SLEEP-WAKE CONFUSION, SOMNAMBULISM, AND A LOST PARADOX: PARASOMNIA CASES FOR THE NEUROLOGIST

Michael Howell

Historical
Sleepwalking: From Dream Enactment to a Disorder of Arousal

The etiology of abnormal nocturnal behaviors (parasomnias) has long puzzled scholars. Reports from Hippocrates (circa 460-370 BCE), Aristotle (384-322 BCE), and Laertius (Circa 200-300) allude to episodes that could be variously interpreted as sleepwalking, REM sleep behavior disorder, or nocturnal epilepsy. The Roman physician Galen (circa 129-200) wrote of spending an entire night sleepwalking only to be awoken after striking a stone (Umanath 2011).

By the renaissance sleepwalking was attributed to dream mentation, often as a window into subconscious psychological conflict. Most notably, in William Shakespeare's Macbeth, sleepwalking Lady Macbeth admits to being a coconspirator in murder as well as her subsequent internal torment. *"Out damned spot! Out, I say! ...What, will these hands never be clean?"*

Sleepwalking understood as a behavioral manifestation of dreaming ended in the mid 20th century with the discovery of the ultradian (NREM/REM) sleep cycle. As sleepwalking did not arise out of intensive dream sleep (REM) but instead predominantly out of deep NREM sleep (Broughton 1968). In 1986, REM sleep behavior disorder was reported, revealing a co-existing disorder of dream enactment (Schenck 1986).

After recognizing the normal ultradian alternations between sleep and wakefulness researchers found periodic cortical arousals every 30-90 seconds in NREM sleep (the cyclic alternating pattern) (Zucconi 1995). That sleep was not a homogenous state of unconsciousness but instead had frequent, non-pathological arousals was a breakthrough in understanding parasomnias (Guilleminault 2005 and 2006).

Sleepwalking episodes captured during PSG investigation demonstrate wake-like cortical activity on scalp EEG. This finding suggests that the name sleepwalking itself is misleading and that these events may be more appropriately perceived as disorders of arousal, with or without ambulation (Schenck 1998).

Over the last two decades reports of complex amnestic nocturnal behaviors have risen in parallel to the widespread use of sedative medications most notably the benzodiazepine receptor agonists (BRA's) (Dolder 2008).

ICSD-3 Criteria

Parasomnias classification is determined (primarily) by the state out of which they arise. NREM-Related Parasomnias include the disorders of arousal: confusional arousals, sleepwalking, and, sleep terrors. Sleep related eating disorder (SRED), is another NREM-Related Parsomnia that for all practical purposes is sleepwalking with eating. REM-Related Parasomnias include REM sleep Behavior Disorder (RBD), recurrent isolated sleep paralysis, and nightmare disorder. In addition, there are several abnormal nocturnal behavior disorders that do not consistently stratify into either sleep state. These conditions, the Other Parasomnias include: sleep enuresis, sleep related hallucinations, and the fantastically named exploding head syndrome (AASM 2014).

This syllabus, and lecture will focus upon the disorders of arousal (with SRED), RBD, sleep enuresis, exploding head syndrome, and sleep related hallucinations. Sleep paralysis will be briefly mentioned.

NREM PARASOMNIAS

Introduction and ICSD-3 Criteria

Disorders of arousal are abnormal nocturnal behaviors with impaired judgment and amnesia. Unlike the ICSD-2, where each individual disorder of arousal had it's own criteria the ICSD-3, published in 2014, has four unifying criteria: recurrent episodes of incomplete awakening from sleep, the patient unable to be redirected during episodes, limited to no dream imagery, as well as partial or complete amnesia. Ambulation out of bed distinguishes sleepwalking from confusional arousals; if the patient eats the parasomnia is SRED. Sleep Terrors, differ from the other disorders of arousal as the patient demonstrates intense fear (episodes typically begin with a scream) and signs of autonomic arousal (mydriasis, tachycardia, tachypnea, diaphoresis) (AASM 2014).

NREM Parasomnia Management

Management of NREM parasomnias, as with all parasomnia management, should initially focus on environmental safety by modifying the sleeping environment. Removal of bedside firearms and other weapons is of paramount importance. Windows, or other exits that could result in a fall, should not be easily accessible. Automatically locking doors are to be avoided as sleepwalkers may ambulate outside of their residence without means of reentry. If necessary, a door alarm is often useful to alert other family members that the patient is ambulating through the house.

Attempts should be made to eliminate sedating agents as well as to identify and treat comorbid sleep and circadian disorders. Most cases of sedative-induced sleepwalking behaviors are terminated following discontinuation of offending medications. Further, sleepwalking typically resolves once the underlying sleep deprivation, obstructive sleep apnea, or restless legs syndrome are effectively addressed (Guilleminault et al 2005; Howell 2012; Howell and Schenck 2012).

When serious nocturnal behaviors persist despite these interventions or in situations with a high probability of injury, pharmacotherapy may be considered. A variety of different therapies, typically benzodiazepines, have been reported as effective for sleepwalking. However, at present, there is a paucity of clinical trial data. Instead, a consensus has arisen, based on case series and small clinical trials. Importantly, national and international agencies that regulate drug approval do not recognize these treatments (Harris and Grunstein 2009; Howell 2012).

The most commonly reported pharmacological treatments for sleepwalking are intermediate- or long-acting benzodiazepines. Most commonly reported agent is clonazepam. The efficacy of clonazepam would be paradoxical as other sedative hypnotics, such as benzodiazepine receptor agonists, frequently induce amnestic nocturnal behavior (Dolder and Nelson 2008). Limiting side effects of clonazepam include morning sedation as well as gait impairment and pertain to its prolonged duration of action.

In conclusion, the most effective sleepwalking therapy is to identify and treat comorbid predisposing, priming, and precipitating conditions. Even subtle sleep-disordered breathing or motor restlessness should be considered as a potential target to resolve sleepwalking (Guilleminault et al 2005; Howell 2012, Howell et al 2015). The patient should also attempt to optimize the duration and circadian timing of sleep. Finally, if pharmacological therapy is utilized, patients should be made aware that evidence supporting these treatments is minimal.

REM PARASOMNIAS
REM Sleep Behavior Disorder

Introduction and ICSD-3 Criteria

Under normal physiological conditions REM sleep is characterized active dream mentation combined with skeletal muscle paralysis. In REM sleep behavior disorder (RBD) the skeletal muscle paralysis is lost leading to dream enactment behaviors such as: punching, kicking, jumping, or thrashing about in bed. These behaviors are potentially injurious to the patient and/or bed partner (Howell 2012, Howell and Schenck 2015).

According to the most recent ICSD-3 criteria a patient has RBD if they have: repeated episodes of sleep-related vocalizations and/or complex motor behaviors, PSG demonstrates that these behaviors occur during REM sleep or due to clinical history of dream enactment presumably arise from REM sleep, and PSG demonstrates REM sleep without atonia. Thus RBD is the only parasomnia that requires a sleep study to confirm the diagnosis (AASM 2014).

Management

The spectrum of dream enactment behavior in Rapid Eye Movement (REM) sleep Behavior Disorder (RBD) ranges from benign hand movements to violent life-threatening actions (thrashing/lunging). The goal of RBD management is to prevent sleep related injury. Thus educating the patient's and bed partner's about the potential dramatic consequences of dream enactment is an important first step as subsequent measures ranging from environmental modification to the treatment of co-morbid sleep disorders will depend upon their adherence and follow through.

If concerning dream enactment persists once ancillary sleep disorders, in particular sleep related breathing disorders, are treated and RBD inducing medications are minimized then medication therapy is reasonable. The most commonly employed agents include low dose (0.25-1.0mg) clonazepam or high dose (6-18mg) melatonin taking at bedtime. However clinicians should be aware that the evidence supporting these therapies is primarily based upon case series, small clinical trials, and expert consensus (Boeve 2010, Howell and Schenck 2015).

As RBD is a prodromal syndrome of alpha-synuclein pathology management should include monitoring for signs of neuro-degeneration. This includes continued careful clinical follow-up for subtle abnormalities of movement and cognition.

Sleep Enuresis

Sleep enuresis is defined by recurrent (at least twice a week) involuntary urination during sleep that has lasted at least 3 months. By the age of six 90% of children have developed 24 hour a day control of micturition. Sleep enuresis is either primary, in a patient who has never developed nocturnal continence, or secondary, in a patient who had previously been continent but then subsequently lost bladder control at night (AASM 2014).

Primary sleep enuresis is often either a failure of the brain to arouse from sleep in response to bladder expansion or due to inappropriate bladder contraction during sleep. Familial cases are common and boys are more commonly affected than girls. The vast majority of primary sleep enuresis cases spontaneously resolve. The most commonly prescribed medication for primary enuresis is desmopressin, an analog of desmopressin, with anti-diuretic properties. Non-pharmacological treatments include: evening fluid restriction, scheduled awakenings, and enuresis bed alarms (Wills and Garcia 2002)

Secondary sleep enuresis is most commonly due to other sleep disorder such as obstructive sleep apnea (OSA). A collapsing airway in combination with increased respiratory effort decreases intrathoracic pressure and subsequently, atrial naturetic peptide is secreted from the heart leading to increased urinary output. In addition OSA also leads to enuresis by impairing cortical arousal through increased homeostatic sleep drive combined with increase autonomic activity. Other etiologies of secondary sleep enuresis include urinary tract disorders, nocturnal seizures, and disorders that lead to increased urine production (AASM 2014).

Exploding Head Syndrome, Sleep Related Hallucinations, and Sleep Paralysis

The sleep-wake transition is associated with experiences that include the exploding head syndrome, sleep related hallucinations (hypnogogic or hypnopompic hallucinations), and sleep paralysis (AASM 2014, Howell 2012).

The theatrically named exploding head syndrome describes a startling auditory hallucination at the initiation of sleep. Patients claim they are awoken buy the sudden loud noise and may describe the feeling as "an exploding head". The character of auditory hallucination varies from simple (a church bell) to complex (the sound of someone pounding on several piano keys). Myoclonic jerks often co-occur with the auditory phenomena.

Sleep related hallucinations (either hypnogogic or hypnopompic) are typically visual and in human or other animal form. They are often associated with anxiety and a foreboding sense of terror. This feeling is heightened if hallucinations are combined with sleep paralysis. Of note, sleep paralysis is often perceived as a sense of dyspnea, from the lack of accessory muscle of respiration (it is a persistence of REM atonia into wakefulness), with frightening dream mentation, such as a demonic presence. Various cultures have paranormal or religious

interpretations to these experiences, as patients without history of a thought disorder, will describe in vivid detail: alien abduction, sexual assault by animals, or demonic possession. The painting by John Henry Fuseli, “The Nightmare” (1781) illustrates REM sleep-to-wake experiential phenomena. The woman in the painting clearly demonstrates the atonia of sleep paralysis combined with frightening visual hallucinations.

These experiential parasomnias most often occur in the setting of either sleep deprivation or comorbid sleep pathology. Sleep Paralysis and sleep related hallucinations are part of the classical quatrad of narcolepsy along with hypersomnolence and cataplexy. These conditions lead to experiential parasomnias by impairing a sharp transition between sleep and wakefulness. Treating underlying sleep disorders and optimizing the duration and circadian timing of sleep will successfully treat the vast majority of cases. REM suppressing agents, antidepressants, can sometimes be useful for challenging cases of sleep paralysis and sleep related hallucinations (Howell 2012, AASM 2014).

References

Allen RP, Walters AS, Montplaisir J, Hening W, Myers A, Bell TJ, et al. Restless legs syndrome prevalence and impact: REST general population study. Arch Intern Med 2005 165:1286-1292.

American Academy of Sleep Medicine. International Classification of Sleep Disorders: Diagnostic and Coding Manual. 3rd Edition ed. Westchester. IL: American Academy of Sleep Medicine; 2014.

Boeve BF. REM sleep behavior disorder: Updated review of the core features, the REM sleep behavior-neurodegenerative disease association, evolving concepts, controversies, and future directions. Ann NY Acad Sci 2010;1184:15-54.

Boeve BF. Idiopathic REM sleep behavior disorder in the development of Parkinson’s disease. Lancet Neurol 2013;12:469-82.

Broughton RJ. Sleep disorders: disorders of arousal? Enuresis, somnambulism, and nightmares occur in confusional states of arousal, not in "dreaming sleep". Science 1968 Mar 8 159:1070-1078.

Canaday BR. Amnesia possibly associated with zolpidem administration. Pharmacotherapy 1996 16:687-689.

Dolder CR, Nelson MH. Hypnosedative-induced complex behaviours : incidence, mechanisms and management. CNS Drugs 2008 22:1021-1036.

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 25:871-875.

Driver-Dunckley ED, Noble BN, Hentz JG, Evidente VG, Caviness JN, Parish J, et al. Gambling and increased sexual desire with dopaminergic medications in restless legs syndrome. Clin Neuropharmacol 2007 30:249-255.

EKBOM KA. Restless legs syndrome. Neurology 1960 10:868-873.

Guilleminault C, Palombini L, Pelayo R, Chervin RD. Sleepwalking and sleep terrors in prepubertal children: what triggers them? Pediatrics 2003 111:e17-25.

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 6:515-521.

Guilleminault C, Kirisoglu C, Bao G, Arias V, Chan A, Li KK. Adult chronic sleepwalking and its treatment based on polysomnography. Brain 2005 128:1062-1069.

Guilleminault C, Kirisoglu C, da Rosa AC, Lopes C, Chan A. Sleepwalking, a disorder of NREM sleep instability. Sleep Med 2006 7:163-170.

Holm KJ, Goa KL. Zolpidem: an update of its pharmacology, therapeutic efficacy and tolerability in the treatment of insomnia. Drugs 2000 59:865-889.

Howell MJ, Schenck CH. Restless Nocturnal Eating: A Common Feature of Willis-Ekbom Syndrome (RLS). JCSM 2012a 8:413-419.

Howell MJ. Parasomnias: an updated review. Neurotherapeutics. 2012b 9:753-775.

Howell MJ, Schenck CH. Rapid Eye Movement Sleep Behavior Disorder and Neurodegenerative Disease. JAMA Neurol 2015;72:707-12.

Hublin C, Kaprio J, Partinen M, Heikkila K, Koskenvuo M. Prevalence and genetics of sleepwalking: a population-based twin study. Neurology 1997 48:177-181.

Iranzo A, Fernandez-Arcos A, Tolosa E, et al. Neurodegenerative disorder risk in idiopathic REM sleep behavior disorder: study in 174 patients. PLoS One 2014;9(2):e89741.

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 11:583-585.

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 96:370-374.

Morgenthaler TI, Silber MH. Amnestic sleep-related eating disorder associated with zolpidem. Sleep Med 2002 3:323-327.

Nihei Y, 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 Jan [Epub ahead of print].

OhayonMM, MahowaldMW, DauvilliersY, KrystalAD, LégerD. Prevelence and comorbidity of nocturnal wandering in the US adult general population. Neurology 2012;78:1583-9

Ondo WG, Lai D. Predictors of impulsivity and reward behavior with dopaminergic agonists. Parkinsonism Relat Disord 2008 14:28-32.

Parksinson J. An Essay on the Shaking Palsy. London:Whittingham and Rowland. 1817.

Pilon M, Montplaisir J, Zadra A. Precipitating factors of somnambulism: impact of sleep deprivation and forced arousals. Neurology 2008 70:2284-2290.

Postuma RB, Gagnon JF, Tuineaig M, et al. Antidepressants and REM sleep behavior disorder: isolated side effect or neurodegenerative signal? Sleep. 2013;36:1579-85.

Poryazova R, Oberholzer M, Baumann CR, Bassetti CL. REM sleep behavior disorder in Parkinson's disease: a questionnaire-based survey. J Clin Sleep Med 2013 Jan 15;9(1):55-9A.

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 12:432-436.

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):871-877.

Pressman MR. Factors that predispose, prime and precipitate NREM parasomnias in adults: Clinical and forensic implications. Sleep Medicine Reviews 2007 11:5-30.

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 24:871-877.

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 11:218-220.

Romenets SR, et al. Rapid eye movement sleep behavior disorder and subtypes of Parkinson's disease. Mov Disord 2012 Jul;27(8):996-1003.

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 14:419-431.

Schenck CH, Mahowald MW. Review of nocturnal sleep-related eating disorders. Int J Eat Disord 1994 May;15(4):343-356.

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 15:159-166.

Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new categorth of parasomnia. Sleep 1985 9:293-308.

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 30:683-702.

Schenck CH, Boeve BF, Mahowald MW. Delayed emergence of a parkinsonian disorder or dementia in 81% of older men initially diagnosed with idiopathic rapid eye movement sleep behavior disorder: a 16-year update on a previously reported series. Sleep Med 2013a;14(8):744-8.

Sixel-Doring F, Trautmann E, Mollenhauer B, Trenkwalder C. Associated factors for REM sleep behavior disorder in Parkinson disease. Neurology 2011;77:1048-54.

Tsai MJ, Tsai YH, Huang YB. Compulsive activity and anterograde amnesia after zolpidem use. Clin Toxicol (Phila) 2007 45:179-181.

Umanath S, Sarezky D, Finger S. Sleepwalking through History: Medicine, Arts, and Courts of Law. Journal of the History of the Neurosciences: Basic and Clinical Perspectives 2011 20;4:253-276.

Videnovic A, Marlin C, Alibiglou L, et al. Increased REM sleep without atonia in Parkinson disease with freezing of gait. Neurology 2013;81:1030-5.

Wills L, Garcia J. Parasomnias: epidemiology and management. CNS Drugs 2002 16:803-10.

Zadra A, Desautels A, Petit D, Montplaisir J. Somnambulism: clinical aspects and pathophysiological hypotheses. Lancet Neurol. 2013 Mar; 12 (3): 285-94.

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 12:147-154.