlled sleep restriction for rhythmic movement disorder. J Pediatr. 2005;147:393–5.
75. Gharagozlou P, Seyffert M, Santos R, et al. Rhythmic movement disorder associated with respiratory arousals and improved with CPAP titration in a patient with restless legs syndrome and sleep apnea. Sleep Med. 2009;10:501–3.
76. Chirakalwasan N, Hassan F, Kaplish N, et al. Near resolution of sleep related rhythmic movement disorder after CPAP for OSA. Sleep Med. 2009;10:497–500.

77. Linscheid T, Copeland A, Jacobstein D, et al. Overcorrection treatment for night-time self-injurious behavior in two normal children. J Paediat Psychol. 1981;6(1):29–35.
78. Strauss C, Rubinoff A, Atkeson B. Elimination of nocturnal headbanging in a normal seven-year-old girl using overcorrection plus rewards. J Behav Ther Exp Psychiatr. 1983;14:269–73.
79. Munezawa T, Kaneita Y, Osaki Y, et al. Nightmare and sleep paralysis among Japanese adolescents: a nationwide representative survey. Sleep Med. 2011;12:56–64.
80. Uhde T, Cortese B, Vedeniapin A. Anxiety and sleep problems: emerging concepts and theoretical treatment implications. Current Psychiatr Report. 2009;11:269–76.
81. Green M. The exploding head syndrome. Curr Pain Headache Rep. 2001;5(3):279–80.
82. Sachs C, Svanborg E. The exploding head syndrome: polysomnographic recordings and therapeutic suggestions. Sleep. 1991;14(3):263–6.
83. Pearce J. Clinical features of the exploding head syndrome. J Neurol Neurosurg Psychiatr. 1989;52(7):907–10.
84. Evans R. Exploding head syndrome followed by sleep paralysis: a rare migraine aural. Headache. 2006;46(4):682–3.
85. Casucci G, d'Onofrio F, Torelli P. Rare primary headaches: clinical insights. Neurol Sci. 2004;25(suppl 3):S77–83.
86. Bamford C, Mays M, Tepper S. Unusual headaches in the elderly. Curr Pain Headache Rep. 2011;15(4):295–301.
87. Okura M, Taniguchi M, Muraki H, et al. Case of exploding head syndrome. Brain Nerve. 2010;62(1):85–8.
88. Poli F, Ricotta L, Vandi S, et al. Catathrenia under sodium oxybate in narcolepsy with cataplexy. Sleep Breath. 2012;16(2):427–34.
89. Zinke J, Rupprecht S, Schwab M, et al. Nocturnal groaning (catathrenia) and epilepsy. Epileptic Disord. 2010;12(2):136–7.
90. Songu M, Yilmaz H, Yuceturk AV, et al. Effect of CPAP therapy on catathrenia and OSA: a case report and review of the literature. Sleep Breath. 2008;12(4):401–5.
91. Guilleminault C, Hagen CC, Khaja AM. Catathrenia: parasomnia or uncommon feature of sleep disordered breathing? Sleep. 2008;31(1):132–9.
92. Iriarte J, Alegre M, Urrestarazu E, et al. Continuous positive airway pressure as treatment for catathrenia (nocturnal groaning). Neurology. 2006;66(4):609–10.
93. Nofzinger E, Reynolds C. REM sleep behavior disorder (Q & A). J Am Med Assoc. 1994;271(11):820.

Chapter 28
Treatment of Parasomnias

Milena Pavlova and Myriam Abdennadher

Overview

The treatment of parasomnia should start with a thorough evaluation of provoking factors. These include various causes of sleep fragmentation, as well as substances that can change the sleep structure. As discussed in earlier chapters (see Chap 7, "Provoking factors"), a higher frequency of events in the same patient can be seen during conditions of stress, medical illness, primary sleep disorders, and some psychiatric conditions that lead to sleep disruption. Epidemiological studies have consistently reported that various sleep fragmenting disorders (shift work, sleep apnea, mood disorders, and others) are seen more frequently among patients with parasomnia [1].

Treatment of Precipitating Factors

Sleep Hygiene

More than a quarter of all adults worldwide have reported some amount of sleep disruption [2]. More concerningly, the amount of sleep that school children and adolescents obtain is frequently insufficient. Thus, it is not surprising that a discussion of sleep hygiene is needed in most cases. Good sleep hygiene, on the other hand may decrease the frequency of parasomnia events [3]. A brief summary of good sleep recommendations is provided in Box 28.1.

M. Pavlova (✉) · M. Abdennadher
Department of Neurology, Brigham and Women's Hospital,
Harvard Medical School, Boston, USA
e-mail: mpavlova1@partners.org

M. Abdennadher
90 St. Marys Street, Unit 3–6, Boston, MA 02215, USA
e-mail: drmed_abd@yahoo.fr

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_28, © Springer Science+Business Media New York 2013

Primary Sleep Disorders

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is common [4], especially in older individuals [5–13]. Each individual event is characterized by airway collapse, which leads to desaturation and subsequently to an arousal. In Chap 7 we describe a patient with confusional arousals that responded to treatment of underlying OSA. Such examples are frequently seen in clinical practice. The most effective treatment of OSA in adults currently is positive airway pressure, other options include dental appliances, upper airway surgery, weight loss, and avoidance of sleep in supine position [14]. In children, OSA as a result of adenotonsillar hypertrophy is common and patients should be evaluated. Treatment of sleep apnea may alleviate parasomnia both in adults [10] and in children [15].

Periodic Limb Movement Disorder

Patients with periodic limb movement disorder (PLMD) frequently also have restless legs syndrome. In children, the disorder is rarer, affecting 1 in 120 school-aged children [16]. In adults, these symptoms can be idiopathic, but can also be associated with anemia, chronic renal disease, or neuropathy. Treatment includes evaluation for iron deficiency (iron supplementation is currently recommended for such patients if ferritin is below 50 pg/ml), dopamine agonists, and gabapentin. In more severe cases, opiate medications are used [17, 18].

Pharmacological Precipitators

A variety of medications can disrupt sleep and thus potentially aggravate parasomnia. Commonly prescribed agents include caffeine-containing medications used in the treatment of migraine and stimulants used for attention deficit disorder. Both categories of medications can have sleep-disrupting effect that is sometimes underestimated or misunderstood by the patients. Other potential precipitators include **beta-blockers**. Randomized studies indicate that they disrupt sleep and can thus provoke events [19]. In situations where beta-blockers are needed, the sleep-disrupting effect can be partially ameliorated by use of melatonin [20].

Zolpidem and zolpidem extended release are among the most prescribed medications for insomnia, accounting for more than 65 % of total sleep aid prescriptions by primary care physicians [21]. Nonetheless, these medications have been reportedly associated with sleepwalking and sleep-eating [22–24]. Some cases were also involved in legal issues such as sleep-driving [25]. A categorical warning has been added to the label of other hypnotics, including eszopiclone and zaleplon.

Selective serotonin reuptake inhibitors (SSRIs) suppress rapid eye movement (REM) sleep and can be associated with sleep fragmentation [26–28]. They have

been associated with a higher occurrence of REM behavior disorder (RBD) and nightmares [29–31]. **Bupropion** has a lesser effect on sleep architecture. However, several authors reported sleepwalking in patients taking bupropion [32, 33].

Safety Measures

Although it may be considered "common sense", it is often necessary to review safety of the sleep environment with the patient. Sharp or otherwise hazardous objects should be removed, and windows and doors secured. More recently, methods that wake the patient up if he/she is leaving the bed have been considered by some clinicians. In a recent case series, success has been reported with a pressurized bed alarm customized with a familiar voice to deliver a calming message during abnormal nocturnal behavior [34].

Pharmacological Treatments of Parasomnia

REM Behavior Disorder

A detailed treatment discussion is provided in the chapter discussing REM behavior disorder (RBD). Briefly, several studies have examined the effectiveness of clonazepam, reporting a very high effectiveness [35]. Smaller studies have reported a beneficial effect of melatonin [36–38].

Non-Rapid Eye Movement Parasomnias

The decision to start pharmacological treatment for non-rapid eye movement (NREM) parasomnia must only be made in select cases, after other options have failed. Many of the patients are younger (see Chap 7, effect of age), and thus potential long-term effects should be discussed with the patients. Sleep-related eating disorder may successfully be treated with topiramate [39]—an antiepileptic medication with weight loss as a side effect. Typical starting doses are 25–50 mg.

For other NREM parasomnias, medications that lead to sleep consolidation have been most widely used in clinical practice. Many clinicians use benzodiazepines or tricyclic antidepressants, which can be helpful in some patients [40]. Schenck et al. also performed two early studies that report a high effectiveness of benzodiazepines (clonazepam and alprazolam) in combined groups of NREM parasomnia and RBD [11, 12]. Both studies included only adult patients. There are no randomized treatment trials available at this time [41].

Case Example

A 44-year-old woman presented with insomnia. She was given zolpidem, based on prior history. At her follow-up visit, she reported that since the start of the medication she had also started to experience abnormal behaviors from sleep: rearranging objects in her room. She was amnestic for the events, but knew about the behaviors because she found objects disarranged in the morning. She also recalled that as a child she had transient symptoms of sleepwalking, which had stopped in adulthood. After the cessation of zolpidem, her abnormal behaviors were resolved.

Practical Points

- Sleepwalking can occur as a result of medications used for the treatment of insomnia.
- Cessation of the provoking medication typically leads to resolution of the events.

Box 28.1 Recommendations for Good Sleep

1. Use sleep homeostasis to help sleep initiation:
   - The average sleep needed for adults is 7–9 h, do not stay in bed longer
   - Avoid late afternoon naps.
2. Use circadian rhythm to help sleep continuity:
   - Regular wake times
   - Allow ample amount of light during the day
   - Avoid light overexposure in the evening.
3. Avoid common sleep fragmenting substances:
   - Avoid afternoon caffeine—last intake ideally at 12:00 noon
   - Avoid alcohol close to bedtime.
4. Stimulus control:
   - Use bed for sleep (and intimacy) only
   - Do not perform other activities, such as watching TV, listening to radio, or eating. Exceptions are soft, continuous (“white”) noises
   - Turn clock, so it is not visible from the bed.

References

1. Ohayon MM, Guilleminault C, Priest RG. Night terrors, sleepwalking, and confusional arousals in the general population: their frequency and relationship to other sleep and mental disorders. J Clin Psychiatry. 1999 Apr;60(4):268–76. (quiz 277).
2. Centers for Disease Control and Prevention (CDC). Youth risk behavior surveillance—United States, 2009. MMWR. 2010;59:1–142.
3. Wills L, Garcia J. Parasomnias: epidemiology and management. CNS Drugs. 2002;16(12): 803–10.
4. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med. 1993 Apr;328(17):1230–5.
5. Pavlova M, Duffy JF, Shea SA. Polysomnographic respiratory abnormalities in asymptomatic individuals. Sleep. 2008 Feb 1;31(2):241–8.
6. Broughton RJ. Mahowald MW, editor. Non-REM arousal parasomnias. In: Principles and practice of sleep medicine. Philadelphia: Saunders; 2000. pp. 693–706.
7. Eliseo T. The hypnotic treatment of sleepwalking in an adult. Am J Clin Hypn. 1975;17(4): 272–6.
8. Reid W, Ahmed I, Levie C. Treatment of sleepwalking: a controlled study. Am J Psychother. 1981;35(1):27–37.
9. Schenck C, Mahowald M. Polysomnographic, neurologic, psychiatric and clinical outcome report on 70 consecutive cases with REM sleep behavior disorder (RBD): sustained clonazepam efficacy in 89.5 % of 57 treated patients. Cleve Clin J Med. 1990;57:9–23.
10. Guilleminault C, Kirisoglu C, Bao G, Arias V, Chan A, Li KK. Adult chronic sleepwalking and its treatment based on polysomnography. Brain. 2005;128(5):1062–9.
11. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW. A polysomnographic and clinical report on sleep-related injury in 100 adult patients. Am J Psychiatry. 1989;146(9): 1166–73.
12. Schenck CH, Mahowald MW. Long-term, nightly benzodiazepine treatment of injurious parasomnias and other disorders of disrupted nocturnal sleep in 170 adults. Am J Med. 1996;100(3):333–7.
13. Gazarian M, Kelly M, McPhee JR, Graudins LV, Ward RL, Campbell TJ. Off-label use of medicines: consensus recommendations for evaluating appropriateness. Med J Aust. 2006;185(10):544–8.
14. Kryger MH, Roth T, Dement WC. Principles and practice of sleep medicine: expert consult premium edition. Philadelphia: Elsevier Saunders; 2010. pp. 1278–94
15. Guilleminault C, Palombini L, Pelayo R, Chervin RD. Sleepwalking and sleep terrors in prepubertal children: what triggers them? Pediatrics. 2003;111:e17–25.
16. Khatwa U, Kothare SV. Restless legs syndrome and periodic limb movements disorder in the pediatric population. Curr Opin Pulm Med. 2010 Nov;16(6):559–67.
17. Lipford MC, Silber MH. Long-term use of pramipexole in the management of restless legs syndrome. Sleep Med. 2012 Dec;13(10):1280–5. doi:10.1016/j.sleep.2012.08.004.
18. Comella CL. Restless legs syndrome: treatment with dopaminergic agents. Neurology. 2002 Feb 26;58(4 Suppl 1):87–92.
19. Yilmaz MB, Erdem A, Yalta K, Turgut OO, Yilmaz A, Tandogan I. Impact of beta-blockers on sleep in patients with mild hypertension: a randomized trial between nebivolol and metoprolol. Adv Ther. 2008 Sep;25(9):871–83.
20. Scheer FA, Morris CJ, Garcia JI, Smales C, Kelly EE, Marks J, et al. Repeated melatonin supplementation improves sleep in hypertensive patients treated with beta-blockers: a randomized controlled trial. Sleep. 2012 Oct 1;35(10):1395–402.
21. Cascade EF, Kalali AH, Reites J. Current status of hypnotic prescribing habits in the United States. Psychiatry (Edgmont). 2007 Sep;4(9):24–5.
22. Hoque R, Chesson AL Jr. Zolpidem-induced sleepwalking, sleep related eating disorder, and sleep-driving: fluorine-18-flourodeoxyglucose positron emission tomography analysis,

and a literature review of other unexpected clinical effects of zolpidem. J Clin Sleep Med. 2009;5:471–6.
23. Doane JA, Dalpiaz AS. Zolpidem-induced sleep-driving. Am J Med. 2008;121:e5.
24. Schenck C, Connoy D, Castellanos M, et al. Zolpidem induced amnestic sleep related eating disorder in 19 patients. Sleep 2005;28(Abstract supplement):A259.
25. Poceta JS. Zolpidem ingestion, automatisms, and sleep driving: a clinical and legal case series. J Clin Sleep Med. 2011 Dec 15;7(6):632–8.
26. McCarley RW, Greene RW, Rainnie D, Portas CM. Brainstem neuromodulation and REM sleep. Semin Neurosci. 1995;7:341–54.
27. Sharpley AL, Cowen PJ. Effect of pharmacologic treatments on the sleep of depressed patients. Biol Psychiatry. 1995 Jan 15;37(2):85–98.
28. Kierlin L, Littner MR. Parasomnias and antidepressant therapy: a review of the literature. Front Psychiatry. 2011;2:71.
29. Lam SP, Fong SY, Ho CK, Yu MW, Wing YK. Parasomnia among psychiatric outpatients: a clinical, epidemiologic, cross-sectional study. J Clin Psychiatry. 2008 Sep;69(9):1374–82.
30. Koponen H, Lepola U, Leinonen E, Jokinen R, Penttinen J, Turtonen J. Citalopram in the treatment of obsessive-compulsive disorder: an open pilot study. Acta Psychiatr Scand. 1997 Nov;96(5):343–6.
31. Markowitz JC. Fluoxetine and dreaming. J Clin Psychiatry. 1991 Oct;52(10):432.
32. Khazaal Y, Krenz S, Zullino DF. Bupropion-induced somnambulism. Addict Biol. 2003 Sep;8(3):359–62.
33. Oulis P, Kokras N, Papadimitriou GN, Masdrakis VG. Bupropion-induced sleepwalking. J Clin Psychopharmacol. 2010 Feb;30(1):83–4.
34. Howell MJ, Arneson PA, Schenck CH. A novel therapy for REM sleep behavior disorder (RBD). J Clin Sleep Med. 2011 Dec 15;7(6):639–44A.
35. Schenck CH, Mahowald MW. REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in SLEEP. Sleep. 2002 Mar 15;25(2):120–38.
36. Kunz D, Mahlberg R. A two-part, double-blind, placebo-controlled trial of exogenous melatonin in REM sleep behaviour disorder. J Sleep Res. 2010 Dec;19(4):591–6.
37. Boeve BF, Silber MH, Ferman TJ. Melatonin for treatment of REM sleep behavior disorder in neurologic disorders: results in 14 patients. Sleep Med. 2003 Jul;4(4):281–4.
38. Aurora RN, Zak RS, Maganti RK, Auerbach SH, Casey KR, Chowdhuri S, Karippot A, Ramar K, Kristo DA, Morgenthaler TI, Standards of Practice Committee. Best practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin Sleep Med. 2010 Feb 15;6(1):85–95.
39. Winkelman JW. Efficacy and tolerability of open-label topiramate in the treatment of sleep-related eating disorder: a retrospective case series. J Clin Psychiatry. 2006 Nov;67(11): 1729–34.
40. Cooper AJ. Treatment of coexistent night terrors and somnambulism in adults with imipramine and diazepam. J Clin Psychiatry. 1987;48:209–10.
41. Harris M, Grunstein RR. Treatments for somnambulism in adults: assessing the evidence. Sleep Med Rev. 2009 Aug;13(4):295–7.

Chapter 29
Use of Alternative Medicines in Parasomnias for Adults and Children

Youngran Chung and Robert C. Dumont

Introduction

Complementary and alternative medicine (CAM) practices are increasingly utilized in the USA for a variety of medical disorders. Patients are interested in using nonpharmacologic options, and physicians are finding these options to be useful especially when there are concerns about adverse reactions from drugs. There are over 18,000 CAM articles cited in PubMed, and integration of these modalities into mainstream medicine is increasing. "Integrative Medicine" is now a growing field in medicine. Depending on the training and expertise of a physician and their staff, CAM treatments may be done at the office, referred out to a specific practitioner (i.e., licensed acupuncturist), or there may be techniques that could be taught and utilized at home by the patient or caregiver (e.g., self-hypnosis). In the approach to using CAM, it is important that the patient receives a comprehensive evaluation and that consideration is given to both conventional and CAM approaches regarding safety and potential effectiveness. Frequently, physicians will turn to CAM as a last resort. However, CAM therapies can sometimes be more effective when introduced early in a pathologic process and importantly most CAM approaches are safer than pharmaceuticals. CAM approaches can be used as a stand-alone therapy, though they are often combined with or used as an adjunct to conventional interventions. Ideally, physicians utilizing CAM approaches should do so in an integrative/holistic manner, looking at other coexisting problems and combining several modalities along with correction of lifestyle imbalances. Some of the more common CAM therapies used for parasomnias are discussed.

Y. Chung (✉)
Department of Pediatric Pulmonary Medicine, Northwestern University Feinberg School of Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA
e-mail: youngran.y@gmail.com

R. C. Dumont
Raby Institute for Integrative Medicine at Northwestern, LLC, Chicago, IL, USA
e-mail: rdumont11@gmail.com

Y. Chung · R. C. Dumont
846 N. Euclid Ave., Oak Park, IL 60302, USA

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_29, © Springer Science+Business Media New York 2013

Acupuncture

Acupuncture is a component of the ancient and comprehensive Chinese medical system, with a complex theory of pathophysiology distinctly different from the Western view. It is frequently complemented by other Chinese medicine (CM) modalities including Chinese herbs, massage, diet and lifestyle modification. The basic tenet of acupuncture is that a disease or illness is caused by a disturbance in the flow of Qi ("life force" or "vital force") which courses through channels or meridians in the body. Acupuncture needles access select points in these channels to reestablish normal flow of Qi.

Acupuncture is indicated for a variety of psychiatric as well as physical disorders, and there is extensive clinical experience in treating sleep disturbances with acupuncture. The acupuncturist's approach is based on CM principles and would view sleep disturbances as a disruption in the connection between a person's body, mind, and spirit. There are specific acupuncture points used in acupuncture for disturbed or restless sleep, nightmares, sleepwalking, sleep talking, and excessive dreams. These concepts and rationale for choice of points are outlined in many acupuncture texts including those specifically addressing pediatric acupuncture [1–4].

The authors have successfully treated nocturnal enuresis with acupuncture, giving the following case as an example: An 8-year-old boy had a history of nocturnal enuresis and recurrent ear infections. Acupuncture was begun with weekly treatments (Korean Hand acupuncture technique: use of press pellets to stimulate acupuncture points on the hands). Within 6 weeks, his enuresis resolved completely as did his recurrent ear infections. He was treated for the six weekly sessions and then two additional monthly treatments. A follow-up 9 months later, confirmed resolution of both enuresis and his recurrent ear infections. In CM, the organ systems are each related to specific sense organs. For example, liver is associated with the eyes and sight, kidney and bladder with the ears. This young boy had characteristics of an underlying "Kidney system" deficiency which was successfully treated by acupuncture.

If there is underlying anxiety, fright, or other psychological and emotional stress associated with these sleep disruptions, acupuncture would also address these aspects as there are acupuncture points and protocols that are specifically used for anxiety and emotional disturbances. Other interventions that are part of the CM approach include use of Tui na before bedtime. Tui na is a Chinese massage that can be self-administered or done by the parents. Moderation of food intake and choices and sometimes Feng Shui (an ancient art form of balancing the energies of any given space by placement or orientation of furniture, plants, etc.) are advised to help settle the mind and regulate the environmental Qi.

While there is literature on efficacy of acupuncture for insomnia, there are very few clinical studies (except in the Chinese language literature) on use of acupuncture for specific parasomnias. However, there are a number of studies on efficacy of acupuncture for enuresis.

In a prospective, randomized, placebo-controlled, single-blind study of 91 children with monosymptomatic nocturnal enuresis, outpatient laser acupuncture-treated

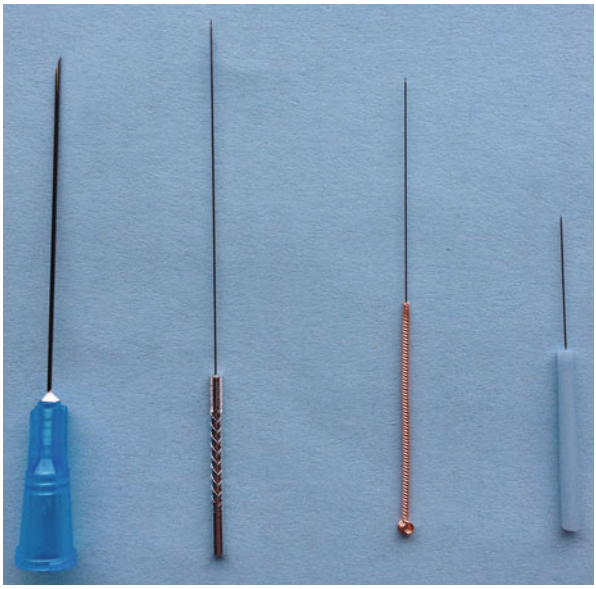


Fig. 29.1 25 Gauge (0.5144 mm) by 1.5 in. needle (extreme *left*) next to acupuncture needles from *right* to *left*: 0.2 × 15 mm, 0.2 × 25 mm, and 0.22 × 40 mm. Syringe needle has cutting edge and acupuncture needles have noncutting points

children were significantly improved compared to placebo, with regard to complete dryness and decrease in mean number of weekly bed-wetting episodes [5]. Another study showed improvement in bladder capacities and number of wet nights per week (decrease in 50 % or more from baseline). They concluded that acupuncture may be beneficial in the treatment of nocturnal enuresis by increasing nocturnal bladder capacity [6]. In a study comparing desmopressin with acupuncture, there was no statistically significant difference between desmopressin therapy and laser acupuncture. The authors concluded that laser acupuncture was a painless, cost-effective, and short-term alternative therapy for children with primary nocturnal enuresis [7].

In general, acupuncture may be more effective if used as part of a comprehensive CM approach rather than in isolation. This has been shown for treatment of enuresis in which, a review reported that the efficacy rate of acupuncture as part of a complete CM approach was higher than alarm therapy for enuresis. They also found that electroacupuncture (low current electric stimulation of needles) enhanced the treatment outcomes [8].

There is a complexity involved in conducting and interpreting clinical acupuncture studies as there are many different variables that can affect outcomes. These variables include: different stimulation devices, variation in acupuncture point selection, and whether acupuncture is used in conjunction with other CM modalities (herbs, massage, and nutrition). Also, there are multiple styles of acupuncture including microsystems (hand, ear, or scalp acupuncture) and different techniques including needle acupuncture, acupressure and the use of non-needle devices (e.g., laser, pellets) to stimulate points (see Figs. 29.1 and 29.2).

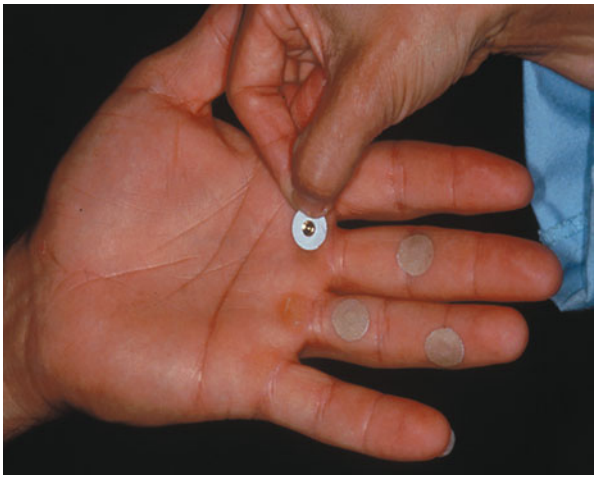


Fig. 29.2 Application of SooJi Chim acupuncture (Korean Hand Therapy) pellets

In skilled hands, acupuncture is a very safe procedure. The needles are applied using a clean needle technique and are almost always single use/disposable even though infection is extremely rare. An analysis by White which included 12 prospective studies that surveyed more than a million treatments showed the estimated risk of a serious adverse event with acupuncture to be 0.05 per 10,000 treatments and 0.55 per 10,000 individual patients [9]. Training in acupuncture for physicians can be found through the American Academy of Medical Acupuncture (AAMA, www.medicalacupuncture.org).

Homeopathy

Homeopathy is one of the most widely used forms of complementary medicines in the world but it is also one of the most misunderstood. The main principle behind homeopathy is "like cures like", or that a substance which may produce a particular constellation of symptoms at a pharmacologic/toxic dose, will cure the same symptoms present in a patient when administered in an ultradiluted form. The basic belief is that homeopathic medicines (also called remedies) stimulate the body's inherent capacity to heal itself; though the true mechanism is not understood. Most homeopathic medicines are derived from natural substances such as botanical, mineral, or animal sources. In the USA, homeopathic medicines have been FDA regulated since 1938 and most are available over the counter.

Homeopathic dilutions can exceed Avogadro's number of 10^{-23}, and therefore, not contain even a single molecule of the original substance. Because of the ultradilute nature of homeopathic medicines, the homeopathic mechanism of action is thought to be to be biophysical rather than pharmacological. Some proponents believe that the manufacturing of a homeopathic medicine imparts a change in the physical properties

of the water diluent. In vitro physiochemical studies suggest this effect [10–12]. Biologic effects of homeopathic dilutions have also been demonstrated at the cellular level [13]. As most homeopathic medicines are so dilute and may not even contain a molecule of the original substance, it would seem implausible that it could have any effect over placebo. However, the predominance of independent systematic reviews of clinical studies concluded that homeopathy does have an effect beyond placebo [14–20].

With regard to parasomnias such as sleep terror, sleepwalking, and bruxism, there are no specific clinical studies, but homeopathic practitioners treat these disorders on a regular basis. For example, homeopathic *Stramonium* is frequently used for nightmares and sleep terrors while homeopathic *Cina* may be used for sleepwalking and bruxism. If there is underlying anxiety as a contributing factor, there may be other homeopathic medicines that could be used adjunctively. Importantly, the choice of a homeopathic medicine for a disorder may be different for each individual. Homeopathy is a holistic approach that takes into consideration not only the particular medical issue at hand, but also other concurrent medical problems including the mental and emotional characteristics of the patient. One of the difficulties of doing homeopathic trials is that the choice of homeopathic medicines have to be individualized, and does not lend itself to the standard randomized controlled study methods. In other words, for the same clinical problem, the choice of homeopathic medicine may differ from person to person because manifestation or expression of the same disease varies depending on the individual.

In the literature, there is only a single clinical trial for homeopathic treatment of nocturnal enuresis; a study comparing safety and efficacy of homotoxicological remedies (a variation of homeopathy) versus placebo and versus desmopressin. This randomized, double-blind, double-dummy controlled trial of 151 children with monosymptomatic nocturnal enuresis, showed full response achieved with homotoxicological remedies, superior over placebo ($p < 0.001$) but less effective than desmopressin [21].

While there is lack of published clinical trials on homeopathy for parasomnias, homeopathy is indicated and has been widely used for a variety of medical disorders including the treatment of various sleep disorders. The authors have treated a number of parasomnia cases with homeopathy. Two examples given here are the treatment of nightmare and sleepwalking. In the first case, a 17-year-old male patient had a history of what appeared to be night terrors as a young child. Once he was able to verbally express himself, he complained of distressing nightmares of a violent nature. These nightmares persisted nightly for years. At the age of 6 years, he was treated elsewhere with homeopathic medicines and the nightmares went away but resurfaced at the age of 13 years. When he was first seen at the age of 17 years, he had been off the original homeopathic medicines for several years as he no longer seemed responsive to them. He was having multiple nightmares every night which interfered with his sleep. Homeopathic treatment was restarted (in a different style approach from what he had previously). Within 3 weeks, his nightmares were reduced to a few per week. They eventually stopped and were completely gone (2 years of follow-up). The second case was of a 12-year-old female patient who had abrupt onset of

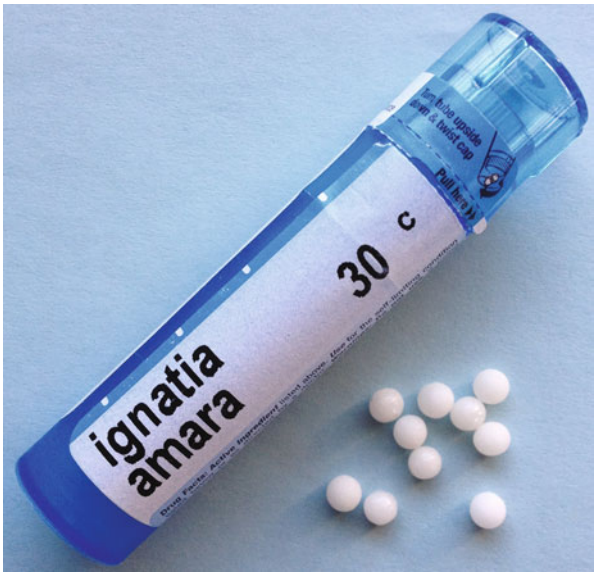


Fig. 29.3 Homeopathic pellets designed for sublingual use. The base pellets are composed of 85 % sucrose and 15 % lactose. The prepared homeopathic dilution is absorbed into the pellet

sleepwalking for a month. This included hazardous activity such as trying to climb out of open windows. Homeopathic treatment was begun and within 2 weeks her sleepwalking episodes decreased significantly. There were no apparent underlying issues of stress.

Due to the nature of their preparation, homeopathic medicines are extremely safe and devoid of drug interactions. They are easy to take and well tolerated at any age (dissolvable sublingual tablet or liquid, see Fig. 29.3). Homeopathic medicines are available over the counter. However, since homeopathic medicines are most effective when selected according to very specific and unique signs and symptoms of that individual, it is best guided by a trained homeopathic practitioner, especially for chronic and complex disorders. A great advantage of homeopathy is its safety and ease of administration (sublingual tablets or dissolved in liquid). Unlike herbs and supplements, homeopathic medicines which have been FDA regulated since 1939, are by nature devoid of pharmacologic ingredients that would interact with drugs or cause side effects. Caution must be taken as some over the counter products labeled "homeopathics" may actually be combined with herbal products.

Homeopathy is a tool that can be learned by health professionals. Courses for homeopathy training in the USA are offered through programs recognized through the American Institute of Homeopathy (www.homeopathyusa.org) and the Center for Education and Development of Clinical Homeopathy (www.cedhusa.org) which offers courses for physicians in the USA and other countries worldwide.

Herbs and Supplements

In a discussion of the potential use of herbs and supplements for the treatment of parasomnias, it is important to appreciate that traditional use of herbs is often based on different paradigms dependent upon the prevailing culture. In CM, nocturnal enuresis could represent several different underlying problems per Chinese medical pathophysiology (i.e., Kidney Yang deficiency, Liver Fire, Spleen Qi deficiency and sinking, Lung Qi deficiency, or Kidney Yin deficiency) [22]. The final diagnosis would be dependent upon other specific symptoms and signs in the patient's history and exam. The choice of herbal formula would then be tailored for that individual patient. The formulas could contain from 5 to 15 different individual herbs; each herb playing its role in the overall disharmony responsible for the symptoms. Finally, the herbal formula would most likely be part of an overall treatment including acupuncture, and more than likely dietary and lifestyle changes. Ayurvedic (Indian) medicine and even certain applications of Western herbal medicine would also use individualized combinations of herbs based on their particular paradigm and as part of an overall holistic/comprehensive approach. With this understanding, as with other individualized approaches, there should be caution in interpreting clinical studies which are based on the Western medical paradigm of "one drug fits all".

Even within the Western biomedical model, both herbs and supplements are used by some health care providers in an individualized, holistic, and comprehensive approach. Rather than treating a particular symptom such as night terrors or restless leg syndrome (RLS) with a specific herb or supplement, the underlying physiologic imbalance causing the problem would be explored and corrected. For example, as some parasomnias have anxiety at their root, herbs and/or supplements would be used to assist with adaptation to stress in this case. Most importantly, these would serve as an adjunctive or supportive measure of a more integrative approach which would also employ Mind/Body techniques. Also, dietary, lifestyle, and psychological/social factors that might play a role in disrupting a normal sleep pattern would be explored and adjusted. This integrated approach is used by Functional Medicine®. As defined by The Institute for Functional Medicine® (www.functionalmedicine.org) "Functional medicine is a science based personalized healthcare approach that assesses and treats underlying causes of illness through individually-tailored therapies to restore health and improve function."

A basic tenet of functional medicine is that the body attempts to maintain a dynamic homeostatic balance while constantly challenged by the complex interaction of environmental influences such as diet, nutrients, exercise, sleep, trauma, emotional and psychological stress, and genetic predispositions. These interactions can overwhelm this homeostatic balance and result in an imbalance of one or more fundamental physiological processes expressed as chronic or recurrent disease.

The primary focus would be to reestablish a healthier lifestyle with emphasis on sleep hygiene while looking for an underlying problem (such as increased stress or anxiety). Safe nonpharmacological approaches are emphasized, and herbs and supplements are frequently used for added support. Conventional drug therapy would

still be considered and utilized, if needed. As a support for underlying anxiety, adaptogenic herbs such as *Eleutherococcus senticosus* (Siberian Ginseng), *Panax ginseng* (Korean Ginseng), *Withania somnifera* (Ashwagandha), and/or *Rhodiola rosea* along with other supplements (i.e., B vitamins) might be used to support adrenal function assisting the body in adapting to stress [23].

For the specific treatment of parasomnias with herbs or supplements, the published clinical evidence is sparse. Herbs traditionally used for nightmares include Passionflower (*Passiflora incarnata*) and Roman Chamomile (*Anthemis nobilis*). The latter is not to be confused with German Chamomile (*Matricaria recutita*), though both are used as anxiolytics. While there are no clinical trials for the use of either Chamomile for parasomnias or as an anxiolytic, Passionflower has a few studies supporting its anxiolytic effects but not strong enough to be conclusive [24]. For night terrors, the serotonin precursor L-5-hydroxytryptophan (L-5-HTP) may provide a safe approach to sleep terrors. Unlike serotonin, it can cross the blood-brain barrier to be converted into serotonin. In a single open study of 45 children undergoing full sleep evaluation including neurological exam, electroencephalography (EEG), and sleep diary, 31 children received treatment of 2 mg/kg of L-5-HTP at bedtime. After 1 month of treatment, 93.5 % (29 out of 31 children) showed improvement, and after 6 months, night terrors disappeared in 83.9 % (26 out of 31 children). This contrasted to persistence of night terrors in 71.8 % (10 out of 14 children) of the control group [25]. For RLS, patients are now routinely evaluated for iron deficiency. While RLS is thought to be caused by a dopaminergic abnormality and can be treated by levodopa in many patients, there is evidence for iron in the treatment of a subset of the RLS population who may have marginal or insufficient CNS iron [26]. In a more recent study, anemia was found in 5 % of 118 patients with RLS as a comorbidity, though a causative relationship was not established in the study [27].

Saint John's Wort has been recommended as a herbal treatment for nocturnal enuresis, though there are no published studies supporting this. Melatonin, known for its sleep-regulating role, was looked at as a potential candidate for enuresis but apparently with no effectiveness. The urinary metabolites (6-hydroxy-melatonin-sulfate (aMT6s)) of children with nocturnal enuresis were not found to be significantly different from healthy controls and a recent study of 24 children (11 melatonin, 13 placebo) showed no difference in sleep cycle or frequency of bed-wetting [28, 29].

Aromatherapy

Aromatherapy is the use of essential oils for the improvement of health and well-being. It is frequently used as adjunctive therapy with a focus on increasing energy, inducing relaxation, and improving mood. It is also used for skin injuries and burns, and for adjunctive treatment of internal disorders, pregnancy, and childbirth.

Essential oils are the aromatic extracts distilled from plant components: flowers, leaves, seeds, fruits, roots, resins, and wood. These essential oils are highly concentrated and more potent than dried herbs; hence, very few oils are used for internal use

due to potential toxicity and mucous membrane irritation. They also have a complex chemistry containing hundreds of unique chemical compounds. These components include terpenes, isoprenes, alcohols, phenols, aldehydes, esters, ketones, oxides, lactones (coumarins), and ethers [30]. Essential oil properties include antiseptic, antibacterial, antifungal, antiviral, anti-inflammatory, analgesic, and expectorant. They also have smooth muscle effects and stimulatory effects on both nervous and immune systems. They easily cross blood-brain barrier and can stimulate the secretion of antibodies, neurotransmitters, endorphins, hormones, and enzymes. The usual mode of use is via the olfactory route (typically via vaporizers and diffusers) or absorption through the skin generally coupled with massage. When used via these methods, essential oils are generally considered safe, though there is caution for internal use. Adverse effects are (reportedly) rare but there is no recognized database or specific reporting system in place. For some oils, repeated/prolonged use could have potential cumulative toxicity (liver, CNS/PNS, kidneys). Skin and mucous membrane reactions can occur from the aldehydes or phenols present in the oils, and some oils may predispose to a (time) limited phototoxicity [30].

Percutaneous absorption is dependent upon epithelial thickness and permeability and amount of surface body area covered. Infants could be particularly vulnerable. Typically, only a very small amount of the therapeutic oil is diluted in a carrier oil such as almond oil. Regular use should be under the guidance of someone with a level of expertise in aromatherapy.

There are several studies supporting the use of aromatherapy/essential oils for mild insomnia and improvement of sleep quality [31–36]. However, there is little discussion of treatment of parasomnias in the aromatherapy literature and no specific clinical studies for parasomnias. One source suggests several essential oils (*Boswellia carterii*, *Citrus limon*, and *Melissa officinalis*) for treatment of nightmares associated with underlying stress [37].

In aromatherapy, as with most therapeutic approaches, it is important to have a solid foundation and understanding with regard to safety and its potential therapeutic uses. There are several professional organizations (the International Federation of Professional Aromatherapists (www.ifparoma.org), Alliance of International Aromatherapists (www.alliance-aromatherapists.org), Canadian Federation of Aromatherapists (www.cfacanada.com), and the National Association for Holistic Aromatherapy (www.naha.org)). There are, however, no recognized professional licensures for aromatherapy. General resources on aromatherapy are available in the references [38, 39].

Hypnosis

Hypnosis can be an extremely versatile tool for the treatment of many different types of physical and behavioral problems. Despite its formal acceptance into medicine by the American Medical Association, American Psychiatric Association, and the American Psychological Association in the 1950s, hypnosis is underutilized and is

still accompanied by misperceptions. Hypnosis is perhaps best defined by Daniel P. Kohen, M.D. as "A spontaneously occurring or induced altered state of awareness (with or without relaxation which may or may not be evident) in which an individual develops a focused concentration on some idea or image with the expressed purpose of maximizing potential, and/or reducing or resolving some problem" [40]. This altered state, also known as a trance or trance state, is a state of focused attention. It is a state which we have all experienced—watching TV or a movie, reading a book, etc.—we are focused in what we are doing and tuning out everything else. It is during this focused state that we are particularly receptive to the suggestions presented. This therapeutic suggestion is often a carefully worded "script" with the goal to achieve the desired therapeutic response. There can often be a considerable overlap with other Mind/Body/behavioral interventions such as progressive muscular relaxation, autogenic training, and use of imagery as these modalities may be used as part of the induction process or in the case of imagery as part of the suggestion (see Chap. 27).

For hypnosis to be effective, good rapport with the patient is extremely important. This is especially important in children, in whom the therapeutic suggestions used in hypnosis are geared toward their age or developmental stage. In all cases, the therapeutic suggestion needs to be tailored to the individual and his/her specific issue. The language used in hypnosis is crucial and is always phrased to be suggestive (rather than commanding) and positive. Finally, all hypnosis is regarded as self-hypnosis. As therapists or medical professionals with training in hypnosis, we serve only as a guide or facilitator. It is the patient that does the work. A hypnotic intervention may be very simple and straightforward.

A very straightforward example is that of a child with recurring nightmares of being chased by an alligator that is traced back to a recent encounter with alligators at a zoo. This might be altered with hypnotic suggestions of a magic wand (and suggestions of what the child could do with the wand) giving the child the power to change the dream into something positive. Despite suggestions given, it is up to the child to determine how he/she would use the wand. It is important to explore the underlying root of the parasomnia and focus on this during hypnosis sessions. Creativity is a vital component.

Case Examples

Two case reports of night terrors in the literature illustrate this last point. A 16-year-old boy presented with night terrors was resistant to other forms of treatment. His night terrors were found to be precipitated by nocturnal noises awakening him from deep sleep. His night terrors were eliminated with posthypnotic suggestions that reduced his awareness of nocturnal sensory stimuli [41]. Another case was a 10-year-old child with a 6-year history of night terrors. He underwent a hypnotic induction using a finger lowering technique in which he would watch them and "go to sleep". He was given suggestions to drop off to sleep gradually for normal cycling of sleep and not dropping too quickly into an extremely deep stage of sleep. The regularity and continual movement of the cycles of sleep were emphasized. His night terrors disappeared [42].

There are several other published studies of hypnosis used for parasomnias including night terrors, nightmares, and nocturnal enuresis. Subjects with severe somnambulism responded well to six brief sessions of hypnosis with sustained improvement after 1-year follow-up [43]. In another study using self-hypnosis for both sleepwalking and night terrors in 27 adults, subjects had a 74 % improvement rate. The average number of office visits required was 1.6, demonstrating the cost-effectiveness of this intervention [44]. A small study involving four children showed the potential benefits of using hypnosis for pediatric sleep terror disorders. The children (aged 8–12 years) had polysomnogram documented sudden arousals out of slow-wave sleep associated with complex behavior. They were initially controlled first with imipramine and then taught self-regulation through self-hypnosis. The imipramine was successfully discontinued and the children remained asymptomatic over 2–3 years of follow-up. Seven other children were reported to be successfully treated without the use of medication [45]. For repetitive nightmares in three subjects, a technique was used that reframed the waking point as the interrupted middle rather than the end of the dream allowing for a more benign completion of the dream. This proved successful in all three subjects after only 1–5 sessions [46]. Hypnosis can provide short- and long-term benefits. A study with 5-year follow-up treated various forms of parasomnias in 36 patients (including 4 children). The treated parasomnias included sleepwalking, nightmares, and night terrors. All underwent one or two hypnotherapy sessions and were then followed up by questionnaire for 5 years. Of them, 45.4 % were either symptom-free or much improved. In the follow-up period, these benefits were seen in 42.2 % at 18 months and 40.5 % at 5-year follow-up [47].

Hypnosis has also been shown to be effective for nocturnal enuresis. The authors have had success using a technique introduced by Daniel Kohen, M.D., giving the suggestion to the child that some part of our brains is awake during sleep (after all, we do not fall out of bed despite moving around in sleep) and that our bladders, controlling the "gates", can talk to this part of the brain while we are asleep and close the gates until that part of the brain wakes us up [40].

Several studies support hypnosis as a treatment for nocturnal enuresis. A comparative study of imipramine ($N = 25$) and self-hypnosis ($N = 25$) revealed similar responses. Of the imipramine-treated, 76 % had a positive response (dry beds), and for the hypnosis group 72 %. After termination of active treatment, the hypnosis group continued practicing self-hypnosis daily through a follow-up period of another 6 months. At 9 months follow-up, 68 % of patients in the hypnosis group maintained a positive response, whereas only 24 % of the imipramine group maintained a dry bed [48]. Reported in an earlier study, there was 77.5 % (31 out of 40 children) resolution of enuresis with only one or two visits in children who were taught self-hypnosis and improvement in 6 others (15 %) [49]. As part of a broader look at hypnosis and other various behavioral issues Kohen and others describe 257 children with nocturnal enuresis also treated with self-hypnosis with a success of 44 % sustained dry nights (12 months) and 31 % with improvement. These last two studies are reviewed along with a more extensive discussion of elimination disorders [50].

Hypnosis can be an effective and cost-efficient intervention. Most importantly, it empowers the patients to manage their own issues. Hypnosis is a skill that any health

professional can learn and utilize for their patients. Hypnosis coursework for health care professionals in the USA is provided by the American Society of Clinical Hypnosis (ASCH, www.asch.net) and the National Pediatric Hypnosis Training Institute (NPHTI, www.nphti.org). The professional organization in Europe is the European Society of Hypnosis (ESH, www.esh-hypnosis.eu).

Summary

CAM practices are frequently being integrated into mainstream medicine. It can be used as a stand-alone therapy or as an adjunct to conventional interventions, and offers safe nonpharmacologic options in the treatment of parasomnias.

Many CAM treatment approaches have minimal or no risk of adverse effects. This is especially true of acupuncture, homeopathy, and hypnosis.

Although there are very few clinical studies utilizing CAM therapies for parasomnias, hypnosis has supportive studies for nocturnal enuresis, sleepwalking, night terrors, and nightmares. Nocturnal enuresis is the most studied parasomnia responding to acupuncture, homeopathy, and hypnosis. Other CAM options such as supplements and aromatherapy, though lacking in clinical studies in parasomnias, may still prove useful in reducing underlying factors such as stress and anxiety. Because of the inherent safety profile of most of these approaches, CAM therapies are worthy of empiric trials for most patients, especially for those with concerns of adverse drug or for whom pharmacologic therapies are not effective. When the use of CAM is entertained, it is best administered by recognized health care practitioners trained in the respective CAM modality.

Practical Points

- Acupuncture is generally safe as the needles are minimally invasive, and well tolerated even by children. However, also available are a variety of non-needle techniques.
- Homeopathy is extremely safe without adverse effects or drug interactions due to the ultradiluted nature of these medicines. Homeopathy is FDA regulated in the USA.
- The essential oils used in aromatherapy are highly concentrated and some can be toxic when taken internally. They are best applied in a diluted form and used via inhalation and external application.
- Hypnosis is a versatile therapeutic approach. It empowers the patient and is easily taught to most people in a practitioner's office.
- Most CAM approaches require an individualized approach, i.e., the therapy is most effective when tailored to the patient's unique presentation and characteristics. This is especially true of homeopathy and acupuncture.

References

1. Loo M. Pediatric acupuncture. New York: Churchill Livingstone; 2002.
2. Loo M, Maguire J. East-West healing: integrating Chinese and Western medicines for optimal health. New York: Wiley; 2001.
3. Maciocia G. The psyche in Chinese medicine: treatment of emotional and mental disharmonies with acupuncture and Chinese herbs. 2nd ed. New York: Churchill Livingstone; 2009.
4. Scott J, Barlow T. Acupuncture in the treatment of children. 3rd ed. Seattle: Eastland Press; 1999.
5. Karaman MI, Koca O, Küçük EV, Öztürk M, Güneş M, Kaya C. Laser acupuncture therapy for primary monosymptomatic nocturnal enuresis. J Urol. 2011;185(5):1852–6.
6. Honjo H, Kawauchi A, Ukimura O, Soh J, Mizutani Y, Miki T. Treatment of monosymptomatic nocturnal enuresis by acupuncture: a preliminary study. Int J Urol. 2002;9(12):672–6.
7. Radmayr C, Schlager A, Studen M, Bartsch G. Prospective randomized trial using laser acupuncture versus desmopressin in the treatment of nocturnal enuresis. Eur Urol. 2001;40(2):201–5.
8. Bower WF, Diao M. Acupuncture as a treatment for nocturnal enuresis. Auton Neurosci. 2010;157(1–2):63–7.
9. White A. A cumulative review of the range and incidence of significant adverse events associated with acupuncture. Acupunct Med. 2004;22:122–33.
10. Rey L. Thermoluminescence of ultra-high dilutions of lithium chloride and sodium chloride. Physica A. 2003;323:67–74.
11. Elia V, Niccoli M. New physico-chemical properties of extremely diluted aqueous solutions. J Therm Anal Calorimetry. 2004;75:815–36.
12. Roy R, Tiller WA, Bell IR, Hoover MR. The structure of liquid water; novel insights from materials research; potential relevance to homeopathy. Mater Res Innov. 2005;94:577–608.
13. Belon P, Cumps J, Ennis M, Mannaioni PF, Sainte-Laudy J, Roberfroid M, et al. Histamine dilutions modulate basophil activity. Inflamm Res. 2004;53:181–8.
14. Linde K, Clausius N, Ramirez G, Melchart D, Eitel F, Hedges LV, et al. Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. Lancet. 1997;20:834–43.
15. Kleijnen J, Knipschild P, ter Riet G. Clinical trials of homeopathy. BMJ. 1991;302:316–23.
16. Cucherat M, Haugh MC, Gooch M, Boissel JP. Evidence of clinical efficacy of homeopathy: a meta-analysis of clinical trials. Homeopathic Medicines Research Advisory Group. Eur J Clin Pharmacol. 2000;56:27–33.
17. Shang A, Huwiler-Müntener K, Nartey L, Jüni P, Dörig S, Sterne JA, et al. Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. Lancet. 2005;2:726–32.
18. Rutten AL, Stolper CF. The 2005 meta-analysis of homeopathy: the importance of post-publication data. Homeopathy. 2008;97:169–77.
19. Reilly D, Taylor MA, McSharry C, Aitchison TC. Is homeopathy a placebo response? Controlled trial of homeopathic potency, with pollen in hayfever as model. Lancet. 1986;2:881–6.
20. Reilly D, Taylor MA, Beattie NG, Campbell JH, McSharry C, Aitchison TC, Carter R, Stevenson RD. Is evidence for homeopathy reproducible? Lancet. 1994;344:1601–6.
21. Ferrara P, Marrone G, Emmanuele V, Nicoletti A, Mastrangelo A, Tiberi E, et al. Homotoxicological remedies versus desmopressin versus placebo in the treatment of enuresis: a randomised, double-blind, controlled trial. Pediatr Nephrol. 2008;23(2):269–74.
22. Maciocia G. Diagnosis in Chinese medicine: a comprehensive guide. New York: Churchill Livingston; 2004. pp. 757–8.
23. Kelly GS. Nutritional and botanical interventions to assist with the adaptation to stress. Altern Med Rev. 1999;4(4):249–65.
24. Miyasaka LS, Atallah AN, Soares BG. Passiflora for anxiety disorder. Cochrane Database Syst Rev. 2007;(1):CD004518.

25. Bruni O, Ferri R, Miano S, Verrillo E. L-5-Hydroxytryptophan treatment of sleep terrors in children. Eur J Pediatr. 2004;163(7):402–7.
26. Allen RP, Earley CJ. The role of iron in restless legs syndrome. Mov Disord. 2007;22 Suppl 18:S440–8.
27. Marin LF, Felicio AC, Santos WA, Prado LB, Prado GF. Clinical correlates of the restless legs syndrome. Arq Neuropsiquiatr. 2012;70(7):529–31.
28. Kirchlechner V, Hoffmann-Ehrhart B, Kovacs J, Waldhauser F. Melatonin production is similar in children with monosymptomatic nocturnal enuresis or other forms of enuresis/incontinence and in controls. J Urol. 2001;166(6):2407–10.
29. Merks BT, Burger H, Willemsen J, van Gool JD, de Jong TP. Melatonin treatment in children with therapy-resistant monosymptomatic nocturnal enuresis. J Pediatr Urol. 2012;8(4):416–20.
30. Tisserand R, Balacs T. Essential oil safety: a guide for health care professionals. London: Churchill Livingstone; 1995.
31. Füssel A, Wolf A, Büter B, Schrader E, Brattström A. Efficient use of sleep pillows in patients suffering from non-organic sleep disorders—a pilot study. Forsch Komplementarmed Klass Naturheilkd. 2001;8(5):299–304.
32. Hirokawa K, Nishimoto T, Taniguchi T. Effects of lavender aroma on sleep quality in healthy Japanese students. Percept Mot Skills. 2012;114(1):111–22.
33. Field T, Cullen C, Largie S, Diego M, Schanberg S, Kuhn C. Lavender bath oil reduces stress and crying and enhances sleep in very young infants. Early Hum Dev. 2008;84(6):399–401.
34. Goel N, Kim H, Lao RP. An olfactory stimulus modifies nighttime sleep in young men and women. Chronobiol Int. 2005;22(5):889–904.
35. Lewith GT, Godfrey AD, Prescott P. A single-blinded, randomized pilot study evaluating the aroma of Lavandula augustifolia as a treatment for mild insomnia. J Altern Complement Med. 2005;11(4):631–7.
36. Lee YL, Wu Y, Tsang HW, Leung AY, Cheung WM. A systematic review on the anxiolytic effects of aromatherapy in people with anxiety symptoms. J Altern Complement Med. 2011;17(2): 101–8.
37. Price S, Price L. Aromatherapy for health professionals. New York: Churchill Livingston; 1995. p. 166.
38. Schnaubelt K. The healing intelligence of essential oils: the science of advanced aromatherapy. 1st ed. Rochester: Healing Arts Press; 2011.
39. Price S, Price L. Aromatherapy for health professionals. 4th ed. New York: Churchill Livingstone; 2011.
40. Kohen D. The American Society of Clinical Hypnosis workshop. Loyola University Medical School, Maywood, IL; 2002.
41. Koe GG. Hypnotic treatment of sleep terror disorder: a case report. Am J Clin Hypn. 1989;32(1):36–40.
42. Kramer RL. The treatment of childhood night terrors through the use of hypnosis–a case study: a brief communication. Int J Clin Exp Hypn. 1989;37(4):283–4.
43. Reid WH, Ahmed I, Levie CA. Treatment of sleepwalking: a controlled study. Am J Psychother. 1981;35(1):27–37.
44. Hurwitz TD, Mahowald MW, Schenck CH, Schluter JL, Bundlie SR. A retrospective outcome study and review of hypnosis as treatment of adults with sleepwalking and sleep terror. J Nerv Ment Dis. 1991;179(4):228–33.
45. Kohen DP, Mahowald MW, Rosen GM. Sleep-terror disorder in children: the role of self-hypnosis in management. Am J Clin Hypn. 1992;34(4):233–44.
46. Kingsbury SJ. Brief hypnotic treatment of repetitive nightmares. Am J Clin Hypn. 1993;35(3):161–9.
47. Hauri PJ, Silber MH, Boeve BF. The treatment of parasomnias with hypnosis: a 5-year follow-up study. J Clin Sleep Med. 2007;3(4):369–73.
48. Banerjee S, Srivastav A, Palan BM. Hypnosis and self-hypnosis in the management of nocturnal enuresis: a comparative study with imipramine therapy. Am J Clin Hypn. 1993;36(2):113–9.

49. Olness K. The use of self-hypnosis in the treatment of childhood nocturnal enuresis: a report on forty patients. Clin Pediatr (Phila). 1975;14(3):273–5.
50. Thomsom L. Hypnosis for children with elimination disorders. In: Westerman W, Sugarman L, editors. Therapeutic hypnosis with children and adolescents. Bethel: Crown House Publishing; 2007. pp. 387–416.

Part VIII
Medicolegal Aspects

Chapter 30
Sexsomnia: A Medicolegal Case-Based Approach in Analyzing Potential Sleep-Related Abnormal Sexual Behaviors

Michel A. Cramer Bornemann

Case Examples

Case 1

SP is an athletic healthy 32-year-old male without any history of illicit drug use and does not have a prior criminal arrest record. He has been divorced from his ex-wife, RP, for the last 6 years. From their tumultuous marriage, they have a 12-year-old daughter, AP, with whom they share joint custody. Though the divorced couple reside in the same community, their daughter primarily resides with her mother and only on very infrequent weekends and rare holidays may spend time with her father with whom there has been but little opportunity to develop a strong trusting relationship. An already tense father/daughter dynamic has been further complicated when SP recently decided to move into the apartment of his current 24-year-old girlfriend, HD, who works the evening shift of an upscale women's boutique specializing in intimate apparel.

Despite considerable misgivings of having her daughter spend the Thanksgiving Holiday with her father at his new girlfriend's apartment, RP decided to allow her daughter to be with her father given her daughter's enthusiasm over the unprecedented holiday invitation. It appears that AP was actually looking forward to the long holiday weekend as HD had also invited her to go shopping at the mall on the Saturday after Thanksgiving as she had that day off. As an "*early Christmas gift*", SP also promised his daughter additional spending money so that she could take advantage of the incredible post-Thanksgiving sales and to enjoy her time with HD. Unfortunately, AP and HD never had the opportunity to go shopping together at the mall ... nor did they have the opportunity to improve the tense dynamic in an otherwise broken household. Instead, it has been alleged on the evening of "*Black Friday*", the day

M. A. Cramer Bornemann (✉)
HealthEast Care Systems of Minnesota,
Saint Paul, Minnesota, USA
e-mail: michel9626@yahoo.com

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*

DOI 10.1007/978-1-4614-7627-6_30,

after Thanksgiving and the beginning of the Christmas Holiday shopping season that SP intentionally and knowingly engaged in sexual misconduct with his daughter, AP, to such an extent that would warrant the charge of sexual assault in the first degree. Specifically, SP was served with two felony counts: (i) Count 1—Aggravated Sexual Assault of a Child, 1st Degree Felony, and (ii) Count 2—Indecency with a Child by Contact, 2nd Degree Felony. In this particular jurisdiction within the United States, when such felonies involve a minor under the age of 14 years, the minimum penalty if convicted is very harsh and often without the opportunity for early parole regardless of the extent of the sexual assault.

On the night of the allegation, SP and his daughter had just turned on cable television in time to catch her favorite show at 10 pm while stretching out comfortably to relax on the very plush sectional sofa in the living room. Earlier, they had chosen a magnificent Christmas tree from a nearby charity lot, the first time they had done such a seasonal task together, and spent the greater portion of the afternoon and evening decorating HD's undersized living room. AP was lying toward the far end of the sofa while her father moved away from the middle and closer towards her so that he could get away from the lower branches of the Christmas tree and attain an unobstructed view of the flat screen television. Both SP and AP were hoping to surprise HD with their festive decorations and were eagerly anticipating HD's return from work later that evening. However, both inadvertently fell asleep on the sofa sometime between 10 and 11 pm.

SP actually remembered very little related to his nocturnal behaviors involving the allegations of sexual assault and indecency concerning the incident involving his daughter that occurred on the evening of "*Black Friday*". Nonetheless, his account of the incident, however sparse his memory has remained consistent when comparing reports from witness summary accounts, police investigator interviews, attorney interviews, and sleep forensics interviews.

As an independent contracted electrician, SP notes that the days leading up to the alleged incident were fraught with long work hours that were compounded by additional family-related responsibilities in anticipation of the coming holiday. A review of his earning statements reveals that SP had worked a total of 60 h over the course of 5 days resulting in a work day average of 12 h per day. Such long work hours were certainly not unusual for SP given his line of work. However, the length of his day was further extended upon finishing his contracted work as SP would do chores and "*odd jobs*" for his extended family to make additional income to minimize anticipated future debts as Christmas was fast approaching. The unpredictable nature of his contracting work, the extended length of his work day, and the stress of the holiday season conspired together to create an untenable situation of persistent fatigue and exhaustion for SP. During these 5 days, SP exhibited a well-defined nocturnal sleep pattern of an approximate sleep onset time of 12:30 am and arising in the morning to his alarm clock at 5 am. SP estimates a total sleep time average of 4 1/2 h which is in sharp contrast to his regular total sleep time of 7 h. Furthermore, SP notes that if there were no constraints placed upon him by either work or family-related responsibilities that his ideal sleep pattern would be a sleep onset time of 11 pm and a consequent sleep offset (or rise time) of 8 am. Clearly, SP had been experiencing a

conflict between his daytime responsibilities, his intrinsic sleep pattern, and his total sleep requirement resulting in marked sleep insufficiency that was most consistent with acute-on-chronic sleep deprivation.

SP notes that he was certainly not under the influence of any alcohol or illicit substances on the night of the allegation and does not take prescription medications, including sedative–hypnotic agents, or over-the-counter medications. SP then recalls that he and his daughter had settled in for the evening in the apartment that he shares with his current girlfriend, HD. SP recalls lying parallel immediately behind his daughter, each in a semirecumbent position, on the large sectional sofa. Their legs were resting comfortably upon the ottoman which was pushed up against the sofa. They were both fully clothed and had yet gotten prepared for bedtime. At 10 pm, he recalls watching the end of "The Simpsons" with "Family Guy", his daughter's favorite program, to immediately follow on the screen. SP does not recall much of "Family Guy" having suddenly fallen asleep. Next, SP notes waking up with the television still on, feeling confused, disoriented, and believing that he was with his girlfriend, HD, while lying on his right-side just behind her on the far end of the sectional sofa. SP states that it was not uncommon for him and his girlfriend to lie beside each other intertwined beneath a comforter on the sofa after a particularly long day to watch television only to fall asleep and never make it to the bedroom. On the night of the allegation, SP does not recall having experienced any dreams or overt behaviors and was never felt sexually aroused.

To his great dismay, SP quickly realized upon direct visualization that it was not his girlfriend that he had been embracing, as HD had not yet returned from work, but instead it was his daughter. Furthermore, as both were partially disrobed, SP "*freaked out*" and "*nauseated*" when he deduced that he may have been "*dry humping*" his daughter instead of merely "*hugging*". SP quickly removed himself from the situation, went to the bathroom, and washed his face with cold water to "gather composure". He returned to the living room to address his daughter and attend to her safety. AP was awake, visibly upset, distant, and did not want to interact with her father in any meaningful fashion.

Approximately 30 min after the incident, HD returned to her apartment to find SP and his daughter watching television on opposite ends of the sofa. They appeared distracted and HD immediately sensed something amiss. She proceeded to go to the kitchen to make her customary late night snack which was also offered to AP but she refused. SP was noted to have left the living room, went to his bedroom, and quickly fell asleep. HD approached AP to inquire as to how she was doing, whereupon AP noted that she was "fine" in an awkwardly far-away tone. As HD was preparing to go to bed, she heard AP crying hysterically and found her "shaking"—appearing very "scared". AP then described to HD what had occurred to her including that "dad fell asleep", "he held me tight", "*was rubbing up and down on my behind*", and "he finally woke up . . . he thought you were me". When asked the duration of the event, AP relayed to HD that "it wasn't long . . . may be 30–45 s . . . I didn't know what to do so I pretended to be asleep". HD was "shocked" as to what she had just heard and directly confronted SP. HD states that SP was very apologetic, believed that "it was an accident", and was "grossed out" for what may have occurred. He did not deny

or attempt to conceal or minimize the possibility of AP's experience. To protect AP, HD sternly ordered SP to immediately move out of their apartment until the situation could be better understood, whereupon SP agreed without incident after packing his essentials.

AP was checked-in to the emergency department triage at a local pediatric hospital by her biologic mother, RP, immediately after the incident at 2:00 am. Medical record documents reveal that the chief complaint was "molested by her father" and the patient's description was "I called my mom because what had happened, but didn't know what". AP underwent a sexual assault forensic assessment. Her appearance during the examination reveals that "she had poor eye contact, was tearful, only will answer with one word answers, shaking uncontrollably". Emergency department social services reported that AP stated that her biological father "was acting weird and pulled down her pants and panties and rubbed his thing on her bottom". AP refused to comply with a recommended genital examination though her panties were taken as potential evidence and later analyzed for DNA. AP was discharged from the emergency department at 6:15 am.

AP provided further details related to her father's inappropriate touch on that "*Black Friday*". This information was relayed to a Child Advocacy Center case worker on December 10 and to a pediatric physician on January 4. AP's description concerning the event has remained consistent. AP remembers watching television on the sofa with her father already asleep beside her. She fell asleep a short time later. She recalls that they were lying close together "feet to feet and head to head". She felt her father move toward her and thought that he was going to embrace her but he did not. Instead, she remembers her father: (1) "touched front with hand ... put hands around stomach ... went down and touched outside ... whole hand under clothes ... skin to skin", (2) pulling down her pants, (3) removing his own pants, and (4) pulling out his penis. She believes that his penis rubbed her behind "*up and down*" and "*maybe* in and out, in and out". Finally, AP notes that this was an isolated instance with her and that it "never happened before". AP also notes that when she stays with her father that she would routinely sleep in a bedroom that he would make available for her and that they typically do no sleep together in very close proximity.

Consequent criminal and clinical investigative endeavors have revealed that SP has a long history of unusual sleep-related nocturnal behaviors that begin as far back as childhood. MO, SP's biologic mother, recalls that her son had at least four significant episodes of "*sleepwalking*" between the ages of 8–14 years. One such memorable episode found her son "*sleepwalking*" into his parent's bedroom eventually making his way into their closet where he urinated in a corner and on his father's shoes. When initially confronted with these behaviors by his parents, SP had no memory for these nocturnal forays nor were these associated with any dreams. MO notes that she never was too concerned about these infrequent behaviors as they resolved by late adolescence. However, by early adulthood and continuing to the present, this apparent childhood "*sleepwalking*" has been supplanted by abrupt nocturnal behaviors with sexualized attributes. HD and a previous girlfriend of SP verify that he has engaged in sexualized behaviors after apparently falling asleep. AP's mother was not made available upon recommendation by opposing legal counsel to either

refute or corroborate such behaviors. Both women note that SP's nocturnal sexualized behaviors were infrequent, typically occur shortly after falling asleep, occur when they were sleeping nearby (i.e., on the bed or sofa) within reach of SP, and were more likely to occur when SP was under considerable stress. These nocturnal behaviors involved a spectrum of behaviors which include affectionate intimate embrace (i.e., "*spooning*"), touch upon the breasts and/or genitals, and/or "*dry humping*". Both women note that these behaviors, in general, were not denied and occasionally encouraged. In the latter, the behaviors may progress to sexual intercourse though the women suspected that SP was "*not entirely there*", appeared "*far away*", was strangely abrupt or aggressive, and were astounded to hear that SP had no memory for the sexual interlude the following morning.

Case 2

GD is 34-year-old male who has been on medical disability due to chronic lower back pain presumably the result of years of physical labor in the construction industry. He lives in a 2-bedroom apartment with his 38 year-old wife, MD, and her 12-year-old daughter from a previous marriage, LK. MD has been employed in the warehouse of an express postal delivery service for the last year and works the overnight shift from 11 pm to 7 am. In the mornings, GD was responsible for ensuring that LK woke up to her alarm so that she could be at her school bus stop by 7:15 am. The transition to junior high school had been difficult for LK as exhibited by her emotional lability with behavioral outbursts regularly directed towards her parents. Often sleeping past her morning alarm, GD would frequently find himself in LK's bedroom to rub or shake her shoulders in order to wake her up for school.

On one particular Wednesday, during 3rd period of school, LK texted a close friend to inform her that she needed to talk to her during the next break. During that lunchtime, LK confided in her friend that her "*father molested her*" that morning. With strong encouragement and support, LK reported to her school's guidance counselor that my "*father did things to me a father should not do to their daughter*". The counselor in turn immediately submitted a mandatory report to the child abuse hotline which resulted in the assignment of a Department of Human Services (DHS) caseworker and began the process of formal criminal charges against GD. A detective interviewed LK to learn that GD had entered her room that morning at 4 am. LK was initially sound asleep in a prone position and thought that she had again slept past her alarm when her stepfather began to rub her shoulders. However, her father repositioned and turned her over onto her back. She could smell the stench of alcohol on his breath as he moved his hand slowly across her abdomen, underneath her undergarments, and onto her genitals. As LK was speaking to the detective, she was tearful, visibly upset, and having difficulty describing the episode. It also turned out that at least 4 similar episodes had occurred over the previous 8 months. In each episode, LK noted that her stepfather would enter her room approximately 2 h before her alarm and in each situation she could smell the odor of alcohol upon

his breath. The latest episode ended in a similar fashion as the previous episodes with her stepfather "*fingering*" her. LK described that "*fingering*" specifically meant deep digital penetration into her vaginal vault with a repetitive in–out motion lasting not more than 1 min. LK stated that GD never uttered a word and did not touch her anywhere else before repositioning the pillows behind her head and closing the door of her bedroom behind him on his way out. When the detective asked LK why she did not attempt to stop or redirect her stepfather's behavior, LK simply noted that she was "*too scared*". LK confided in the detective that no one else had known about the "*abuse*", including her mother, as she was afraid her mother would not believe her and that such disclosure could "*tear the family apart*".

Later that afternoon, local law enforcement officials and the detective arrived at GD's apartment to place him in custody. He was first asked if anything unusual had happened the prior evening whereby he succinctly responded, "*I have no idea what you are talking about*". He was then confronted with the allegations of possible "*abuse and molestation*" and was read his Miranda Rights. GD was stunned, became belligerent, and initially resisted arrest. While in police custody, he provided little information only declaring that, "*I didn't do it"* and "*she's lying*". GD's wife, MD, was also surprised but above all concerned about the veracity of the allegations and eventually put her full support behind her husband. After being served with the formal count of aggravated sexual assault of a child, 1st Degree Felony, GD eventually posted bail whereupon he and his wife remained together while living in their 2-bedroom apartment. LK provisionally moved in with her biologic father who without delay filed for permanent custody.

MD had not been aware of GD engaging in any significant unusual or bizarre nocturnal behaviors during their 2 years of marriage, though on the two evenings in the week when they would sleep together she infrequently would wake up with him kissing and embracing her. She was never sure with these behaviors whether her husband was asleep but assumed this was an expression of his longing for her given that the intimate aspect of their relationship had taken a severe setback after she started her routine overnight work schedule. GD states that his mother recalls only two "*sleepwalking*" episodes as a child but one was especially memorable as he was found attempting to climb out of a 2nd floor window near his bunk bed. His "*sleep talking*" was a source of amusement to friends with sleepovers throughout adolescence. These nocturnal behaviors disappeared completely by early adulthood with the exception of rare occurrences of uncharacteristic asocial behaviors which GD associated with nights of significant alcohol use.

As to the charge of aggravated sexual assault, GD relayed a very different account to his defense attorney. He stated that on the evening of the allegation, he had run out of his prescription opiates and decided to medicate his unbearable low back pain with vodka. He explained that he drank a bottle of vodka until he "*fell asleep*" in the living room recliner. GD was not sure at what time he fell asleep but began drinking "*sometime after midnight*". GD then recalled being awoken by a feeling that "*someone was touching him*". GD further described this to his defense attorney as a feeling that was a combination of being in a state that was a "*dream/half-asleep*". Next, GD looked up, felt "*drugged*", and saw a "*topless, woman, beckoning me into*

the hallway". The woman was described as very tall, having radiant flowing golden silver hair, an ivory complexion, and an hour glass figure. She did not say a word . . . "*But it was as if we were communicating as I followed her down the hallway, into her bedroom, and onto her bed*". GD felt sexually aroused as he touched the beguiling woman . . . and "*then stopped and returned to his room*". GD states that he does not recall waking up his daughter that morning and believes that she got to the bus stop on her own accord without difficulty that day.

In both criminal cases, legal assistants performed medical literature reviews on an extensive array of search terms including sleep disorders, sleepwalking, dreams, and sexual assault. In the latter criminal case, the influence of alcohol was also introduced into the search field. After reviewing the results of the literature search, both criminal defense teams were relieved that they had arrived at the foundation of their probable defense. Regrettably, their defense was for a clinical condition that they had never before encountered in criminal law and thereby had never presented its supporting argument in a court of law. Thus, in regard to sleep-related abnormal sexual behaviors, it was necessary for the defense attorneys associated with each criminal case to retain the services of a credible sleep medicine expert to develop a "*Sleepwalking Defense*" for their respective clients. Such a sleep medicine expert would allow the attorneys to understand this clinical condition and to assist them in the further investigation of the case for the development of a possible defense of the criminal charges. Of course, key elements related to cases involving sleep-related abnormal sexual behaviors, or "*sexsomnia*", would include: (i) establishing that this is a formally recognized clinical disorder that may be effectively diagnosed and managed, (ii) commenting upon its prevalence and epidemiology, (iii) describing its underlying pathophysiologic mechanisms, (iv) detailing the possible spectrum and pattern of sexualized behaviors, and (v) commenting upon the individual's mental state when in the midst of such an episode. Lastly, features unique to each case would need to be addressed including: (i) the progression of "*sleepwalking*" from childhood into adulthood. (ii) the relationship between sexual repression, sexualized dreams, and wish fulfillment, and (iii) the role of alcohol as a trigger for sleepwalking and, in particular, "*sexsomnia*".

Clinical Discussion

Introduction

Sleep-related abnormal sexual behaviors are formally recognized to be within the disorders of arousal from non-REM sleep by the International Classification of Sleep Disorders (ICSD) 3rd edition. Of the subtypes of disorders of arousal (DOA), such sexualized behaviors are most often associated with confusional arousals but may also be associated with sleepwalking. This condition has been referred to by many terms, often interchangeably, in the medical literature and popular media including "*Atypical sexual behavior during sleep", "Sexual behavior in sleep"*, "*sexsomnia*,"

and "*sleep sex*". Similar to other parasomnias, sleep-related abnormal sexual behaviors have experienced a tremendous growth in general awareness and it is clear that it may be associated with a host of major interpersonal and clinical consequences. Articles which report on sleep-related abnormal sexual behaviors have appeared in many popular journals within recent years including WebMD, Psychology Today, and Newsweek [1]. Salacious stories involving young women and "*sleep sex*" with subsequent marital discord and trips to the therapist's couch are not uncommon in the tabloid press, particularly in the United Kingdom.

Despite the increased general awareness and formal clinical recognition, much confusion remains about sleep-related abnormal sexual behaviors particularly as a multitude of medical, psychiatric, and toxic conditions may have similar features or may mimic this condition. Accurate diagnosis is not only essential as it translates into an effective clinical management strategy with the most favorable benefit-to-risk ratio but also has significant legal and social implications. For instance, the "*Sleepwalking Defense*" has been looked upon favorably by defense attorneys and has been successfully applied in cases involving "*sexsomnia*" resulting in a complete acquittal, as in *State of Oregon v. James Kirchner* [2]. However, the penalty can be harsh if convicted such as in aggravated sexual assault if the victim is a minor who is 14 years of age or younger at the time of the crime. In many jurisdictions within the United States in such cases, the minimum penalty if convicted will be no less than 25 years with no chance for early parole. Despite some success in the court of law, many in the legal community remain skeptical over the legitimacy of "*sexsomnia*" as demonstrated by a recent update put forth by the National Center for the Prosecution of Child Abuse entitled "*Overcoming the Sleep Disorder Defense*" [3]. Sleep physicians who cannot only diagnose and manage sleep-related abnormal sexual behaviors but those who also interface with the legal community would appear to be particularly well poised to navigate this terrain which continues to be challenging and may have far-reaching implications.

Prevalence/Epidemiology

The classification of sleep-related abnormal sexual behaviors within the DOA from NREM Sleep recognizes the unitary nature of these parasomnias which is critical in understanding the spectrum of associated behaviors and/or cognitive states that are often linked. It has long been accepted that DOA in children, including confusional arousals, sleepwalking, and sleep terrors, is not necessarily uncommon. In a Canadian study that followed children between the ages of 2 ½ to 6 years, approximately 14.5 % of these children at any one particular time displayed sleepwalking [4]. In adults, a United Kingdom telephone survey of 4,972 individuals, revealed a prevalence of sleepwalking of 2.0 % and of confusional arousals of 4.2 % [5]. A Finnish cohort of 11,220 individuals aged 33–60 years provides not only the prevalence of sleepwalking in an adult population but also insight into its natural history [6]. In this study, adult men were more likely to sleepwalk compared to adult women

(3.9 vs. 3.1 %). Furthermore, those who reported sleepwalking often or sometimes in childhood did so as adults for 24.6 % of men and for 18.3 % of women. In adults who continue to sleepwalk, there was more than 84 % positive history of sleepwalking in childhood. In regards to frequency, sleepwalking was only reported as "*weekly*" in 0.4 % for both genders. Lastly, the prevalence of parasomnias declines as children grow as supported by a Canadian study of 664 boys and 689 girls [7].

Over the past few years, there has been without a doubt an increased awareness for "*sexsomnia*" or "*sleep sex*" amongst the general public that has been fervently driven by a host of media outlets. In 2005, "*sexsomnia*" was even offered as a controversial diagnosis on the popular American medical television drama series "House M.D." on episode 17, "Role Model". Despite increased awareness of parasomnias amongst clinicians, the prevalence of sleep-related abnormal sexual behaviors remains poorly defined. Trajanovic et al. [8] and Mangan et al. [9] used internet web-based surveys to assess a difficult to reach clinical population and concluded that sleep-related abnormal sexual behaviors are much more common than previously thought. Though internet web-based surveys certainly have distinct advantages including access to unique populations, it also has many inherent methodological problems including sampling and nonresponse issues. Thus, a true estimate of the prevalence of sleep-related abnormal sexual behaviors in the general community cannot be derived from these studies. Insight into the prevalence of sleep-related abnormal sexual behaviors in a clinical population has been offered in a retrospective analysis of medical records of sleep medicine patients by Chung et al [10]. Using a patient response questionnaire of 832 patients at a sleep disorders clinic, 7.6 % (63/832) were considered to have symptoms suggestive of "*sexsomnia*". Though this study reflects an inherent selection bias toward a sleep disorder clinic and cannot necessarily be extrapolated to the general community, its findings are consistent with the DOA—these behaviors, sleep-related abnormal sexual behaviors, are not necessarily uncommon.

Sleep-related abnormal sexual behaviors also have significant implications that reach outside the clinical realm. Sleep Forensics is a growing field most often associated with the "*Sleepwalking Defense*" in cases of homicide [11]. Cramer Bornemann and Mahowald at WorldSleep2011 in Kyoto, Japan, commented in their plenary presentation entitled "Violent Parasomnias—Forensic Implications" that a growing percentage of their sleep forensics work now involves assessing cases of potential sleep-related abnormal sexual behaviors [12]. Cramer Bornemann also presented at the 33rd International Congress on Law and Mental Health in Amsterdam, The Netherlands, in 2013 that over 33 % of the 250 forensics cases submitted for formal review from 2006–2012 are associated with charges of sexual assault.

State Dissociation and Sleep-Related Behaviors

It has long been thought that the unconscious mind, whether asleep or in a state of hypnosis, may reveal itself in words, mental images, or behaviors though its meanings remained obscured from the conscious mind by a formidable barrier of

repression. However, a breakdown of this psychic censorship may occur with "*dream-enactment*" behaviors, or "*sleepwalking*", which allow those with special interpretive skills to have privileged access into the motivations of the unconscious mind. Ultimately, a vast majority of these interpretations involve some degree of an attempt at inner conflict resolution or "*wish fulfillment*". Such dream theories when applied to sleep-related behaviors, such as those developed and influenced by Sigmund Freud, have been largely supplanted by modern scientific disciplines, including cognitive neuroscience and somnology, that are driven by rigorous methodology that require hypotheses that are both testable and verifiable. Nevertheless, the pseudoscience of certain aspects of "*Dream Theory*" continues to hold sway over the general public as supported by the everlasting success of dream interpretation manuals and the belief in the metaphorical significance of dream symbolism. Particularly in cases with legal implications, it is important to recognize when older, now discredited, paradigms for understanding human behavior remain in play. For instance, in a case involving a sexual-related offense potentially explained by sleep disorder, it would not be uncommon for the defense attorney to first develop an argument beginning with an inquiry into sexual frustration/repression, sexualized dreams, and even suppressed sexual fantasies. An ability to separate commonly held public bias from scientific objectivity is often the first step in clinical analysis.

Recent advances in neurophysiology coupled with refined neurodiagnostic imaging modalities now reveal that the three states of being (Wake, NREM Sleep, and REM Sleep) are modulated by a host of influences including the degree of aminergic and cholinergic neurochemical bias, CNS activation, and the degree of endogenous vs. exogenous input. Under normal physiologic conditions which include homeostatic drive and circadian rhythmicity, the process of state declaration is maintained in a stable and predictable fashion throughout a 24 h period. However, as the components of sleep frequently dissociate and oscillate, sleep and wake may be rendered into a state that is not yet fully declared, thereby finding itself in a temporary unstable state. Thus, sleep and wake, as well as its associated consciousness and unconsciousness, are not dichotomous states as they occur on a spectrum and are considered evanescent [13].

Parasomnias are the result of such state dissociation. Previously, Wake, NREM sleep, and REM sleep were thought to be the 3 states that once physiologically declared were mutually exclusive or an all-or-none condition. Recent research has revealed the combinations of one or more of these states is possible and results in unusual physiologic combinations with unstable states with altered levels of consciousness [14]. Such state dissociations are the consequence of timing or switching errors in the normal process of the dynamic reorganization of the CNS as it moves from one state to another. Elements of one state persist, or are recruited, erroneously into another state, often with fascinating and dramatic consequences. In such situations, higher cognitive function is absent, if not severely impaired, while the potential for motor capacity for the most part has been retained. The concept of state dissociation (Fig. 30.1) in humans helps to explain such phenomena as: hypnogogic hallucinations, REM sleep behavior disorder, and the DOA—including sleepwalking and sleep-related abnormal sexual behaviors [15–19].

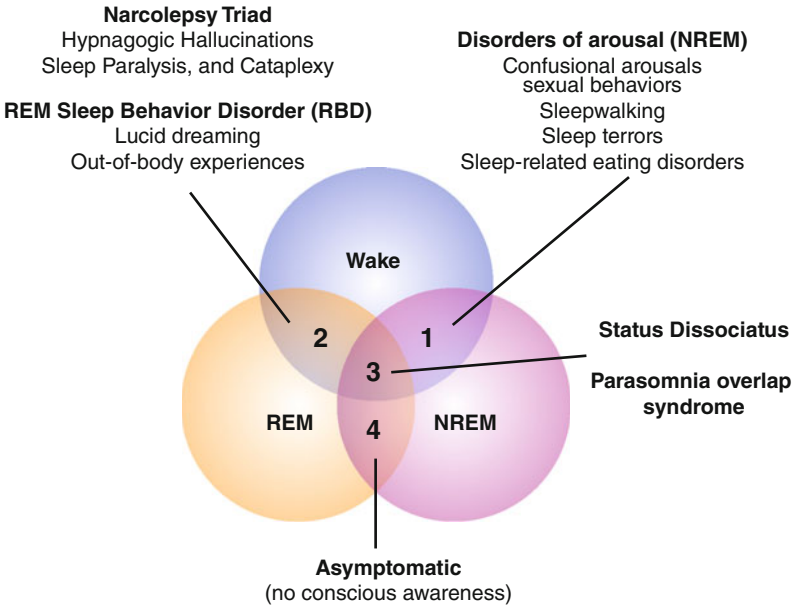


Fig. 30.1 Areas of overlap among states of being. (Data from Mahowald MW, Schenck CH [69])

Clinical Behavioral Analysis

Cases 1 and 2 involve young men who have had relatively few nocturnal behaviors in adulthood causing in little, if any, negative personal consequences. The implications of these nocturnal behaviors only became apparent when it directly involved their daughter, or step-daughter, which generated a mandatory reporting process culminating in felony criminal sexual assault charges with harsh consequences if convicted—a minimum penalty of 25 years of incarceration. Both cases shared many similar features including: (i) a childhood history corroborated by their mothers of "*sleepwalking*", (ii) nocturnal behaviors associated with the allegations that occurred during the first 1/3rd of the sleep period, (iii) behaviors that were without obvious premeditation, motivation, and/or intent, (iv) the behaviors that were atypical and not necessarily consistent with the character of the individual when awake, and (v) a behavioral pattern associated with the allegation that was suggestive of a sleep-related abnormal sexual behavior. Accordingly, pursuing a defense based upon a DOA from NREM sleep would not be unreasonable as these particular features of the two cases would appear to be a perfunctory fit of the "Guidelines to Assist in the Determination of the Putative Role of an Underlying Sleep Disorder in a Specific Violent Act" put forth by Cramer Bornemann and Mahowald [20]. However, these two cases diverge on several key features and it may be the details of these features which may have both major clinical and legal implications. Relevant divergent features between the

two cases include: (i) childhood frequency of "*sleepwalking*", (ii) the proximity between the parties involved, (iii) frequency of potential sleep-related abnormal sexual behaviors, (iv) the influence of sleep deprivation, (v) the influence of alcohol, and (vi) relevance of dreams at the time of the episode.

Schenck et al. provide the most comprehensive review of sexual behavior in sleep which included parasomnias and nocturnal seizures amongst other conditions [21]. Schenck et al. were able to collect and characterize 31 cases of parasomnia-related sexual activity of which a significant portion of these were published case series collected from Guilleminault et al. [22] and Shapiro et al. [23]. Interestingly, in their analysis of the 31 cases of parasomnia-related sexual activity not all were attributed to a DOA from NREM sleep as 3 cases were associated with REM sleep behavior disorder (RBD) while obstructive sleep apnea was comorbid in 4 cases. In cases of parasomnia-related sexual activity, there was a mean age of 32 years and a striking male predominance with a reported 4:1 male/female ratio. Age of onset of "*sleep sex*" for both genders was during early adulthood. A full range of sleep-related sexual behaviors with self and/or bed partners or others were reported, including masturbation, sexual vocalizations, fondling, sexual intercourse with climax, and sexual assault/rape. In terms of behavioral patterns, the females almost exclusively engaged in masturbation and sexual vocalizations, whereas the males were more apt to engage in fondling and sexual intercourse with females. Schenck et al. also point out that histories of multiple NREM sleep parasomnias were common with confusional arousals being predominant.

According to Schenck et al., sleep-related sexual activity was noted to be far more injurious to the bed partner than to the affected person in the parasomnia group. Adverse psychosocial consequences were common though pleasurable sexual experiences had also been reported by cosleepers [21]. A further analysis of the cases highlighting parasomnia-related sexual activity presenting as sexual fondling or sexual intercourse in Schenck et al. reveals that the vast majority of these cases occur with the affected individuals in close proximity to one another. Schenck et al. did note a case involving apparent parasomnia-related sexual intercourse between "*platonic*" friends who were not in close proximity to one another as they each initially fell asleep in separate rooms. However, this case appears to be contaminated by significant alcohol use "*after a night out drinking*" [24]. Though the issue of "*sexual RBD*" remains problematic on several accounts and at the very least is an atypical variant of RBD, it has been well-established that sleep-related abnormal sexual behaviors are primarily are DOA from NREM sleep for which the predominant form appears to arise from confusional arousals.

As close proximity is a key feature associated with injurious or violent behaviors arising from DOA from NREM sleep, it is not at all surprising that the cases featured by Schenck et al. exhibit close proximity to also be a key feature in parasomnia-related sexual activity. Once sleep-related abnormal sexual behaviors have adverse and/or injurious consequences, one must remain cognizant for their potential forensic implications and consider these also as asocial violent behaviors. Again, additional insight into the potential behavioral patterns of sleep-related abnormal sexual behaviors may be gathered from the study of confusional arousals. Pressman reviewed

32 cases of violence associated with DOA from NREM sleep (confusional arousals, sleep walking, and sleep terrors) drawn from medical and legal literature to determine the role of physical contact and proximity between affected individuals [25]. Of the 32 cases, Pressman identified 10 cases that were consistent with confusional arousals. Close proximity was found in 100 % of these cases and in 6 of the 10 cases the victim touched the sleeping individual or attempted to arouse them. This review supports the basic principle that in DOA from NREM sleep that the "*sleepwalker does not seek out their victim*". Typically, the situation is often circumstantial arising from the confluence of close proximity and/or triggered by direct physical contact set in motion, perhaps, by lack of foresight for the preexisting condition. Though untreated parasomnias are a chronic condition with potential for recurrent outbursts, Pressman notes in his review that significant cases of DOA from NREM sleep with forensic implications against other individuals tend to be isolated instances which almost never occur more than once. Thus, when additional claims with potential forensics implications are discovered in the investigation in a medicolegal case which broadens the criminal charges upon the defendant, sleep-related abnormal sexual behaviors as an argument for the defense should become suspect. In these cases, influences that may be more likely to be associated with inappropriate asocial or violent sexual behaviors should be pursued.

Central Pattern Generators and Fixed Action Patterns

That a broad spectrum of behaviors may arise in the absence of conscious wakefulness promotes an inquiry into potential mechanisms for complex behaviors including sleep-related abnormal sexual behaviors. The widely held impression that the brainstem and other more "*primitive*" neural structures primarily participate in elemental rather than behavioral activities is inaccurate. There is clear evidence that a broad spectrum of motor behaviors may originate from these more primitive structures—without involvement of more rostral neural structures. The axis involving central pattern generators (CPGs) and fixed action patterns (FAPs) is one potential mechanism to account for behaviors that arise from the platform of sleep which are without consciousness or intent. CPGs are dedicated networks of nerve cells that contain information that are necessary to activate different motor neurons in an appropriate sequence and intensity to generate motor patterns [26]. The fixed action pattern (FAP) is an indivisible behavioral sequence that when initiated will run to full completion. FAPs are invariant and are produced by a neural network known as the innate releasing mechanism in response to an external stimulus known. FAPs are considered to be "*hard wired"* task-specific behavioral patterns that are ubiquitous in the animal kingdom and provide a species-dependent survival advantage with their immediate efficient neurologic processing. As an example, one such FAP in humans is the palmar and plantar grasp reflexes which may be elicited shortly after birth in newborns and persist up to 6 months. This FAP appeared through evolution amongst primates,

so that the newborn can hold to the mother's hair and not fall off if she were to move suddenly.

The concept of CPGs has been well-recognized by Neurologists especially those who study the cortical and brainstem networks responsible for modulating rate and amplitude of mastication, swallowing, and breathing. When swallowing dysfunction occurs as a result of neurodegenerative conditions such as Parkinson's disease and amyotrophic lateral sclerosis (ALS), consideration for a potential disturbance of the underlying CPG has provided additional insights into the underlying pathology which may yield future therapeutic dividends [27, 28]. It has long been recognized that there are many similarities between certain parasomnias and epileptic seizures, most notably nocturnal frontal lobe epilepsy (NFLE). Moreover, Tassinari et al. recognized that many behaviors related to certain parasomnias and epileptic seizures share similar features suggestive of a stereotyped inborn FAPs initiated by CPGs [29]. Tassinari recognized CPGs as genetically determined neuronal aggregates in the mesencephalon, pons, and spinal cord that were linked from an evolutionary perspective with innate primal behaviors essential for survival. Instinctive behaviors that are consistent with the CPG/FAP axis can be divided into 5 behavioral categories including: (i) Alimentary such as chewing and swallowing, (ii) Defensive/predatory postures including territorial biting, (iii) Emotional including facial expressions and vocalizations, (iv) Locomotion including cyclic leg movements, and (v) Copulatory including repetitive pelvic thrusting.

In higher level primates, CPGs are predominantly inhibited by the influence wielded by the neomammalian cortex. Tassinari provides a neuroethologic model of brief temporary behaviors initiated by CPGs that may arise without consciousness under certain conditions from the platform of sleep. Thus, through the many transitions inherent within sleep, a period of state instability may occur resulting in state dissociation. Keep in mind that many of the CPGs are located in the brainstem and in close proximity to processes that govern the transitions from wake to sleep and from NREM to REM. In this state, aberrant neuronal impulses, or switching errors, may occur which may unleash CPGs that otherwise would have been suppressed in a fully declared state. This in turn can generate FAPs resulting in the abrupt onset of aberrant motor and/or emotional expressions that are inappropriate for the setting and uncharacteristic of the awake neocortical-mediated diurnal behaviors. FAPs are task-specific behavioral patterns that on outward appearance might be mistaken as motivated conscious behavior driven by intent. However, FAPS are instinctive patterned behaviors that are mechanistic and by nature have not been processed through higher order cognitive executive functions.

As a neuroethologic concept, the CPG/FAP axis sets a framework for future research by promoting a naturalistic approach through careful behavioral observation and methodical data collection to better understand the spectrum of sleep-related abnormal sexual behaviors for which the duration and complexity of behaviors remain not fully defined. This concept is particularly useful in sleep forensics as sleep-related abnormal sexual behaviors tend to have patterned behaviors and medicolegal referrals involving sexual assault continue to increase. Analysis of the behavioral details consistent (or inconsistent) within any component of the 5 behavioral categories of

the CPG/FAP axis often provides insight into assessing the degree of likelihood of sleep-related abnormal sexual behavior for a given case.

For example, in Case #1, SP was unfortunately in close proximity to his daughter, AP, when he inadvertently fell asleep. Isolation of the behavioral pattern reveals a relatively brief and simple behavioral pattern that was described as "*dry humping*". This patterned behavior is consistent with repetitive pelvic thrusting recognized within the copulatory category of behavioral patterns of the CPG/FAP axis. Though this feature alone does not provide conclusive evidence to account for SP's behavior on the night of the criminal allegation, it is one element which should be weighted favorably when reviewing the case in its entirety and determining the likelihood of sleep-related abnormal sexual behavior as the cause for the criminal complaint. In contrast, isolation of behavioral patterns in Case #2 reveals a more complex scenario consisting of several distinct processes in which the defendant, GD, engaged. These processes include the defendant: (i) walking from his recliner in the living room to his daughter's bedroom and opening her bedroom door, (ii) turning over his daughter, LK, from a prone to supine position, (iii) engaging in digital vaginal penetration, (iv) repositioning his daughter's pillows, and (v) closing his daughter's bedroom door as he made his way back to his recliner in the living room. Surely when defense options are limited, one may attempt to argue that any single feature separated from the complex scenario may be consistent with a parasomnia. However, in terms of DOA from NREM sleep, this case begins with a fundamental flaw as close proximity is not an essential feature. In cases with multiple processes, applying behavioral isolation to each process may be especially useful. If each isolated process is inconsistent with a CPG patterned behavior, consideration needs to be given that the processes expressed are in actuality that of a higher order cognitive executive function. Functions of the prefrontal cortex that are most relevant to self-conscious awareness are commonly termed "*executive functions*" [30] and are not consistent with behaviors that arise from sleep. An individual's ability to shift or adapt from one situation to the next and evidence of the ability to initiate dynamic problem solving strategies are examples of higher order cognitive executive functions and are generally not consistent with behaviors that arise from confusional arousals, including a sleep-related abnormal sexual behavior. Evidence of behaviors in Case #2 that are inconsistent with CPG/FAP behavioral constructs as they suggest involvement of higher order cognitive executive function include GD turning over his daughter (problem-solving), repositioning her pillows (problem-solving), and closing her bedroom door upon leaving (shift/adaptability). As in Case #1, though GD's behaviors are in sharp contrast with the CPG model, it is but a conceptual approach and does not alone absolutely exclude sleep-related abnormal sexual behaviors in his case. However, it should be a weighted feature in the final analysis of his case and coupled with lack of close proximity the likelihood of an argument in favor of a Parasomnia ("*Sleepwalking Defense*") appears to have been seriously eroded.

Associated Clinical Conditions and Influences

As reflected in the ICSD-3, Parasomnias are now firmly placed upon a foundation of a unitary State Dissociation paradigm. Disorders of arousal from NREM sleep are the most impressive and the most frequent of the parasomnias and it should come as no surprise that the most common cause of sexual behavior in sleep linked in the literature appears to be associated with confusional arousals though a few cases revealed an atypical association with RBD [22, 31]. Many endogenous and exogenous factors can affect state cycling/synchronization including: (i) Age, (ii) Sleep deprivation, (iii) Shift work, (iv) Hormonal factors, (v) Medical and/or mental health conditions, (vi) Pharmaceutical/toxic influences, and (vii) Environmental stressors. Clinically significant expressions of errors in state transitions seldom appear allowing one to deduce that the drive for complete state declaration must indeed be very robust given the unremitting neuronal cycling and the ever-present array of endogenous and exogenous influences upon the system. Unfortunately, from both a clinical and legal perspective, only few of these factors have been reported to be associated with sleep-related abnormal sexual behaviors though, again, characteristic features attributed to DOA from NREM sleep may provide additional insights. Sleep deprivation appears to be one such potentiating influence for those prone to confusional arousals or sleep walking. Studies by Montplaisir et al. suggest that sleepwalkers suffer from a dysfunction of the mechanism responsible for sustaining stable slow-wave sleep and that these individuals are particularly at risk when exposed to increased homeostatic sleep pressure [32].

Several reports have revealed an association between sexual behavior in sleep with OSA [23, 31, 33, 34] or Upper Airway Resistance Syndrome [23]. Shapiro et al. describe a case of sleep-related abnormal sexual behavior likely to be the direct result of untreated OSA as the sexual behaviors resolved with therapeutic intervention for the OSA. In this case, the subsequent recurrences of sleep-related abnormal sexual behaviors were related to withdrawal of the therapy [23]. Mahowald and Schenck also document a case of OSA that was associated with confusional arousals, sleep talking, and sleep-related abnormal sexual behaviors. In the latter condition, the patient's wife had noted that this emerging intimacy had completely resolved at the 1-month and 3-month CPAP compliance visits noting only that when the CPAP mask did not stay on his face was he prone to mildly groping her [35].

Generally regarded as a DOA from NREM sleep when arising as a primary sleep disorder, sleep-related abnormal sexual behavior can be associated with other medical conditions or influences, some of which had already been commented upon (Table 30.1). Dissociative disorders, not to be confused here with the concept of state dissociation, in the realm of mental health has been defined as conditions that involve the breakdown of memory, awareness, identity, and perception. This condition can easily mimic and be mistaken for a parasomnia when these have a nocturnal pattern or are subjectively associated with sleep. Conditions related to mental health are important to rule-out in medicolegal cases as this may determine the difference between a full acquittal, as offered by a parasomnia, and long-term mental health

Table 30.1 Other conditions associated with sexual behavior in sleep

REM sleep behavior disorder
Obstructive sleep apnea (OSA)
Epilepsy
Sleep-related dissociative disorders
Medications
Alcohol/illicit drug use
Malingering

institutional management. There are several dissociative disorders recognized by the DSM-IV including depersonalization disorder, dissociative amnesia, and dissociative fugue. Nocturnal episodes of dissociation may arise in 25 % of these patients. When assessed with objective measures, these episodes appear to arise from well-established EEG wakefulness near sleep onset or after established sleep though the subjective presentation was one that is compellingly sleep-related [36]. Plante and Winkelman in a 2008 review on psychiatric considerations in parasomnia discuss the differential diagnosis of unusual parasomnias and sleep-related dissociative disorders including sexualized behaviors [37].

Disorders of arousal from NREM sleep, particularly sleepwalking, have long been linked to individuals with mental health conditions through a broad range of medications either taken alone or in combination. Recently, Ohayon et al. assessed the prevalence and comorbid conditions of nocturnal wandering in the American general population. Nocturnal wandering is an abnormal state of consciousness which would include sleepwalking. In this cross-sectional study of 19,136 noninstitutionalized adults, Ohayon et al. found nocturnal wandering to have lifetime prevalence of 29.2 % and prevalence the previous year of 3.6 %. The study was particularly notable as the selective serotonin reuptake inhibitors (SSRIs) were associated with an increased risk of nocturnal wandering. These medications appear to precipitate events in individuals with a prior history of nocturnal wandering [38]. However, the literature only notes a single report where Escitalopram, an SSRI, has been associated with unusual sexual behavior in sleep [39]. Sedative–hypnotic agents, most notably the benzodiazepine and non-benzodiazepine class, have also been associated with sleepwalking. From the non-benzodiazepine class, Zolpidem has received much attention and has prompted much more serious warning labels in part due to its adverse effects including sleep-related eating disorder [40–43] and sleep-related driving [44, 45]. Again, there is a paucity of reports in the literature which ascribe an association between Zolpidem and sexual behavior in sleep [43, 46].

Despite previously held unsubstantiated beliefs coupled with popular media attention given to the association between alcohol and sleepwalking, there is no compelling scientific research data to support that a reasonable amount of alcohol will either elicit or prime the sleepwalking or sleep-related abnormal sexual behaviors [47]. Conservative estimates of the prevalence of sexual assault suggest that 25 % of American women have experienced sexual assault, including rape. Approximately 50 % of these cases involve alcohol consumption by the perpetrator, victim, or both [48, 49]. In year 2009, Connor et al. reported the results of a 12-month population-based survey on 16,480 New Zealanders to describe the prevalence of physical and

sexual assault and its association with alcohol use by the perpetrator [50]. This report revealed that nearly 7 % of men and 3 % of women reported having been physically assaulted. Sexual assault was reported in 1 % of women and 0.4 % of men with 45 % being assaulted more than once. More than 50 % of all sexual assaults involved a perpetrator who was reported to have been drinking. In medicolegal cases involving voluntary intoxication and addressing consequent culpability, alcohol binge drinking remains underappreciated in its involvement with antisocial behavior including inappropriate and/or uncharacteristic sexual behaviors. Alcoholic blackouts are episodes of amnesia that are primarily anterograde such that the alcohol impairs the ability to form new memories while the individual is intoxicated but does not erase memories before the toxic insult. These episodes may present as a Korsakoff-like syndrome which may go undetected by both law enforcement officers and healthcare providers with the individual capable of participating in seemingly purposeful, salient, and emotionally charged events for which they will have no memory. Although much is known about the effects of alcohol on decrements in motor performance, there is also compelling evidence that indicates acute alcohol use impairs the performance of frontal lobe-mediated tasks such as those that require judgment and impulse control [51]. Studies involving college students reported a high prevalence of risky behaviors during blackouts, including sexual activity with acquaintances and strangers and instigating other violent behaviors [52]. The alcoholic blackout clearly represents one of the many behaviors that may mimic parasomnias, especially sleep-related abnormal sexual behaviors, which are arguably exponentially much more prevalent and thus should be given appropriate weight when attributing likely causation in criminal allegations.

Malingering is infrequently encountered in a clinical setting in regard to sleep-related abnormal sexual behaviors and would appear to be more of a concern in a legal setting where it may be raised by the prosecution in opposition to the formulation of an anticipated defense. Here, a defendant may attempt to avoid culpability or punishment of an alleged criminal behavior including as sexual assault by feigning amnesia or "*memory blackouts*". As a useful starting point, the DSM-IV-TR suggests malingering should be suspected with any combination of the following: (i) medicolegal context, (ii) marked discrepancies between subjective complaints and objective findings, (iii) lack of cooperation with evaluations and/or treatment, (iv) presence of antisocial personality disorder. There are many validated clinical tools for consideration to begin the process of assessing or to rule out Malingering including the Shipley Institute of Living Scale (Shipley), the Minnesota Multiphasic Personality Inventory (MMPI-2), and the Test of Memory Malingering (TOMM) to name but a few. In medicolegal cases involving minors, concerns related to pedophilia often arise, especially when it involves a potential history of repeated abuse with the same victim or allegations involving other minors. In these situations, extreme caution should be exercised with consideration for outside consultation to include involvement of personnel specialized in psychosexual interviews and evaluations.

Forensics Analysis

The Role of Mens Rea in Forensics Analysis

There is now a greater degree of civic responsibility placed upon the field of sleep medicine given the legal community's growing recognition of sleep's broad implications on behavior ranging from cognitive impairment related to sleep deprivation in personal and public safety, pharmaceutical toxicity, and complex parasomnias. Sleep-related abnormal sexual behaviors have become of increasing concern to the legal community, most likely outpacing other violent parasomnias. The recognition of this clinical condition has been reflected by several seminars in the United States providing credits for Continued Legal Education (CLE) with the most notable being the Oregon Criminal Defense Lawyers Association seminar on "Sex Cases—When a Child Is Involved" in the Fall of 2011. Sleep Forensics (see Box 30.1) was born of the need to address civic responsibility while appreciating that advances in neuroscience have social implications and attempts to facilitate discourse between the two disparate disciplines of law and sleep medicine within currently held rules and regulations of the legal system.

Anglo-American law has traditionally defined criminal offenses as requiring both an *actus reus* and a *mens rea*. The state (or prosecution) must prove both types of elements in order to secure a conviction. Criminal law presumes that most human behavior is voluntary and that individuals are consciously aware of their acts. Based upon a straightforward world view, humans were embodied within the law possessing skills of practical deductive reasoning in an otherwise predictable environment. To be found guilty of a crime, a person must be in a certain mental state, called *mens rea* (guilty mind), necessary to have committed a crime, and have accomplished the physical components of the criminal act, called *actus reus*. From a neuroscientific point of view, the criminal act or *actus reus* component of the crime is of less interest than the essential element of *mens rea* in regard to both mechanism of behavior and culpability. In a medicolegal case involving potential sleep-related abnormal sexual behaviors, the element of *mens rea*, the mind, or that most complex of all organs—the brain, firmly becomes the fulcrum from which all will hang in the balance.

The application of sleep forensics is best based upon an adaptable conceptual approach utilizing the most current principles of cognitive neuroscience bolstered upon the framework of state dissociation as opposed to static precepts which simply lists or highlights diagnostic criteria and extrapolates associations with criminal behavior. In terms of sleep-related abnormal sexual behaviors, one needs to distinguish between a case that is purely clinical and whether it also has medicolegal implications. Cases with medicolegal implications are challenging as a clinical diagnosis may not be sufficient as it does not temporally address the *mens rea* of the criminal allegation. For instance, according to Ohayon et al. [38], nocturnal behaviors are not uncommon and a clinical history of some form of DOA from NREM sleep in childhood can often be uncovered with a retrospective lens . . . but this information does not necessarily provide a compelling legal argument. One primary goal of the

sleep forensics approach is to isolate salient cognitive elements at the moment of the criminal allegation in order to render an opinion on the defendant's *mens rea*. Elements of a dynamic forensics approach may also be applied in difficult clinical cases to provide direction toward a possible diagnosis.

Process Fractionation as a Tool to Assess Cognition

Sleep physicians on a daily basis appreciate, by interpreting polysomnographic studies, the state-determined uniformity of physiologic events that are consistent from patient to patient. The maintenance of physiologic homeostasis appears maintained in NREM whereas REM appears discordant and ostensibly oppositional. Even thermoregulation in REM is not consistent with man's phylogeny taking on a temporary poikilothermic status despite well-developed preoptic hypothalamic integrative mechanisms for homeothermy. Other normal state-dependent physiologic variations include REM-dependent penile tumescence and, of course, the inhibition of spinal motor neurons in causing motor paralysis or REM with muscle atonia [53]. Physiology during the process of the sleep period is state dependent as regions of the brain are selectively activated and/or deactivated as it transitions between NREM and REM. The changes in physiology are, to a degree, strikingly dramatic and repetitive in nature that one can often infer the sleep state based upon these changes alone. To analyze a process, such as sleep, and isolate its individual components in order to deduce its underlying state, NREM vs. REM, is a method called "*process fractionation*".

As noted earlier, higher order executive functions reside within the prefrontal cortex, specifically the dorsolateral prefrontal cortex (DLPFC), and are most relevant in discussions related to conscious awareness when assessing *mens rea*. Executive functions include self-observation, planning, prioritizing, and decision-making abilities that are based upon basic cognitive capacities together with attention, working memory, temporal memory, and behavioral inhibition [30, 54]. The transition from wake to NREM is characterized by frontal deactivation as reported by several positron emission tomography (PET) studies [55, 56] and quantitative EEG studies [57, 58]. Deactivation increases with the deepening of NREM sleep [59] and is maintained in the transition from NREM to REM sleep [60]. Interestingly, with the onset of REM sleep, limbic-related prefrontal cortex is reactivated sometimes to levels that exceed those of wake but the DLPFC remains deactivated [61, 62]. Dreams in REM are likely a combination of this latter neuroanatomical activation/deactivation which culminates in an experience of internally generated visual impressions, episodically strong unmodulated emotions, loss of logical rigor, and uncritical acceptance of the event that regularly lead to temporary delusion. Thus, in dreams, one typically assumes one is awake when in fact one is actually asleep. This all underscores the fact that the mind is a very poor judge of its own causation and of information processing by the brain. Also important are the implications for *mens rea* as PET and quantitative EEG studies support that the DLPFC is essentially "*off-line*" and inaccessible during sleep.

Wake, NREM sleep, and REM sleep are modulated by the degree of aminergic and cholinergic neurochemical bias, CNS activation, and the degree of endogenous vs. exogenous input. These states are orchestrated by a control system in the pontine brainstem through a reciprocal interconnection between aminergic inhibitory neurons and cholinergic excitatory neurons. The activity levels of these two groups of neurons also have an inverse relationship whereby the activity of the aminergic cells attains its peak during wake, declines during NREM sleep and is at its nadir during REM sleep. In contrast, cholinergic cells exhibit an opposite pattern of activity. The changes in brain state that result in normal and abnormal changes in the state of the mind all share a common process: an alteration in the influence of lower centers, principally located in the brainstem, upon the thalamus and cortex located in the upper brain. This means that consciousness, too, is state dependent [13, 63]. Given that the mind is a poor judge of its own causation and errors in the determination of its own state are common, how can one retrospectively determine the degree of consciousness . . . as in criminal case potentially explained by a sleep-related abnormal sexual behavior? As sleep physicians analyze physiologic components in a polysomnographic study to deduce NREM from REM, so, too, can one apply process fractionation and isolate components of consciousness to determine whether a behavioral pattern was consistent with that which arose from the platform of sleep.

The American Law Institute's Model Penal Code (MPC) of 1962 attempts to provide guidance to difficult relationships between *mens reus* and *actus reus* including a culpability requirement for each material element of the offense. Voluntariness is the first step in establishing *mens rea* which if successfully proven by the state then proceeds to assess liability. As voluntariness is absolutely fundamental to *mens rea*, it is shocking that the MPC never explicitly defines the term "*voluntary*". Furthermore, as voluntariness is to *mens rea*, consciousness is to voluntary conduct. Despite being impressively progressive for its time, the MPC ultimately arrived at a static dichotomous all-or-none perception of consciousness that is out of step with contemporary thought and certainly not consistent with current neuroscientific principles or constructs of consciousness [64]. A revision of the MPC was performed in the early 1970s but there have been no systematic reviews to assess the MPC against scholarly criticisms since the initial publication. In cases involving sleep-related abnormal sexual behaviors with forensic implications, if the behavior arose from sleep, one can then also deduce that the DLPFC was "*off-line*" and not accessible. The implications for this association with *mens rea* are self-evident leaving the court system to render a decision accordingly—but a decision nonetheless educated with the current constructs of cognitive neuroscience.

The legal paradigm that consciousness is a relative dichotomy is in stark contrast with that of cognitive neuroscience and clinical medicine. After all, the Glasgow coma scale, which evaluates level of consciousness after a head injury by assessing ocular, verbal, and motor responses, is not based upon a binary value but rather a scale from 3 to 15. Consciousness has been defined as our awareness of our environment, our bodies, and ourselves. To be human is also to have awareness of awareness and to have "*meta-awareness*"—an awareness of oneself. To better understand the human

Table 30.2 Ten components of consciousness

Attention	Selection of input data
Perception	Representation of input data
Memory	Retrieval of stored representations
Orientation	Representations of time, place, and persons
Thought	Reflection upon representations
Narrative	Linguistic symbolization of representations
Emotion	Feelings about representations
Instinct	Innate propensities to act
Intention	Representations of goals
Volition	Decisions to act

mind and to develop an experimental approach, cognitive neuroscience now recognizes at least 10 distinct components that constitute consciousness [65]; Table 30.2.

The consciousness state paradigm recognizes that all 10 components of consciousness change to varying degrees as the brain changes state and does so in a repetitive and stereotyped manner over the sleep–wake cycle. At sleep onset, consciousness is altered in predictable ways which begin with loss of awareness of the outside world. With a Stage I EEG, some individuals may experience short-lived dreams but their content departs progressively from their previous waking experience. As brain activation falls, consciousness is further modulated when entering into NREM stage II sleep and may be obliterated as the EEG spindles, which reflect independent oscillation of the thalamocortical system, block both external and internal signals within the brain. Arousal from NREM stage III/IV is difficult and often requires frequent and repeated challenges with noxious stimuli. Once awakened, individuals may demonstrate confusion and disorientation that may last several minutes with a strong tendency to return to sleep. This process has been labeled sleep inertia and is particularly acute during recovery from sleep deprivation [66]. In NREM stage IV, the brain is maximally deactivated and responsiveness to external stimuli is at its lowest level. Vivid dreams seem to be most correlated with REM stage sleep such that it has been suggested that dreaming is our conscious experience of brain activation in sleep. The changes with each component of consciousness appear to be of such dramatic magnitude that strong inferences can be made about the major physiological underpinnings of consciousness [67]; (Table 30.3). The consciousness state paradigm sets a foundation for both clinical translational research and forensics investigation as it is well-suited for the method of process fractionation in attempting to determine the state of a behavior. In the latter, it may be a beneficial tool to provide additional guidance in an otherwise challenging clinical case involving Sexual Behaviors in Sleep, but is above all a useful tool in addressing *mens rea* in cases with legal implications.

Therefore, in sleep-related abnormal sexual behaviors, process fraction will attempt to discover components of consciousness that are consistent with NREM sleep as this will also directly account for the underlying mechanisms which contain the neurochemical bias and the degree of CNS activation/deactivation of pivotal neuroanatomical centers to account for such outwardly bizarre irrational behaviors. The consciousness state paradigm complements the concept of state dissociation and affirms many of clinical findings associated with components of consciousness

Table 30.3 Contrasts in components of consciousness between states. (From Hobson JA. [65]. Modified and reprinted with permission from Cambridge University Press)

	Wake	NREM	REM	Causal Hypothesis
Sensation & Perception	Vivid, externally generated	Dull or absent	Vivid, internally generated	Presynaptic inhibition, Blockade of sensory input
Thought	Logical and progressive	Logical and perseverative	Non-logical and bizarre	Loss of attention memory and volition leads to failure of sequencing and rule inconstancy; analogy replaces analysis
Attention	Intact, vigilant	Lost	Lost	Decreased aminergic modulation causes a decrease in signal to noise ratio
Orientation	Intact	Unstable	Unstable	Internally inconsistent orienting signals are generated by cholinergic system
Emotion	Inhibited	Weak	Episodically Strong	Cholinergic hyperstimulation of amygdala and related temporal lobe structures
Instinct	Inhibited	Weak	Episodically Strong	Cholinergic hyperstimulation of hypothalamus and limbic forebrain triggers CPG/FAP axis
Aminergic Inhibition (-)				Aminergic Inhibition (-)
Cholinergic Excitation (+)				Cholinergic Excitation (+)

in DOA from NREM sleep. In this regard, it comes as no surprise that both Schenck et al. and Pressman in their reports document significant, or complete, amnesia immediately after sleep-related abnormal sexual behaviors or violent confusional arousals with a relative paucity of dream content [21, 25].

Summary and Closing Case Statements

Sexual behaviors in sleep may be the result of many conditions or influences. When confronted by a patient, or client, potential conditions or influences will need to be considered to develop an appropriate differential diagnoses from which an effective strategy can ensue to either confirm or refute that the sexual act occurred in/from sleep. This initial step in exclusion is imperative not only to proceed toward optimal

clinical management but also because only few of these medical conditions offer the potential for a complete acquittal of all criminal charges in a court of law. Sexual behaviors in sleep occur through a diverse pathophysiologic process appearing through a common pathway attributable to DOA from NREM sleep. Under this parasomnia subtype, they are given the term sleep-related abnormal sexual behaviors and are most often associated with confusional arousals, though sleep walking has been reported as well. As had been supported by the ICSD-2 and now the ICSD-3, polysomnography is not required for the diagnosis in DOA from NREM sleep and their subtypes, including sleep-related abnormal sexual behaviors. Though polysomnography may be of utility to evaluate for the presence of other conditions such as REM sleep behavior disorder or OSA when clinically suspected, polysomnography is not routinely performed as part of a medicolegal evaluation in part as this diagnostic tool is not temporally associated with the crux of the legal focus upon *mens rea* with the criminal allegation (See Box 30.2). Once diagnosed, potentiating influences such as sleep deprivation and OSA should be addressed and treated. Effective treatment for sleep-related abnormal sexual behaviors has been reported in the literature with the clonazepam which is a benzodiazepine, though its mechanism of action is not well understood [68].

Case 1 and 2 have many similarities including a childhood history of sleepwalking reported by their mothers, nocturnal behaviors that persisted into adulthood, sexualized behaviors noted by female partners that were apparently benign, and amnestic sexualized behaviors involving their (step) daughters with legal implications. From a clinical perspective, it is no surprise that the nocturnal behaviors were not of clinical concern to either of the defendants despite the apparent chronicity of the behaviors as they were not a cause for alarm until the behaviors impacted a vulnerable individual under inappropriate circumstances. It is also no surprise that legal defense teams associated with both defendants each independently determined after extensive literature-based research that a "*Sleepwalking Defense*" was the most likely avenue to formulate a compelling argument as a foundation for an acquittal. Case 1 and 2 (Table 30.4) highlight the measures taken to assess challenging nuanced cases where the forensic implications may be the impetus for the clinical assessment. In these situations, a comprehensive approach in the assessment of sexual behavior in sleep is recommended including a thorough understanding of the epidemiology, natural history, and diagnostic criteria for both DOA from NREM sleep and its subtype—sleep-related abnormal sexual behavior. Strength in the determination for both the clinical condition and the forensic inquiry as related to *mens rea* is enhanced by applying tools to further assess internal consistency between NREM and its associated components of consciousness.

Case 1 exemplifies an individual who has a strong clinical history of nocturnal behaviors in childhood and into adulthood that closely matches what one would expect as the natural progression for one who has an unremitting DOA from NREM sleep. Furthermore, into adulthood, other conditions, including the possibility of toxic contamination, have been excluded and his nocturnal forays appeared to be primed by sleep deprivation. Based upon a comprehensive retrospective clinical analysis, there is a strong likelihood that this individual had a DOA in childhood (Diagnosis—Sleep walking) and has one as an adult (Diagnosis—sleep-related abnormal sexual behaviors). From a forensics perspective, the behaviors that are temporally associated with

Table 30.4 Clinical and forensics summary of Case # 1 vs. Case # 2. (Data from Cramer Bornemann MA [20])

	Case #1	Case #2
Clinical history of vhildhood sleepwalking	Strong	Moderate
Clinical history of "*sexsomnia*" in adulthood	Strong	Weak
Potentiating factors for DOA NREM	Sleep deprivation	Absent
Relevant behavior occurred within 2 h of Sleep	Yes	Yes
Relevant behavior was abrupt, immediate, senseless, w/o apparent premeditation	Yes	Yes
Close proximity, victim happened to be present nearby	Yes	No
With return to consciousness, dysphoric emotional response, no attempt at concealment	Yes	No
Contamination by other conditions (Alcohol, medications, psychiatric, etc.)	No	Yes Irresponsible alcohol use Possible opiate influence
Behavior consistent with CPG/FAP axis	Yes (pelvic thrusting)	No
Process fractionation—components of consciousness consistent with changes found in NREM	Yes Amnesia, orientation lost, emotion—episodically strong, instinct—episodically strong	No Evidence of attention and orientation, dream recall less likely in NREM
Clinical assessment Pediatric diagnostic probability	Childhood sleepwalking <Strong>	Childhood sleepwalking <Moderate>
Clinical assessment Adult diagnostic probability	Adult "sexsomnia" <Strong>	Adult "sexsomnia" <Weak>
Sleep forensics Parasomnia "*sexsomnia*" *d*efense	*Charge* 1: Sexual assault *Charge* 2: Indecency	*Charge*: Sexual assault

the criminal allegations are also consistent with the CPG/FAP axis as well as having the appropriate component of consciousness. Thus, it appears very likely that the behaviors in Case 1 arose from the platform of sleep from which it can then be deduced that DLFPC was "*off-line*". Case 1 presents a compelling clinical history with strong diagnostic support but more importantly arrives at a medical opinion which directly connects the behaviors and the state of consciousness with the criminal allegations to *mens rea* so that the court of law can proceed with an informed decision.

Based upon a comprehensive retrospective clinical analysis, Case #2 at best is an individual that had a DOA in childhood (Diagnosis—Sleep walking) but as an adult a diagnosis for sleep-related abnormal sexual behaviors seems weak—or at least premature. The progression from rare sleep walking episodes in childhood into adulthood also does not take a characteristic profile as the defendant's rare occurrences of nocturnal uncharacteristic asocial behaviors were associated with nights

of significant alcohol use. Given that there is no compelling evidence to support responsible alcohol use as a trigger for sleep walking, it appears likely that these behaviors are directly attributable to the degree of alcohol intoxication. It is also interesting to note that there is no significant progression of any type of DOA from NREM sleep from the end of childhood up to the time of the criminal allegations. Thus, the clinical history and progression is relatively weak. From a forensics perspective, in the evaluation of behavior that are temporally associated with criminal allegations, it is first important to exclude likely causative factors as parasomnias with forensic implications are quite unusual. Case #2 is clearly contaminated with inappropriate degree of alcohol consumption with the possibility of opiate influence. Further evaluation applying the CPG/FAP axis and process fractionation also reveals other inconsistencies which include evidence of dream mentation and higher order executive functioning. Though the patient did exhibit amnesia which is a consistent finding in individuals with having just experienced a confusional arousal, it is also consistent with alcohol binge drinking. Though no one particular element would completely exclude a "*Sleepwalking Defense*", the totality of inconsistencies taken together result in a case for which a meritorious argument in favor would be extremely difficult to fathom.

Sexual behaviors in sleep are perhaps not as uncommon as once thought and can take on many expressions. The public's fascination with "*sexsomnia*" may equate this condition with unrestrained libidinous sexual intercourse between strangers but the most common expression of this condition may be an inappropriate and unwanted emerging intimacy between individuals who by tacit agreement have chosen to sleep in close proximity. It would be understandable that this condition would have a tendency to be underreported especially if the behaviors were relatively benign, occurred between individuals in a committed relationship, and was not a source of relationship discord. However, significant concern arises when those who are prone to this condition, either by mere circumstance or by poor judgment, find themselves in close proximity with a vulnerable individual, such as a minor, or with an individual who misinterprets the behavior. The sleep forensics experience in the United States has revealed an alarming increase in the number of cases of sexual assaults purported to be attributed to "*sexsomnia*" where the perpetrator is an adult male and the victim is a minor under the age of 14 years. If such legal cases are indeed a bellwether, a proposal could be made for more rigorous controlled epidemiologic studies into this condition to better define its prevalence and characteristics as part of public policy to ensure personal and public safety—especially in those who cosleep with children. Despite its increasing recognition, there also remains significant skepticism, if not disdain, related to "*sexsomnia*" by reports refuting this condition by the National District Attorneys Association's National Center for Prosecution of Child Abuse [3]. To counteract both media driven bias and the general skepticism emanating from an adversarial-driven court system, one should be equipped with a combination of cognitive neuroscience constructs and of salient clinical acumen to navigate the topology of sexual behavior in sleep to provide the most appropriate patient-centered care and to be a resource to the legal community when indicated.

Practical Points

- Sleep-related abnormal sexual behaviors are formally recognized as a clinical or pathologic subtype within the DOA from non-REM sleep by the ICSD-3.
- Sleep-related abnormal sexual behaviors are most often associated with confusional arousals. As such, if another individual is engaged with these behaviors, proximity is often a key element.
- A full range of sleep-related sexual behaviors with self and/or bed partners or others have been reported, including masturbation, sexual vocalizations, fondling, and sexual intercourse. There is an association between gender and the prevalence of the type of sleep-related sexual behavior.
- There is no compelling clinical-based evidence to support that alcohol is a priming influence for sleep-related abnormal sexual behaviors. Behaviors arising from irresponsible alcohol use or overt alcohol intoxication should be viewed for what it is and clinically managed accordingly.
- Amnesia is a featured element in NREM parasomnias, including sleep-related abnormal sexual behaviors.
- Sleep-related abnormal sexual behaviors are not associated with psychiatric conditions and are not the result of sexual frustration/repression or "*wish fulfillment*". Parasomnias can be best understood upon the neuroscientific construct of state dissociation.
- Concerning sleep-related abnormal sexual behaviors with forensic implications including criminal allegations, arriving solely at a clinical diagnosis is insufficient. In these cases, one also needs to address *mens rea*. Here, behavioral pattern analysis and process fractionation may prove to be useful tools to assess cognition at the time of the allegation.

Box 30.1: Sleep forensics definition
The application of the principles and tools of neuroscience as applied to somnology and sleep medicine that have been widely accepted under international peer-review to the investigation in understanding unusual, irrational, and/or bizarre human behaviors associated with criminal allegations which is to undergo further examination in a conflict resolution legal atmosphere and/or courtroom.

Box 30.2: The utility of polysomnography in medicolegal cases
Even frank sleepwalking during a formal sleep study would only indicate that the individual was a sleepwalker—not that sleepwalking was involved at the time of the crime. Thus, a diagnostic tool as polysomnography would not be temporally associated with any questions related to *mens rea* in a criminal allegation. Furthermore, despite incredible advances in the neurosciences, several

cautionary notes must be provided which could unfairly bias the jury. The first is a condition that has been called by Stephen Morse, University of Pennsylvania Law School, as "Brain overclaim syndrome" [70, 71]. In general, the public has an overfascination with new developments in science and will often prematurely grant scientific statements as sheer truth, though those arguments cannot be conceptually or empirically sustained. As Michael Gazziniga, member of the President's Council on Bioethics comments, "there is apprehension that high-tech biomedical appearance of the neuroscience tests will carry undue weight with juries, especially jurors whose expectations about the use of forensic science have been conditioned by television courtroom dramas" [72, 73]. In a court of law, the undisciplined use of scientific technical data is a real concern especially given the public misperception that science is a field that deals with absolute certainties when in actuality it is a field that reflects probabilities of occurrence. In many ways, the legal community has misrepresented the nature of science for many years and continues to attempt to do to so in an admittedly adversarial environment.

References

1. Underwood A. It's called 'sexsomnia'. Newsweek. 2007 Jun 11;149(24):53.
2. Reese SE. Beautiful words: State v. James Kirchner. The Oregon Defense Attorney. 2008; November/December:24–5.
3. Badawy RS. Sexsomnia: overcoming the sleep disorder defense. National District Attorneys Association's National Center for Prosecution of Child Abuse. 2010;22(4):1–7.
4. Petit D, Touchette E, Tremblay RE, Boivin M, Montplaisir J. Dyssomnias and parasomnias in early childhood. Pediatrics. 2007 May;119(5):e1016–25.
5. Ohayon MM, Guilleminault C, Priest RG. Night terrors, sleepwalking, and confusional arousals in the general population: their frequency and relationship to other sleep and mental disorders. J Clin Psych. 1999 Apr;60(4):268–76; quiz 77.
6. Hublin C, Kaprio J, Partinen M, Heikkila K, Koskenvuo M. Prevalence and genetics of sleepwalking: a population-based twin study. Neurology. 1997 Jan;48(1):177–81.
7. Laberge L, Tremblay RE, Vitaro F, Montplaisir J. Development of parasomnias from childhood to early adolescence. Pediatrics. 2000 Jul;106(1 Pt 1):67–74.
8. Trajanovic NN, Mangan M, Shapiro CM. Sexual behaviour in sleep: an internet survey. Soc Psych Psych Epid. 2007 Dec;42(12):1024–31.
9. Mangan MA, Reips UD. Sleep, sex, and the web: surveying the difficult-to-reach clinical population suffering from sexsomnia. Behav Res Meth. 2007 May;39(2):233–6.
10. Chung SA, Yegneswaran B, Natarajan A, Trajanovic N, Shapiro CM. Frequency of Sexsomnia in sleep clinic patients. Sleep. 2010;3:A226.
11. Vlahos J. The case of the sleeping slayer. Sci Am. 2012;307:48–53.
12. Cramer BMA, Mahowald MW. Violent parasomnias—forensic implications. Sleep and Biological Rhythms. 2011;9(4):217.
13. Hobson JA. REM sleep and dreaming: towards a theory of protoconsciousness. Nat Rev Neurosci. 2009 Nov;10(11):803–13.

14. Mahowald MW, Cramer BMA, Schenck CH. State dissociation, human behavior, and consciousness. Curr Top Med Chem. 2011;11(19):2392–402.
15. Mahowald MW, Schenck CH. Dissociated states of wakefulness and sleep. Neurology. 1992;42:44–52.
16. Mahowald MW, Schenck CH. Dissociated states of wakefulness and sleep. In: Lydic R, Baghdoyan HA, editors. Handbook of behavioral state control: cellular and molecular mechanisms. Boca Raton, FL: CRC Press; 1999. pp. 143–58.
17. Nelson KR, Lee SA, Schmitt FA. Does the arousal system contribute to near death experience? Neurology. 2006;66:1003–9.
18. McNally RJ, Clancy SA. Sleep paralysis, sexual abuse, and space alien abduction. Transcult Psych. 2005;42:113–22.
19. McNally RJ, Clancy SA. Sleep paralysis in adults reporting repressed, recovered, or continuous memories of childhood sexual abuse. Anxiety Disorders. 2005;19:595–602.
20. Cramer BMA, Mahowald MW. Sleep forensics. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. 5th ed. Philadelphia: Elseviers Saunders; 2011. pp. 725–33.
21. Schenck CH, Arnulf I, Mahowald MW. Sleep and sex: what can go wrong? A review of the literature on sleep related disorders and abnormal sexual behaviors and experiences. Sleep. 2007 Jun;30(6):683–702.
22. Guilleminault CM, Moscovitch A, Yuen K, Poyares D. Atypical sexual behavior during sleep. Psychosom Med. 2002;64(2):328–36.
23. Shapiro CM, Trajanovic NN, Fedoroff JP. Sexsomnia—a new parasomnia? Can J Psych Rev. 2003 Jun;48(5):311–7.
24. Ebrahim IO. Somnambulistic sexual behaviour (sexsomnia). J Clin Forensic Med. 2006 May;13(4):219–24.
25. Pressman MR. Disorders of arousal from sleep and violent behavior: the role of physical contact and proximity. Sleep. 2007 Aug;30(8):1039–47.
26. Grillner S. The motor infrastructure: from ion channels to neuronal networks. Nat Rev Neurosci. 2003 Jul;4(7):573–86.
27. Hunter PC, Crameri J, Austin S, Woodward MC, Hughes AJ. Response of parkinsonian swallowing dysfunction to dopaminergic stimulation. J Neurol Neurosurg Psychiatry. 1997 Nov;63(5):579–83.
28. Aydogdu I, Tanriverdi Z, Ertekin C. Dysfunction of bulbar central pattern generator in ALS patients with dysphagia during sequential deglutition. Clin Neurophysiol. 2011 Jun;122(6):1219–28.
29. Tassinari CA, Rubboli G, Gardella E, Cantalupo G, Calandra-Buonaura G, Vedovello M, et al. Central pattern generators for a common semiology in fronto-limbic seizures and in parasomnias: a neuroethologic approach. Neurol Sci. 2005;26:s225–s32.
30. Goldberg E. The executive brain: frontal lobes and the civilized mind. 1st ed. New York, NY: Oxford University Press; 2001.
31. Della MG, Dittoni S, Frusciante R, Colicchio S, Losurdo A, Testani E, et al. Abnormal sexual behavior during sleep. J Sex Med. 2009 Dec;6(12):3490–5.
32. Zadra A, Pilon M, Montplaisir J. Polysomnographic diagnosis of sleepwalking: effects of sleep deprivation. Ann Neurol. 2008;63:513–9.
33. Hurwitz TD, Mahowald MW, Schluter JL. Sleep-related sexual abuse in children. Sleep Rev. 1989;18:246.
34. Rosenfeld DS, Elhajjar AJ. Sleepsex: a variant of sleepwalking. Arch Sex Behav. 1998 Jun;27(3):269–78.
35. Schenck CH, Mahowald MW. Case 24: Sexsomnia and obstructive sleep apnea. In: Culebras A, editor. Sleep neurology: common and uncommon presentations. 1st ed. New York: Cambridge University Press; 2010.
36. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW. Dissociative disorders presenting as somnambulism: polysomnographic, video and clinical documentation (8 cases). Dissociation. 1989;11(4):194–204.

37. Plante DT, Winkelman JW. Parasomnias: psychiatric considerations. Sleep Med Clin. 2008;3(2):217–29.
38. Ohayon MM, Mahowald MW, Dauvilliers Y, Krystal AD, Leger D. Prevalence and comorbidity of nocturnal wandering in the U.S. adult general population. Neurology. 2012 May 15;78(20):1583–9.
39. Krol DG. Sexsomnia during treatment with a selective serotonin reuptake inhibitor. Tijdschrift voor psychiatrie. 2008;50(11):735–9. (Sekssomnia tijdens behandeling met een selectieve serotonineheropnameremmer).
40. Miranda M, Seijas D, Castillo JL, Perez JC. Zolpidem induced sleep related eating disorder. Revista medica de Chile. 2010 Aug;138(8):1067–9. (Trastorno Alimentario del Sueno inducido por el hipnotico Zolpidem).
41. Hoque R, Chesson AL Jr. Zolpidem-induced sleepwalking, sleep related eating disorder, and sleep-driving: fluorine-18-flourodeoxyglucose positron emission tomography analysis, and a literature review of other unexpected clinical effects of zolpidem. J Clin Sleeep Med. 2009 Oct 15;5(5):471–6.
42. Yun CH, Ji KH. Zolpidem-induced sleep-related eating disorder. J Neurol Sci. 2010 Jan 15;288(1–2):200–1.
43. Schenck CH, Connoy DA, Castellanos M, et al. Zolpidem-induced amnestic sleep-related eating disorder (SRED) in 19 patients. Sleep. 2005;28(Abstract Supplement):A259.
44. Pressman MR. Sleep driving: sleepwalking variant or misuse of z-drugs? Sleep Med Rev. 2011 Oct;15(5):285–92.
45. Poceta JS. Zolpidem ingestion, automatisms, and sleep driving: a clinical and legal case series. J Clin Sleep Med. 2011 Dec 15;7(6):632–8.
46. Schenck CH. Paradox lost: midnight in the battle-ground of sleep and dreams. Minneapolis, MN: Extreme Nights, LLC; 2005.
47. Pressman MR, Mahowald WM, Schenck CH, Cramer BMA. Alcohol-induced sleep-walking or confusional arousal as a defense to criminal behavior: a review of scientific evidence, methods and forensic implications. J Sleep Res. 2007;16:198–212.
48. Abbey A. Acquaintance rape and alcohol consumption on college campuses: how are they linked? J Amer Coll Heealth. 1991 Jan;39(4):165–9.
49. Abbey A, Zawacki T, Buck PO, Testa M, Parks K, Norris J, et al. How does alcohol contribute to sexual assault? Explanations from laboratory and survey data. Alcohol Clin Exp Res. 2002 Apr;26(4):575–81.
50. Connor J, You R, Casswell S. Alcohol-related harm to others: a survey of physical and sexual assault in New Zealand. New Zeal Med J. 2009 Sep 25;122(1303):10–20.
51. Weissenborn R, Duka T. Acute alcohol effects on cognitive function in social drinkers: their relationship to drinking habits. Psychopharmacol. 2003;165(3):306–12.
52. White AM, Jamieson-Drake DW, Swartzwelder HS. Prevalence and correlates of alcohol-induced blackouts among college students: results of an e-mail survey. J Amer Coll Health. 2002;51(3):117–31.
53. Chase MH, Morales FR. Subthreshold excitatory activity and motoneuron discharge during REM periods of active sleep. Science. 1983 Sep 16;221(4616):1195–8.
54. Fuster JM. The prefrontal cortex: anatomy, physiology, and neuropsychology of the frontal lobe. Philadelphia: Lippincott, Williams, & Wilkins; 1997.
55. Maquet P, Degueldre C, Delfiore G, Aerts J, Peters JM, Luxen A, et al. Functional neuroanatomy of human slow wave sleep. J Neurosci. 1997 Apr 15;17(8):2807–12.
56. Kajimura N, Uchiyama M, Takayama Y, Uchida S, Uema T, Kato M, et al. Activity of midbrain reticular formation and neocortex during the progression of human non-rapid eye movement sleep. J Neurosci. 1999 Nov 15;19(22):10065–73.
57. Finelli LA, Borbely AA, Achermann P. Functional topography of the human nonREM sleep electroencephalogram. Euro J neurosci. 2001 Jun;13(12):2282–90.
58. Werth E, Achermann P, Borbely AA. Fronto-occipital EEG power gradients in human sleep. J Sleep Res. 1997 Jun;6(2):102–12.

59. Hofle N, Paus T, Reutens D, Fiset P, Gotman J, Evans AC, et al. Regional cerebral blood flow changes as a function of delta and spindle activity during slow wave sleep in humans. J Neurosci. 1997 Jun 15;17(12):4800–8.
60. Maquet P, Peters J, Aerts J, Delfiore G, Degueldre C, Luxen A, et al. Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. Nature. 1996 Sep 12;383(6596):163–6.
61. Braun AR, Balkin TJ, Wesenten NJ, Carson RE, Varga M, Baldwin P, et al. Regional cerebral blood flow throughout the sleep-wake cycle. An H2(15)O PET study. Brain. 1997 Jul; 120(Pt 7):1173–97.
62. Nofzinger EA, Mintun MA, Wiseman M, Kupfer DJ, Moore RY. Forebrain activation in REM sleep: an FDG PET study. Brain Res. 1997 Oct 3;770(1–2):192–201.
63. Muzur A, Pace-Schott EF, Hobson JA. The prefrontal cortex in sleep. Trends Cogn Sci. 2002 Nov 1;6(11):475–81.
64. Denno DW. Crime and consciousness: science and involuntary acts. Minn Law Rev. 2002 December;87(2):269–400.
65. Hobson JA. States of consciousness: normal and abnormal variation. In: Zelazo PD, Moscovitch M, Thompson E, editors. The Cambridge handbook of consciousness. 1st ed. New York: Cambridge University Press; 2007.
66. Dinges DF, Pack F, Williams K, Gillen K, Powell JW, Ott GE, et al Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. Sleep. 1997;20(4):267–77.
67. Hobson JA. Normal and abnormal states of consciousness. In: Velmans M, Schneider S, editors. The Blackwell companion to consciousness. 1st ed. Oxford: Blackwell Publishing; 2007. pp. 101–13.
68. Harris M, Grunstein RR. Treatments for somnambulism in adults: assessing the evidence. Sleep Med Rev. 2009 Aug;13(4):295–7.
69. Mahowald MW, Schenck CH. Dissociated states of wakefulness and sleep. Neurol. 1992 Jul;42(7 Suppl 6):44–51; discussion 2.
70. Morse SJ. Brain over claim syndrome and criminal responsibility: a diagnostic note. Ohio State Journal of Criminal Law. 2006;3:397.
71. Morse SJ. Brain and blame. Sem Clin Neuropsy. 1996 Jul;1(3):222–35.
72. Gazzaniga MS. The law and neuroscience. Neuron. 2008 Nov 6;60(3):412–5.
73. Garland B, editor. Neuroscience and the law: brain, mind, and the scales of justice. NewYork: Dana Press; 2004.

Chapter 31
Forensic Aspects of the Parasomnias

Karl Doghramji, Solange Margery Bertoglia and Clarence Watson

Historical Overview

For centuries, medical and nonprofessional publications have reported cases of violent, sleep-related behaviors. The range of such behaviors has been broad, including shoplifting, striking others, rape, and even murder [1–5]. Many of these have engendered large-scale interest among the public, especially those that have become the focus of legal attention. Only recently have they become of interest to the scientific community.

Although violent behaviors during sleep are relatively uncommon, they are not unusual and are thought to affect 2 % of the population, as noted by a UK survey of 4,972 men and women between the ages of 15–100 years [6]. Fortunately, only a minority of these behaviors result in legal liability to those who suffer from the disorders that cause them. Historically, however, those that have made their ways to the legal system have posed profound challenges to traditionally held legal theories of criminal culpability. Scholars have wrestled with the question of whether individuals who commit such acts should be held criminally accountable. One of the earliest accounts is that of Dr. Alexander Bonkalo, who described a 1791 criminal case in Selesia involving a man who killed his wife with an axe during his sleep.

K. Doghramji (✉)
Professor of Psychiatry, Neurology, and Medicine Medical Director, Jefferson Sleep Disorders Center Program Director, Fellowship in Sleep Medicine, Thomas Jefferson University, 211 South Ninth Street, Suite 500, Philadelphia, PA 19107, USA
e-mail: karl.doghramji@jefferson.edu

S. Margery Bertoglia
Department of Psychiatry and Human Behavior, Thomas Jefferson University, 833 Chestnut Street, Suite 210, Philadelphia, PA 19107, USA
e-mail: solange.margery@jefferson.edu

C. Watson
Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
e-mail: cwatson@watsonforensics.com

Two Pala Plaza, Ste. 300, Bala Cynwyd, PA 19004, USA

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6_31, © Springer Science+Business Media New York 2013

Lawyers for the defendant argued that the man was not fully awake at the time of the killing as the act occurred because of a condition they referred to as "sleep drunkenness" (*Schlaftrunkenheit*) [7]. They argued that the defendant was asleep when he acted, and, therefore, did not possess the freedom of will to commit the crime. Writings by Dr. Benjamin Rush regarding somnambulism in the early nineteenth century appear consistent with the defense's argument offered in the 1791 criminal case. Rush likened somnambulism to mental illness, as he wrote: "Like madness it is accompanied with muscular action, with incoherent, or coherent conduct, and with that complete oblivion of both, which takes place in the worst grade of madness" [8]. In his 1855 Monograph on Mental Unsoundness, Francis Wharton, a Philadelphia lawyer and legal scholar, wrote: "*Somnambulism* is not a mere intensified dream, but *in foro medico*, must be treated as a morbid independent state, and in a legal point of view, every act shown to have been committed under its influence is to be disconnected with voluntary moral agency" [9]. Wharton further offered a guide for considering somnambulism in criminal cases: "(a) a general tendency to deep and heavy sleep must be shown, out of which the patient could only be awakened by violent and convulsive effort; (b) before falling asleep, circumstances must be shown producing disquiet which sleep itself does not entirely compose; (c) the act under examination must have occurred at the time when the defendant was usually accustomed to have been asleep; (d) the cause of the sudden awakening must be shown. It is true that this cannot always happen, as sometimes the start may have come from a violent dream; (e) the act must bear throughout, the character of unconsciousness; (f) the actor himself, when he awakes, is generally amazed at his own deed, and it seems to him almost incredible. Generally speaking he does not seek to evade responsibility, though there are some unfortunate cases in which, the wretchedness of the sudden discovery, overcomes the party himself, who seeks to shelter himself from the consequences of a crime of which he was technically, though not morally, guilty" [9]. Dr. Isaac Ray, the father of American forensic psychiatry, also did not believe that an individual should be held criminally responsible for behaviors occurring during sleep. In his 1853 book chapter, Legal Consequences of Somnambulism, Dr. Ray stated, "as a somnambulist does not enjoy the free and rational exercise of his understanding, and is more or less unconscious of his outward relations, none of his acts during the paroxysms, can rightfully be imputed to him as crimes" [10]. However, as we will see below, attitudes regarding legal responsibility for parasomnia-induced violence have varied throughout the years.

Parasomnia Behaviors Associated with Legal Consequences

Prior to discussing the legal principles that have been raised in conjunction with the violent parasomnias, we would like to present notable examples of the types of violent parasomnia behaviors that have been the subject of legal attention. In doing so, we will also clarify certain characteristics of each case that have figured prominently in the jury's decision. We have divided these into three types: those that

lead to violence or result in injury to others, those that result in self-injury, and those associated with inappropriate sexual behavior.

Parasomnia Behaviors Associated with Injury to Others

The first successfully-defended case, documented in the US courts, involving a sleepwalking defense was that of *Massachusetts v. Tirrell*. Mr. Tirrell was accused of murdering a prostitute and setting fire to a brothel in 1846 [11, 12]. Tirrell's attorney claimed that he had been a sleepwalker throughout his life and that the act of murder occurred during an episode of sleep drunkenness, a period of impaired consciousness upon awakening. This contention was supported by the testimony of a physician. The outcome of the case may have been significantly swayed by the eloquence of Tirrell's defense attorney. Nevertheless, the case set forth a number of other such defensive stances in later years. The legal principles underlying these defenses are elaborated in greater detail later, yet in may similar cases, juries seem to have been influenced by a variety of factors, including whether the event seemed out of character for the defendant and whether the behavior appear to be too "complex" to be accepted as something that the defendant would have engaged in while asleep.

An example of the former stance is the case of *R. v. Parks* [13] in which Parks drove to his parents-in-law's house, with whom he got along, by all accounts. He killed his mother-in-law, left the father-in-law seriously injured, and then turned himself over to the police. It appeared that Parks had planned to visit his parents-in-law the day before and that, on the day of the event, was found wandering in their house. He had attacked his in-laws when they attempted to restrain him. Despite the highly "complex" nature of these actions, the jury agreed with Mr. Parks' defense that his actions were the result of an automatism, primarily because his actions were seen as being out of character when compared with his typical behavior and personality patterns while awake. In contrast, a 37-year-old man suffering from polysomnographically established severe sleep apnea syndrome was found to be guilty of first degree murder [14]. The jury reasoned that there was substantial motive for the murder, including a history of spousal and child abuse and a note written by the victim around the time of the shooting describing her intention to take the children and leave the suspect. In that case, the defendant called the police and claimed that he was awakened by the sound of a gunshot, only to find that he had actually shot his wife. The defense contended that the severe nature of his sleep apnea may well have led to a confusional arousal, which, in turn, may have led to the violent act, yet the history of domestic violence was the deciding factor. The case of *California v. Reitz* [15] bears some similarity to this case. Reitz beat, stabbed, and killed his girlfriend. During the trial, he stated that he woke up and found her dead just after he had dreamt about being in a fight with an intruder. He had a history of sleepwalking and bipolar disorder and had consumed alcohol and recreational substances on the night of the event. As part of his evaluation, he was sent to a sleep clinic and the test "revealed not only a propensity to sleepwalk, but Reitz also suffered a significant

night terror that was caught on tape." Nevertheless, his conviction was upheld and he was sentenced to 26 years to life in prison. The critical factor was the discovery that he had been violent toward his girlfriend in the past and had even threatened to kill her.

As noted above, the "complexity" of the parasomnia appears to be another important factor influencing jury decisions. An example is the case of Scott Falater who claimed to have killed his wife while sleep walking [16]. Falater was described as a "deeply religious, mild-mannered, teetotaling, financially stable, seemingly devoted husband." Mr. Falater had a history of sleepwalking and a polysomnograph indicated that he fitted "the profile of a sleepwalker." Still, he stabbed his wife 44 times, rolled her into the swimming pool, held her head under the water, and disposed of the body. A neighbor witnessed the drowning and saw Falater trying to quiet the barking dog. Falater also sustained a cut during the incident for which he applied a band aid. The jury felt that his behavior was too complex and premeditated to be consistent with a parasomnia, and he was found guilty of first degree murder.

Scientific discovery has, more recently, been emerging as a factor in jury decisions. Emerging scientific knowledge regarding the pathophysiology of REM sleep behavior disorder (RBD), for example, has swayed jury decisions. Defenses have been able to successfully argue that dreaming can be violent even in the most docile of individuals, yet physiologic abnormalities beyond their control allow violent content to be enacted. A case in point is that of Brian Thomas in Wales, [17] who was accused of strangling his wife during his sleep. Mr. Thomas had a long history of sleepwalking, due to which he and his wife had resorted to sleeping in separate bedrooms. However, during holidays, the couple would share a bed in a camper. Thomas reported that on the night of the murder, the couple had been disturbed by "boy racers." Apparently dreaming, Thomas reported imagining that they had broken into the van and that he fought with them to defend the couple against imagined danger. He subsequently woke up, and after realizing what had happened, called for help using the emergency line. Mr. Thomas, contended the defense, was likely suffering from RBD. His imagined struggle with strangers was actually enacted as a violent act against his wife, leading to her strangulation. Thomas' defense was augmented by supporting testimony by friends and family members, all of whom noted that he was a devoted husband and father, and a good friend. In the end, the jury found him not guilty.

Parasomnia Behaviors Associated with Self-Injury

Self-inflicted injury is common in the parasomnias. Schenck et al. reported that ecchymoses, lacerations, and fractures were common in a series of 100 parasomnia patients. Behaviors leading to these included falling out of bed, running into walls or furniture, jumping out of windows, walking into lakes, among others [18]. Such behaviors have not, however, commonly posed legal questions, with the exception of those leading to death. In such cases, the primary forensic question is whether

the death was caused by suicide or a parasomnia, as life insurance carriers are more likely to deny or to limit payment of life insurance claims to beneficiaries in cases where the death is due to suicide. Such cases also raise questions of importance for family members, for whom an accurate determination of the cause of death is of emotional significance, especially considering the social and religious ramifications of suicide. Mahowald et al. [19] reported the case of a college student who was killed after being struck by a truck, as he ran onto a highway from behind the pillars of an overpass, while dressed only in boxer shorts. He had a personal and a family history of sleepwalking, yet had no history of depression or other emotional conditions; in fact, he had made several concrete plans for his future. A review of events just prior to the accident indicated that he was sleep deprived. He had recently reported, to his roommate, that he had a dream in which he was "running a foot race with someone from a nearby small town." Although the case was originally deemed a suicide, a subsequent review led to the recommendation, to the medical examiner, to change the cause of death to "accidental death due to sleepwalking."

Another case was that of a 12-year-old girl [20] who woke up to find that she had a deep laceration on her neck. She was taken to the hospital, where the laceration was deemed to be intentionally self-inflicted despite the patient's claims to the contrary. Her claims of amnesia for the event were dismissed, and she was admitted to a psychiatric unit. She had a history of sleepwalking and no prior history of psychiatric difficulties. Upon further review, the incident was considered to be the result of a non-rapid eye movement (NREM) parasomnia. Although the case was not brought to the attention of the legal system, one could foresee legal problems arising from such a case, with claims being made regarding misdiagnosis, resulting in the unnecessary use of psychotropic medications and psychiatric hospitalization, particularly if the later involves involuntary civil commitment.

Parasomnia Behaviors Associated with Sexual Behavior

Inappropriate sexual behaviors occurring during sleep in the context of parasomnias have been well documented and described in greater detail in Chap. 21. As noted, behaviors are varied, including making sexual sounds, indecent self-exposure, masturbation, and even rape. These are generally regarded as being consequences of NREM parasomnias. Parasomnia-related sexual behaviors are likely under-reported because of the natural reluctance to expose such intimate details to others. Nevertheless, some cases have been brought to the attention of legal authorities, usually involving unwilling partners. As in the cases of injury to others, the courts have dealt with the cases in highly variable fashion.

A frequently discussed case is that of Jan Luedecke, a resident of Canada, who fell asleep on the couch next to a woman while attending a party [21]. She later accused him of rape. The defense claimed that the event represented a parasomnia, in support of which it brought forth evidence that the defendant had a history of sleepwalking and that he had been sleep deprived immediately prior to the incident. The Court of Appeals upheld the sexual assault acquittal. The case was particularly controversial

owing to the revelation that the defendant's sleep deprivation the night before was the result of another party, during which he had ingested "magic mushrooms" and had consumed alcohol.

Sexsomnia cases can be particularly problematic from a legal standpoint if the object of the activity is a minor. An example is the case of a 45-year-old man referred for an evaluation to a sleep clinic after he was charged with sexual battery [22]. The case report notes that he woke up and went downstairs, where his teenage daughter and her friend had fallen asleep. He fondled his daughter's friend. The patient reported having had no memory of the event and expressed bewilderment and guilt when he discovered what had happened. He had a history of sleepwalking, during which he would wander throughout the house while mumbling and take objects from one room to the other. He had no history of psychiatric or legal problems. He was lost to follow-up.

In 2009, Foss Hodges was acquitted of child molestation charges [23]. Foss had allegedly molested a seven-year-old girl while she was sleeping at his home. His defense claimed that this had occurred in the context of a parasomnia. Foss had a history of sleep-related behavior such as talking and urinating in a closet. He also had a history of sexual behavior during sleep, including intimacy with his wife and fondling male friends during a ski trip. Foss drank alcohol and took an antihistamine tablet on the night of the alleged molestation. The child involved in the case stated that he appeared asleep and that she had to wake him up, after which Foss discovered that his head was resting on the child's chest. He subsequently contacted the County Department of Family and Children Services.

Legal Concepts Involved in Criminal Responsibility

Actus Reus and Mens Rea

The primary question posed by the parasomnias that result in injury to others is that of criminal culpability. The defense's position is typically centered on the notion that "a person would not be considered criminally responsible for acts occurring during 'sleep'" [11]. In order to find an individual culpable of any crime, the law requires the presence of two elements at the time of the crime: *actus reus* and *mens rea* [11]. The ancient Latin phrase, "*actus non facit reum nisi mens sit rea*" or "the deed does not make a man guilty unless his mind is guilty" forms the basis of this legal tradition. The *actus reus* element represents the guilty *act* involved in a crime. The *mens rea* element represents the guilty *intent* to commit a crime. Successful legal defenses often nullify either the *actus reus* or the *mens rea* related to the relevant criminal charges in order to eliminate or reduce a defendant's culpability.

In cases where a violent act is committed during sleepwalking, it is often the *actus reus* requirement that first comes under fire, as the presence of an *actus reus* element implies that the defendant's actions were voluntary. The American Law Institute Model Penal Code (MPC) states: "a person is not guilty of an offense unless his

liability is based on conduct that includes a voluntary act or the omission to perform an act of which he is physically capable" [24]. Even more relevant in criminal cases involving sleepwalking, the MPC further stated that bodily movements during unconsciousness or sleep are *not* considered voluntary acts. At the core of this view is the idea that a person's mental state during sleep is incapable of weighing the consequences of behaviors or refraining from those behaviors. While the *actus reus* is often the target in legal defenses, theoretically, legal defenses in sleepwalking cases can also be viewed as negating the *mens rea* requirement. In doing so, the legal defense would seek to establish the absence of the guilty *intent* (because of the lack of conscious awareness) to commit a crime, in addition to demonstrating that the defendant did not act voluntarily [25].

Automatism, Unconsciousness, and Insanity

Legal systems have varied internationally in their treatment of criminal cases involving somnambulism. Historically, sleepwalking defenses have included the legal theories of automatism, unconsciousness, and insanity [26]. The definitions of and distinctions between these legal theories are illustrated in the cases below. Generally, countries outside of the US have utilized the theory of automatism as the foundation of the sleepwalking defense. US courts, on the other hand, have used all three theories to support the sleepwalking defense.

In the forensic arena automatisms are regarded as automatic, unconscious, and involuntary behaviors in a mental state where a person is capable of action but is not conscious of what he is doing. Accordingly, the automatism defense negates the *actus reus* requirement of a voluntary act [27]. In the UK and Canada, the legal defense of automatism has been explicitly divided into two categories, insane and non-insane automatism. A Canadian legal case, *R. v. Quick*, described the legal distinction between the two automatism categories [28]. A non-insane automatism is thought to be caused by external factors, such as a hypoglycemia due to injected insulin. On the other hand, an insane automatism is thought to be caused by internal factors, such as organic disorders or mental illness. This distinction holds particular legal significance, as the consequences of acquittal associated with either defense vary dramatically. An acquittal based on an insane automatism defense would result in commitment to a mental health institution, whereas a successful non-insane automatism defense would result in release from legal custody.

Despite this legal distinction and the current scientific knowledge regarding parasomnias, the sleepwalking defense is categorized as a non-insane automatism defense in the UK and in Canada [13]. The notorious Canadian case of *R. v. Parks* illustrates this approach [13]. In that case, Ken Parks was accused of killing his mother-in-law and seriously injuring his father-in-law after driving miles from his home. Parks' defense argued that he was asleep during these behaviors and presented a non-insane automatism defense. Parks was subsequently acquitted at trial on the basis of that defense and released from custody.

In the US, the sleepwalking defense has been asserted only rarely and US courts have been inconsistent in their legal approach to this defense [29]. In parallel with international courts, US courts have considered the sleepwalking defense using a variety of theories, including automatism, unconsciousness, and insanity. However, US courts have not bifurcated the automatism defense into insane and non-insane categories.

The first successful sleepwalking defense case in the US took place in Massachusetts in 1846 [12]. In that case, Albert Tirrell was accused of murdering a prostitute and setting fire to a brothel. His attorney argued that Tirrell had been a sleepwalker throughout his life and that "Tirrell had committed the deed, if he committed it [the crimes] at all, in the unconsciousness of sleep" [30]. The Massachusetts jury acquitted Tirrell after two hours of deliberation. US cases subsequent to the Tirrell decision illustrate the varied approaches to the sleepwalking defense taken by US jurisdictions.

The 1879 case of *Fain v. Commonwealth* involved Mr. Fain, a man with a history of sleepwalking. He fell asleep in the lobby of a hotel and when the porter tried to wake him up he shot and killed him. After going outside, he told a witness that he had shot someone, but did not know who it was. After he was informed of the identity of the victim, he expressed sorrow for what he had done. He was initially found guilty but the conviction was reversed on appeal when evidence of a prior history of sleepwalking was introduced, along with additional evidence indicating that he had recently been subjected to sleep deprivation as a result of his child-care obligations. The court of appeals of Kentucky in the *Fain* case expressed its view that a defendant who was sleeping at the time he shot and killed his victim was *unconscious* at the time of the shooting and, accordingly, was unable to understand the circumstances and consequences of his behavior [31]. In the 1974 California case, *People v. Sedeno*, the sleepwalking defense was also viewed to be subsumed within unconsciousness defense [32]. In that case, the Supreme Court of California found that the California Penal Code's exemption of acts occurring while unconscious included acts performed during sleepwalking. The underlying premise of the defense is that an unconscious person does not possess the requisite mental state to weigh actions that would otherwise amount to criminal behavior.

Nevertheless, US courts have also resorted to the automatism defense in sleepwalking cases. In the 1997 decision of *McClain v. Indiana*, the Supreme Court of Indiana held that a criminal defendant was entitled to present evidence of sleepwalking behaviors as an automatism defense [33]. Defendant McClain was instructed by police to get out of the street because he was walking in traffic, when he hit one of the officers and an altercation ensued. McClain was charged with aggravated battery, battery against police officers, and resisting law enforcement. McClain's defense was that the sleep deprivation (had slept just 3 hours in the 48 hours prior to his arrest) prevented McClain from forming the necessary intent for the crimes charged. The Supreme Court of Indiana held that he was entitled to present evidence of sleepwalking behaviors as an automatism defense, because "[e]vidence of automatism is relevant to the issue of voluntariness." Accordingly, the court highlighted the necessary component of the actus reus requirement—the voluntary act.

Despite the use of the automatism and unconsciousness defenses, US courts have, over time, blurred the distinction between these, making them functionally equivalent [13]. In fact, many US courts use the two terms synonymously [34]. As a result, the sleepwalking defense can be raised under either scheme in various US jurisdictions. Notably, both approaches represent *complete* defenses, in which case, an acquittal would result in complete release from the charges and legal detention.

Some US courts have also considered the sleepwalking defense as a variant of the insanity defense. Generally, the insanity defense undermines the *mens rea* requirement by establishing that at the time of the crime, a mental disease or defect was present that impaired the defendant's ability to know or appreciate the nature of his act or to conform his behavior to the requirements of the law. In the 1910 case, *Tibbs v. Commonwealth*, the Court of Appeals of Kentucky held that the only defense available for acts occurring during sleepwalking was the insanity defense [35]. In the 1925 case, *Bradley v. State*, the Texas Court of Criminal Appeals overturned a murder conviction, holding that the trial court erred in not applying the insanity defense where the defendant claimed to be sleepwalking at the time of the crime [36].

Later cases in the US clearly rejected the use of the insanity defense in sleepwalking cases. In the 1975 case, *State v. Caddell*, the Supreme Court of North Carolina, while acknowledging sleepwalking as a form of unconsciousness, stated that the defenses of insanity and unconsciousness are distinct because "unconsciousness at the time of the alleged criminal act need not be the result of a disease or defect of the mind" [34]. The Supreme Court of Wyoming also made this distinction in *Fulcher v. State* in 1981 [37]. The Wyoming court reasoned that without such distinction, a person who was unconscious, but not mentally ill, at the time of the crime would face commitment at a mental institution when acquitted and further noted that commitment of such an individual to a mental institution for rehabilitation would be of no value. The Supreme Court of Indiana, citing *Fulcher* in *McClain v. Indiana,* agreed with the distinction between the insanity and unconsciousness defenses, while holding that the automatism defense was more appropriate in the context of sleepwalking.

In general, therefore, US courts do not favor the use of the insanity defense in sleepwalking cases. One legal scholar makes the point as follows: "[m]odern courts and scholars have abandoned the classification of sleepwalking as an insanity defense, primarily because criminally insane defendants are often committed to a mental institution for mental rehabilitation, an inappropriate treatment for sleepwalkers" [38].

Legal Responsibility of Treating Physicians

As in any other medical condition, physicians managing patients who suffer from parasomnias are expected to diagnose, treat, and advise their patients of the risks associated with a particular sleep disorder in accordance with accepted standards of medical care. Failure to do so introduces the risk of liability in negligence actions filed by patients alleging injuries caused by that failure. The question as to what

additional responsibilities are assumed by physicians managing patients who engage in parasomnia-related violence has not been well defined.

Physicians may have a responsibility to third parties who are at risk for injury, or who are injured by, parasomnia-related violence. The often cited case example of physicians' legal responsibility to third parties to prevent harm threatened by their patients is the 1976 California case, *Tarasoff v. Regents of the University of California* [39]. In that case, the Supreme Court of California found physicians liable for failing to properly intervene after learning that their patient expressed intent to physically harm a third party, Tatiana Tarasoff, and found that the doctors' negligence stemmed from their failure to take steps to warn or protect the intended victim. Following the decision, some state jurisdictions adopted similar views as the California court, whereas other states declined to find physician liability in Tarasoff-like situations. But, unlike cases that involve a patient's verbal expressions of intent to harm third parties, parasomnia-related violence cases do not typically involve a patient's conscious intent to harm a third party.

Nevertheless, it should be noted that there is case law supporting physician liability when a patient has injured a third party, despite the absence of conscious intent to cause harm. Examples include cases of patients' impaired driving secondary to a medical condition. The 2005 Massachusetts case, *Medina v. Pillemer*, [40] involved a pedestrian who was struck by a vehicle, which was being driven by a patient with a recently diagnosed seizure disorder secondary to a malignant brain tumor.

This medical condition had caused him to lose control of the vehicle. The pedestrian sued the neurologist in charge of the patient's care for negligently failing to advise the patient to refrain from driving. The court found that the physician had a legal duty to exercise reasonable care for potential victims by advising his patient to avoid driving.

While other state courts have found physicians to be liable in similar situations, some jurisdictions have disagreed. In a 1996 Kansas case, *Calwell v. Hassan*, [41] two bicyclists sued a neurologist after they were hit by his patient who suffered from an unspecified sleep disorder. According to reports, the patient had fallen asleep at the wheel, striking the bicyclists head-on. In their lawsuit, the bicyclists alleged that the doctor's failure to warn his patient regarding driving was the proximate cause of their injuries. Nevertheless, the court found that the neurologist was not obligated to the bicyclists, reasoning that the driver should have known, in accordance with common knowledge, that she should not have driven while drowsy. The court held that a physician has no duty to warn a patient of information that the patient should otherwise already be aware.

Despite the lack of guidance regarding the legal responsibility of treating physicians in cases involving parasomnia-related violence, it is prudent for physicians to advise their patients of any significant safety risks associated with their particular parasomnias, including the risk of violence. As part of treatment management discussions with the patient, treating physicians should provide recommendations to the patients aimed at promoting the safety of the patient and individuals close to them. These safety measures are discussed in greater depth in various chapters in this book.

Role of the Physician as Expert Witness

Expert Witness Qualifications

Sleep medicine specialists are likely to be called as expert witnesses during the legal proceedings of cases of violence that are suspected of being based upon a parasomnia. Such cases pose challenges that go beyond those that are seen in typical forensic matters, as juries typically look at parasomnia defenses with a great deal of skepticism. In addition, "objective" medical evidence, such as sleep study results, is typically lacking in these cases because parasomnias are rarely captured in the context of the sleep laboratory, even after the fact.

The American Sleep Disorders Association, the predecessor of the American Academy of Sleep Medicine, and the American Academy of Neurology have published guidelines for physicians wishing to be expert witnesses in this area [42, 43]. According to these guidelines, the expert witness should possess a current, valid, and unrestricted license; be a Diplomat of the American Board of Sleep Medicine; be familiar with and involved with the clinical practice of sleep medicine; and be impartial and not become a partisan or advocate of the case. The expert witness's fees should relate to time and effort, not depend upon the outcome, and should not exceed 20 % of the expert's annual income. The expert witness should be willing to submit the testimony for peer review and should make records from previous testimonies available to the attorneys and expert witnesses involved in the case. In cases involving psychiatric aspects, it is preferred that the expert witness not be involved in the treatment of the evaluee, as the doctor–patient relationship can influence the expert witness' objectivity and affect the therapeutic relationship [44].

The Forensic Evaluation

The expert witness should inform the evaluee, at the outset, that the material that is shared during the interview is not strictly confidential and that it can be included in the report to the attorney, the court, or the institution requesting the evaluation. The evaluation should have a special focus on the evaluee's sleep history, narrative of the event, and the review of records and collateral information.

Sleep History and Narrative of the Event

A general medical and psychiatric evaluation, sleep-related evaluation, and a detailed, clinically focused, diagnostic evaluation of the event form the bedrock of the forensic evaluation. Readers are referred to Chap. 4 of this book for a detailed description of the diagnostic evaluation of parasomnias. The event should be understood in detail, with special focus on the characteristics of the event that support or refute the probability of a true parasomnia. Some authors have theorized that three factors

must coexist for an event to be consistent with a NREM parasomnia, the absence of any of which makes the occurrence less consistent with a parasomnia [45]. These include (1) *predisposing factors* such as a familial pattern or a long-standing history of prior behaviors of a similar nature; (2) *priming factors* that increase slow-wave sleep and increase the arousal threshold, such as stress, sleep deprivation, fever, and medications; and (3) *precipitating factors*, which set the sleepwalking episode in motion by causing an arousal during slow-wave sleep, such as being touched, environmental noises, acute pain, periodic limb movements during sleep, and sleep apnea.

Mahowald and Schenck [46] have proposed guidelines that incorporate those that had been previously suggested by others [7, 47, 48]. They propose that the evaluation of each case along the lines of seven distinct elements can assist in determining the "putative role of an underlying sleep disorder in a specific violent act." These include the following: (1) Suspicion of a sleep disorder, based on the clinical characteristics of the evaluee and based on a history of a specific, identified, sleep disorder; (2) the duration of the event is brief, usually minutes; (3) the behavior is "abrupt, immediate, impulsive, and senseless." Alternatively, the act can be goal-directed, yet it is "inappropriate to the total situation, out of character for the individual, and without evidence of premeditation;" (4) in the case of events that lead to injury to others, the victim is either the brunt of an act that was not specifically meant for him, yet he happened to be present in the vicinity of the evaluee. The victim may also have inadvertently served as the stimulus that led to the critical, parasomnia-inducing arousal; (5) upon return to consciousness, the person who committed the act is perplexed or horrified by the event and does not attempt to escape or conceal the evidence; (6) following the event, the evaluee has some degree of amnesia for the event and "there is evidence of lack of awareness on the part of the individual during the event;" (7) in the case of the NREM parasomnias, the act can occur upon awakening or at least 1 hour after the onset of sleep. The authors also recommend the consideration of the events preceding the violent act, which may have promoted the likelihood of the act, such as prior sleep deprivation and the use of sedative hypnotics, or events that may have triggered the act, such as an observed attempt by someone to awaken the evaluee.

Collateral Information

The examiner should request access to all available information, including past medical records, police reports, and victim's report. These records can provide support, or refute the evaluee's claims. For example, a police report can support the claim of being confused and distressed after the act and of making no attempt to conceal the act. It can also provide a different perspective regarding the event; if a discrepancy between the evaluee's account and that of the police is identified, it should be clarified with the evaluee. For example, witness reports stating that the evaluee made an attempt to conceal evidence or made comments that suggested that the act seemed premeditated should be presented to the evaluee for explanation. Bed partners and

cohabitants can also provide information regarding a history of parasomnia-related behaviors. Third-party witnesses who are not directly affected by the outcome of the case may provide more credible information. For example, in a case of a parasomnia resulting in what appears to be a suicide, family members' accounts can be less credible than a roommate's account if family members are the potential beneficiaries of an insurance payment.

Laboratory Testing

As noted earlier, results of prior tests can be of assistance in establishing the absence or presence of medical conditions prior to the event, and which may have contributed to the event. However, testing following the event may be less useful unless it reveals diagnostic abnormalities with a presumed onset prior to the event. For example, a case can be made that sleep apnea syndrome diagnosed by polysomnography following a violent parasomnia may have afflicted the evaluee prior to the event, if it can be established that major changes in medical status or weight did not take place subsequent to the event. Nonetheless, many of the abnormalities uncovered during polysomnography and other laboratory tests, when performed following the event, can be nonspecific in nature, and their causal attribution to the event is often problematic.

Practical Points

- Patients who suffer from parasomnias should be warned regarding the possibility of violent and sexually inappropriate acts during sleep.
- Physicians treating parasomnias may also have a legal responsibility to warn third parties who are at risk for injury from their patients' behaviors.
- The forensic evaluation for parasomnia-related violence must include a comprehensive sleep-related, medical, and psychiatric evaluation.
- As claims that violent acts are sleep-related cannot be substantiated by definitive tests, the forensic evaluation must also take into account key characteristics involved in the genesis of the sleepwalking episode, with particular emphasis on predisposing, priming, and precipitating factors.

References

1. Mahowald MW, Bundlie SR, Hurwitz TD, Schenck CH. Sleep violence—forensic science implications: polygraphic and video documentation. J Forensic Sci. 1990 Mar;35(2):413–32.
2. Mahowald MW, Schenck CH. Dissociated states of wakefulness and sleep. Neurology. 1992 Jul;42(7 Suppl 6):44–51; discussion 52.
3. Mahowald MW, Schenck CH, Rosen GM, Hurwitz TD. The role of a sleep disorder center in evaluating sleep violence. Arch Neurol. 1992 Jun;49(6):604–7.

4. Mahowald MW, Schenck CH. Parasomnias: sleepwalking and the law. Sleep Med Rev. 2000 Aug;4(4):321–39.
5. Zorick FJ, Salis PJ, Roth T, Kramer M. Narcolepsy and automatic behavior: a case report. J Clin Psychiatry. 1979 Apr;40(4):194–7.
6. Ohayon MM, Schenck CH. Violent behavior during sleep: prevalence, comorbidity and consequences. Sleep Med. 2010 Oct;11(9):941–6.
7. Bonkalo A. Impulsive acts and confusional states during incomplete arousal from sleep: criminological and forensic implications. Psychiatr Q. 1974;48(3):400–9.
8. Rush B. Of dreaming, incubus, or night mare, and somnambulism. Medical inquiries and observations upon the diseases of the mind. 5th edn. Philadelphia: Grigg and Elliot; 1835. pp. 298–303.
9. Wharton F. A monograph on mental unsoundness. Philadelphia: Kay and Brother; 1855. pp. 119–30.
10. Ray I. A Treatise on the medical jurisprudence of insanity, 3rd edn. Boston: Little, Brown & Co.; 1853.
11. Weiss KJ, Watson C, Markov D, Del Busto E, Foubister N, Doghramji K. Parasomnias, violence and the law. J Psychiatry Law. 2011;Summer:249–86.
12. Brown SG. The life of Rufus Choate. 6th edn. Boston: Little, Brown, & Co.; 1898.
13. Fenwick PRv. Parks. 2 SCR. 1992;5:871–347.
14. Nofzinger EA, Wettstein RM. Homicidal behavior and sleep apnea: a case report and medicolegal discussion. Sleep. 1995 Nov;18(9):776–82.
15. Sleep Forensic Associates. California v. Reitz. 2004. http://sleepforensicsassociates.com/caseStudies/cases-sleepwalking.php. Accessed: 12 Oct 2004.
16. Rubin P. A killer sleep disorder. Scott Falater, a mild-mannered Mormon family man, inexplicably stabbed his wife 44 times, then drowned her in the family pool while a neighbor watched. His defense? He was sleepwalking. 1998. http://www.phoenixnewtimes.com/1998-11-19/news/a-killer-sleep-disorder/. Accessed: 19 Nov 2012.
17. Morris S. Devoted husband who strangled wife in his sleep walks free from court. Prosecution drops case against chronic sleep disorder sufferer who killed wife during bad dream on holiday. 2009. http://www.guardian.co.uk/uk/2009/nov/20/brian-thomas-dream-strangler-tragedy. Accessed: 12 Oct 2012.
18. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW. A polysomnographic and clinical report on sleep-related injury in 100 adult patients. Am J Psychiatry. 1989 Sep;146(9):1166–73.
19. Mahowald MW, Schenck CH, Goldner M, Bachelder V, Cramer-Bornemann M. Parasomnia pseudo-suicide. J Forensic Sci. 2003 Sep;48(5):1158–62.
20. Shatkin JP, Feinfield K, Strober M. The misinterpretation of a non-REM sleep parasomnia as suicidal behavior in an adolescent. Sleep Breath. 2002;6:175–9.
21. Kari S. Ontario court upholds ‘sexsomnia’ acquittal. Toronto man may appear before mental health board. 2008. http://www.nationalpost.com/news/story.html?id=292924. Accessed: 12 Oct 2012.
22. Rosenfeld DS, Elhajjar AJ. Sleepsex: a variant of sleepwalking. Arch Sex Behav. 1998 Jun;27(3):269–78.
23. Peters, Rubin, & Sheffield Trial and Appellate Lawyers. Jury takes less than two hours to acquit hodges. 2009. http://www.justiceingeorgia.com/news/index.php?id=15. Accessed: 12 Oct 2012.
24. American Law Institute. Model penal code. Philadelphia:American Law Institute; 1962.
25. Grant E. While you were sleeping or addicted: a suggested expansion of the automatism doctrine to include an addiction defense. U Ill L Rev. 2000:997.
26. Bourget D, Whitehurst L. Amnesia and crime. J Am Acad Psychiatry Law. 2007;35(4):469–80.
27. Arboleda-Florez J. On automatism. Curr Opin Psychiatry. 2002;15:569–76.
28. R. v. Quick QB 1973:910.
29. Horn M. A rude awakening: what to do with the sleepwalking defense? B C L Rev. 2004;46:149–82.

30. Harris R, Kerr JM. Before and at trial: what should be done by counsel, solicitor and client. Northport:Edward Thompson Co.; 1890.
31. Court of Appeals of K. Fain v. The commonwealth. 1879;78:183.
32. 10 Cal.3d 703. People v. Sedeno. 518 P 2d 913 1974:913.
33. Ind. N.E. 2nd. McClain v Indiana. 1997;678:104.
34. NC S.E.2d. State v. Caddell. 1975:348.
35. Ky. S.W. Tibbs v. Commonwealth. 1910;128:871.
36. Tex. Crim. App. S.W. Bradley v. State. 1925;277:147.
37. Wy P. Fulcher v. State. 1981;633:142.
38. Horn M. A rude awakening: What to do with the sleepwalking defense? B C L Rev. 2004;46:149.
39. P.2d Cal. Tarasoff v. Regents of the University of California. 1976;334:551.
40. Mass. L. Rep. Medina v. Pillemer. 2005;20:352.
41. P.2d Kansas. Calwell v. Hassan. 1996;925:422.
42. Williams MA, Mackin GA, Beresford HR, Gordon J, Jacobson PL, McQuillen MP et al. American academy of neurology qualifications and guidelines for the physician expert witness. Neurology. 2006 Jan 10;66(1):13–4.
43. American Sleep Disorders Association. ASDA guidelines for expert witness qualifications and testimony. APSS Newsletter. 1993;8:23.
44. Strasburger LH, Gutheil TG, Brodsky A. On wearing two hats: role conflict in serving as both psychotherapist and expert witness. Am J Psychiatry. 1997 Apr;154(4):448–56.
45. Pressman MR. Factors that predispose, prime and precipitate NREM parasomnias in adults: clinical and forensic implications. Sleep Med Rev. 2007 Feb;11(1):5–30; discussion 31–3.
46. Mahowald MW, Schenck CH. Sleep-related violence: forensic medicine issues. In: Chokroverty S, editor. Sleep disorders medicine: basic science, technical considerations, and clinical aspects. Philadelphia: Elsevier; 2009. pp. 654–60.
47. Walker AE. Murder or epilepsy? J Nerv Ment Dis. 1961 Nov;133:430–7.
48. Glasgow GL. The anatomy of automatism. N Z Med J. 1965 Sep;64(397):491–5.

Index

S. V. Kothare, A. Ivanenko (eds.), *Parasomnias,*
DOI 10.1007/978-1-4614-7627-6, © Springer Science+Business Media New York 2013

R