

Parasomnias

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Parasomnias are undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousal from sleep. Parasomnias may occur during non-rapid eye movement sleep (NREM), rapid eye movement sleep (REM), or during sleep-wake transitions.

Parasomnias may be characterized by abnormal sleep-related complex movements, behaviors, emotions, perceptions, dreams, and autonomic nervous system activity. Parasomnias are clinical disorders because of the resulting injuries, sleep disruption, adverse health effects, and untoward psychosocial effects. The clinical consequences of the parasomnias can affect the patient, the bed partner, or both.

Human consciousness consists of three essential states: Wake, NREM sleep, and REM sleep. The three states are modulated by a host of influences, including the degree of aminergic and cholinergic neurochemical activity, central nervous system (CNS) activation, and the degree of endogenous versus 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-hour period. However, as the sleep-wake cycle oscillates, the usually distinct states of consciousness may be rendered into a state that is not fully declared, resulting in a temporarily unstable state of dissociation. Thus, sleep and wake can be viewed as occurring on a spectrum rather than being entirely dichotomous states.

Parasomnias are the result of such state dissociation. Combinations of these states may result in unstable states of altered consciousness manifesting as parasomnias. Disorders of arousal, such as sleepwalking, sleep terrors, and confusional arousals, are an admixture of wakefulness and NREM sleep. Higher cognitive function is severely impaired, if not absent, while the potential for motor capacity has, for the most part, been retained. REM sleep behavior disorder (RBD) is an admixture of REM sleep coupled with waking or NREM sleep levels of tonic or phasic EMG activity. All three states may be present in the same individual as an overlap of disorders.

The co-mingling of basic states of consciousness results from different forms of pathophysiology. In disorders of arousal, no identifiable neuropathology is present, but functional changes in cerebral activity during NREM sleep are present. These changes result in a brain in which certain areas are deactivated (asleep), and others remain activated (awake). This CNS activation, with concomitant skeletal muscle and autonomic nervous system activation, is believed to reflect a functional disabling of or damage to brain areas usually responsible for inhibiting these activities during sleep. Additionally, sleep inertia, sleep state instability, and locomotor/central pattern generators are thought to contribute to NREM parasomnias.

NREM disorders of arousal frequently appear to involve the disinhibition of “basic drive states” or motor functions such as fleeing, feeding, sex, and aggression. It has been postulated that central pattern generators elicit primal fixed action patterns that the prefrontal cortex would otherwise inhibit during wake. In this regard, aggression is typically abrupt in onset and characterized by apparent instinctual defensive posturing instead of complex and procedural behaviors. These can emerge in pathologic forms with the parasomnias, as seen with sleep-related aggression and locomotion, sleep-related eating disorder (SRED), and abnormal sleep-related sexual behaviors. Some patients with a disorder of arousal may enact the terminal part of a long dream. In contrast, RBD often results from serious neuropathology related to alpha-synuclein in many cases. Initially, this neuropathology affects the area of the brain responsible for inhibiting muscle tone during REM sleep, and dreams may be enacted. In the case of REM-related behaviors, the experience and activity reflect the actual, often aggressive content of a dream. It is frequently possible to correlate observed movements with later descriptions of the dream. The initial appearance of RBD symptoms is often followed years later by the development of neurodegenerative disorders, particularly Parkinson's disease and related synucleinopathies.

Abnormal sleep-related movements comprise a separate category of disorders, detailed in the section on sleep-related movement disorders. Unlike parasomnias, which typically entail more complex movements and behavior, sleep-related movement disorders encompass a broad range of predominantly simple motoric activities: myoclonic, repetitive, rocking, rhythmic, grinding, cramping, fragmentary, dystonic, or dyskinetic movements or tremors, which are not usually associated with dream mentation or experiential concomitants.

Parasomnias involve sleep-related behaviors and experiences over which there is no conscious, deliberate control. There are ten core categories of parasomnias listed in the International Classification of Sleep Disorders, 3rd Edition. Only one of the core categories, RBD, requires video-polysomnographic documentation as one of the essential diagnostic criteria. However, for most other parasomnias, video-polysomnographic monitoring can provide corroborative documentation supporting the clinical diagnosis and help to exclude other disorders or mimics that are part of the differential diagnosis. When combined with thorough clinical interviews, video-polysomnography is a powerful discriminating tool for identifying the cause of sleep-related injury in adults.

Considerable advances have taken place in understanding the neurophysiologic aspects of abnormal arousals from slow wave sleep that are key in the pathophysiology of the disorders of arousal. In addition, advances in understanding the clinical aspects of these NREM sleep parasomnias have occurred, particularly regarding their prevalence and severity in adults.

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NREM-Related Parasomnias

Disorders of Arousal (From NREM Sleep)

This group of NREM-related disorders, which includes confusional arousals, sleepwalking, and sleep terrors, arises as a result of incomplete arousals from deep sleep. The concept of “sleep state dissociation” has been elaborated to explain the occurrence of neurophysiologic features of both wakefulness and sleep in the Disorders of Arousal. These conditions share: (1) similar genetic and familial patterns; (2) similar pathophysiology of partial arousals from deep sleep; and (3) similar priming by sleep deprivation and biopsychosocial stressors. Disorders of arousal may be triggered by sound, touch, or other stimuli. They are associated with absent or minimal cognitive functioning and partial or complete amnesia for the episode. These disorders are not secondary to psychiatric disorders, nor are they generally secondary to neuropathology or head injury.

General Diagnostic Criteria for Disorders of Arousal

Criteria A-E must be met

- A. Recurrent episodes of incomplete awakening from sleep.¹
- B. Inappropriate or absent responsiveness to efforts of others to intervene or redirect the person during the episode.
- C. Limited (e.g., a single visual scene) or no associated cognition or dream imagery.
- D. Partial or complete amnesia for the episode.

- E. The disturbance is not better explained by another current sleep disorder, medical disorder, mental disorder, or medication/substance use.

Notes

1. The events usually occur during the first third of the major sleep episode.
2. The individual may continue to appear confused and disoriented for several minutes or longer following the episode.

Confusional Arousals

ICD-9-CM Code: 327.41

ICD-10-CM Code: G47.51

Diagnostic Criteria

Criteria A-C must be met

- A. The disorder meets general criteria for a NREM disorder of arousal.
- B. The episodes are characterized by mental confusion or confused behavior that occurs while the patient is in bed.
- C. There is an absence of terror or ambulation outside of the bed.

Notes

1. There is typically a lack of autonomic arousal such as mydriasis, tachycardia, tachypnea, and diaphoresis during an episode.

Sleepwalking

ICD-9-CM Code: 307.46

ICD-10-CM Code: F51.3

Alternate Names

Somnambulism.

Diagnostic Criteria

Criteria A and B must be met

- A. The disorder meets general criteria for NREM disorders of arousal.
- B. The arousals are associated with ambulation and other complex behaviors out of the bed.

Sleep Terrors

ICD-9-CM code: 307.46

ICD-10-CM code: F51.4

Alternate Names

Night terrors, pavor nocturnus.

Diagnostic Criteria

Criteria A-C must be met

- A. The disorder meets general criteria for NREM disorders of arousal.
- B. The arousals are characterized by episodes of abrupt terror, typically beginning with an alarming vocalization such as a frightening scream.
- C. There is intense fear and signs of autonomic arousal, including mydriasis, tachycardia, tachypnea, and diaphoresis during an episode.

Essential Features

Disorders of arousal consist of behaviors that are usually initiated during partial arousals from slow wave (N3) sleep. Most episodes are brief, but they may last as long as 30 to 40 minutes in some children. Sleep talking and shouting may accompany these events. The eyes are usually open during an episode and, not uncommonly, are wide open with a confused “glassy” stare. The patient with a disorder of arousal may be very difficult to awaken and, when awakened, is often confused. There is usually amnesia for these episodes, although adults may remember fragments of episodes. Dream-like mentation is sometimes reported in adults. Other high-level cognitive functions such as attention, planning, coherent social interaction, and intent are absent. Because disorders of arousal usually originate from slow wave sleep, they most often emerge in the first third or first half of the typical sleep period. They may occur during other times of increased slow wave sleep, such as during recovery sleep following sleep deprivation. They rarely arise from a daytime nap.

Disorders of arousal are encountered most commonly in children and typically resolve by puberty but may persist (or, infrequently, arise de novo) in adolescence or adulthood.

Confusional Arousals: Confusional arousals, unlike sleepwalking, occur with the patient in bed. When the patient leaves the bed, sleepwalking has been initiated. Confusional arousals often start with the individual sitting up in bed and looking about in a confused manner.

Sleepwalking: Sleepwalking episodes typically begin as confusional arousals. Sleepwalking episodes can also begin with the individual immediately leaving the bed and walking or even “bolting” from the bed and running. Highly inappropriate, agitated, resistive, belligerent, or violent behavior can also occur. Behaviors can be simple and non-goal-directed, or complex and protracted, and may involve inappropriate sexual activity with oneself or an individual nearby, such as a bed partner. The ambulation may terminate spontaneously, at times in inappropriate places, or the sleepwalker may return to bed, lie down, and continue to sleep without reaching conscious awareness at any point. The sleepwalking individual is disoriented in time and place, with slow speech, severely diminished mentation, and blunted response to questions or requests. There is often prominent anterograde and retrograde memory impairment. Despite diminished external perception due to blockade of sensory input, the individual may appear to be awake with eyes open during some or most of an episode, with reduced vigilance and impaired cognitive response.

Sleep Terrors: Sleep terrors differ from other disorders of arousal in that the events are often initiated by a cry or piercing scream and accompanied by autonomic nervous system and behavioral manifestations of intense fear. There is often marked autonomic discharge, with tachycardia, tachypnea, flushing of the skin, diaphoresis, mydriasis, and increased muscle tone. The person usually sits up in bed and is unresponsive to external stimuli. If awakened, the individual is confused and disoriented. However, bolting out of bed and running is not uncommon in adults and can be associated with violent behaviors, especially if attempts are made to block or restrain the individual. Incoherent vocalizations may accompany the sleep terror episode. Sometimes there is prolonged inconsolability associated with a sleep terror in children or adults. A rare form of sleep terror is parasomniac choking, in which sleepers suddenly awaken from deep sleep with an intense, distressing feeling that an object is stuck in their throats and choking them, despite normal patency of the airways.

Associated Features

Disorders of arousal are devoid of higher cognitive functions such as planning, memory from before an incident, formation of a memory during an incident, proper social interaction, or recognition of others. Patients exhibiting disorders of arousal are not consciously aware, and behaviors are often thought to be “automatic” in nature. Self-injury may occur as well as injury to others nearby. In clinical populations, dreams of imminent danger (e.g., the ceiling collapsing, being buried alive, an intruder about to attack), accompanied by the need to escape, are frequent dream scenarios with NREM parasomnias in adults. Dreaming can occur with sleepwalking and sleep terrors, including elaborate dreaming with dream-enacting behaviors.

Disorders of arousal, particularly sleepwalking, can involve normal, routine behaviors that are inappropriate only in regard to their timing. More often, however, sleepwalking involves inappropriate behaviors, such as urinating in a wastebasket, moving furniture around haphazardly, or climbing out a window. Sleepwalkers can sometimes navigate in familiar surroundings but are prone to bumping into objects or falling. A sudden arousal consistent with sleep terrors may escalate into agitated sleepwalking, panicky running, or other potentially dangerous behaviors. Self-injury is not unusual and, when resulting in death, has been given the term “parasomnia pseudosuicide.” Cuts, bruises, and other injuries may occur—often to the surprise of the sleepwalker once awake. Sleepwalkers are reported to have a high pain tolerance. Therefore, knife cuts, burns, and other self-injury sustained during sleepwalking may not awaken them. Pain perception in response to such injuries during sleepwalking episodes may be reduced or absent, allowing the individual to remain asleep despite the injury.

Violence to others also can occur with adult sleepwalking, especially in men. The sleepwalker does not generally seek out the eventual victim of violence. More typically, a person attempting to block, grab, restrain, redirect or awaken a sleepwalker during an episode may be violently attacked, even if they are family members or friends. This confrontation may result in a form of primitive defensive aggression by the sleepwalker, including pushing, hitting, kicking, or throwing objects. This pattern also has been reported in the sleep laboratory when technical personnel have attempted to return sleepwalking patients to bed. In extreme cases, victims have been stabbed with knives or blunt objects. Such inappropriate and violent behaviors have legal and forensic implications. Sleepwalkers have been arrested and charged with assault and battery, attempted homicide, homicide, and sexual assault with indecency.

The child with calm sleepwalking may quietly walk toward a light or to the parents’ bedroom. Occasionally, children walk toward a window or door or even go outside, with obvious attendant risk.

There is a growing literature on excessive daytime sleepiness being a common associated feature of sleepwalking in adults.

Clinical or Pathologic Subtypes

Sleep-related abnormal sexual behaviors are primarily classified as confusional arousals in that they typically occur without any behaviors outside of the bed (or chosen sleeping accommodation) but have also been less commonly associated with sleepwalking. Other terms for this condition include “*atypical sexual behavior during sleep*,” “*sexsomnia*,” and “*sleep sex*.” Sleep-related abnormal sexual behaviors often have significant interpersonal, clinical, and occasional criminal consequences. The set of abnormal sexual behaviors and experiences during disordered arousals includes prolonged or violent masturbation, sexual molestation and assaults (of minors and adults), initiation of sexual intercourse (including disregard of the menstrual status of the bed partner - in contrast to waking intercourse for those individuals), spontaneous orgasms, and loud, sexual vocalizations during sleep—followed by morning amnesia. The preponderance of patients have also been diagnosed with a NREM sleep parasomnia, most often confusional arousals but on occasion sleepwalking or sleep-related eating disorder. Obstructive sleep

apnea (OSA), sleep-related bruxism, and certain medications, including sodium oxybate and zolpidem, have triggered sexsomnia.

A parasomnia overlap disorder (with or without OSA), in which RBD and a NREM parasomnia are comorbid in a patient with sexsomnia, may complicate the diagnosis of each condition. A careful review of the history, including input from the bed partner, and use of video-polysomnography may facilitate the identification of these presentations. Finally, complex sexual behaviors during sleep can be manifestations of epileptic seizures.

Demographics

Both sexes are affected equally. Disorders of arousal are especially prevalent among children and adults younger than 35 years. The prevalence rate of confusional arousals and sleepwalking are similar.

The prevalence of confusional arousals in children three to 13 years of age in a large population-based study was 17.3%. The lifetime prevalence of confusional arousals has recently been reported as 18.5%. The prevalence among adults older than 15 years is 2.9% to 4.2%.

The lifetime prevalence of sleepwalking has been estimated to be as high as 18.3%. Although a more recent, large meta-analysis found a 6.9% estimated lifetime prevalence of sleepwalking, with a current prevalence rate for sleepwalking within the last 12 months being 5% in children and 1.5% in adults. A study of “nocturnal wandering” that likely included many sleepwalkers reported a lifetime prevalence of 29.2%. A Swedish study of children aged 6-16 years found the incidence of sleepwalking to be 40%. One earlier epidemiological study found that up to 4.3% of adults sleepwalk. Peak prevalence of sleepwalking has been estimated to be at 10 years.

The prevalence of sleep terrors has not been studied as thoroughly. Prevalence rates of 1% to 6.5% in children and 2.2% in adults have been reported, with a prevalence rate of 2.3% to 2.6% in the 15 to 64-year-old age group, before falling to 1% in the older than 65 years age group. Other studies have reported the intermittent appearance of sleep terrors in 25% of children younger than five years. The peak prevalence of sleep terrors has been estimated to be at 1.5 years.

Predisposing and Precipitating Factors

Disorders of arousal are most often evaluated with respect to predisposing, priming, and precipitating (triggering) factors. A simultaneous co-occurrence of these factors is often thought necessary to precipitate a disorder of arousal. However, an explanation for the night-to-night variability of occurrence is lacking.

A genetic predisposition has been hypothesized, and several studies have identified different genetic loci and modes of inheritance (see Familial Pattern, below). Furthermore, disorders of NREM arousal have a

high prevalence of the HLA DQB1*05:01 genotype, supporting the concept of a common genetic background for these NREM parasomnias.

Many priming factors for disorders of arousal, especially sleepwalking, have been identified. Sleep deprivation and situational stress are the most potent factors.

Parkinson's disease is associated with sleepwalking in 9% of patients, most of whom also had video-PSG-demonstrated REM sleep behavior disorder. Less common medical triggers for sleepwalking include hyperthyroidism, migraines, head injury, encephalitis, and stroke, among others

OSA and other sleep-related respiratory events may trigger disorders of arousal in both children and adults. Treatment of comorbid conditions may reduce or eliminate the occurrence of disorders of arousal. Disorders of arousal may also be triggered by environmental stimuli such as contact with the bed partner, telephone calls, pagers, messaging from electronic devices, and a host of other stimuli. It is clinically important to note that first responders, physicians, and others on call (such as police officers and firefighters), with sleep disruption and cumulative sleep deprivation, may be vulnerable to such stimuli, increasing the potential for inappropriate responses and behavior.

Travel, sleeping in unfamiliar surroundings, febrile states in children, physical or emotional stress in adults, and the premenstrual period in women may precipitate episodes. Internal stimuli, such as a distended bladder, or external stimuli, such as noise or light, can also precipitate episodes. Many medications may trigger sleepwalking, particularly benzodiazepine receptor agonists and other gamma-aminobutyric acid (GABA) modulators; antidepressants and other serotonergic agents; antipsychotics; and β -blockers. The strongest evidence for medication-induced sleepwalking was for zolpidem and sodium oxybate. Alcohol has been identified in previous reports as a potential sleepwalking trigger.

However, the amnesia associated with disorders of arousal makes these reports unreliable. More recent evidence-based reviews have found no compelling relationship between alcohol and disorders of arousal. In addition, there is no evidence indicating that behavior resulting from alcohol intoxication can be distinguished from behavior resulting from a disorder of arousal. Thus a disorder of arousal cannot be diagnosed in the context of alcohol intoxication. This assertion holds for any claim that an intoxicated person fell asleep and then engaged in an arousal disorder episode since "passing out" from alcohol intoxication cannot be distinguished from actual sleep by any observer. Likewise, the association between therapeutic doses of sedative-hypnotic drugs and apparent parasomnias should be carefully distinguished from the expected effects of drug abuse or misuse that result in CNS depression. Investigations of drivers who had accidents attributed to drug-related sleep-driving are reported to show that: 1) blood levels of prescribed sedative-hypnotics exceeded therapeutic ranges; 2) the individuals failed to take the medication at the correct time or remain in bed for sufficient time following ingestion; or 3) the individuals combined sedative-hypnotics with other CNS depressants or alcohol. Driving with a high blood level of a sedative-hypnotic can result in significant cognitive and motor impairment. Serious accidents can result. Sleep driving and other complex behaviors in this population are more likely to have resulted from drug misuse and abuse rather than true parasomnias. The ICSD-3R advocates that disorders of arousal should

not be diagnosed in the presence of alcohol intoxication or the setting of sedative-hypnotic exposure resulting in elevated blood levels.

There is no significant association between childhood disorders of arousal and psychopathology. Although many adult sleepwalkers may have a past or current history of nonpsychotic depressive and anxiety disorders, it does not appear that the psychiatric disorder and sleepwalking are tightly linked. In addition, when the two conditions emerge in close temporal proximity, control of the psychiatric disorder often does not control the parasomnia, for which additional treatment is required. However, depressive disorders, sedating antidepressants, and nonbenzodiazepine hypnotics have been identified as significant risk factors.

Familial Pattern

Genetic factors appear to play an important role in all disorders of arousal. However, research data exist primarily for patients who sleepwalk. Sleepwalking has a familial pattern. The rate of childhood sleepwalking increased with the number of affected parents: 22% when neither parent has the disorder, 47% if one parent is affected, and 61% when both are affected. Parental history of sleepwalking predicts the incidence and persistence of sleep terrors in children. Population-based studies of monozygotic and dizygotic twins suggest that genetic factors have a role in 65% of cases of sleepwalking. Different models of modes of inheritance, including multifactorial, recessive with incomplete penetrance, and autosomal dominant trait with reduced penetrance, have been proposed, based primarily on analysis of family histories. However, these findings are not sufficiently specific to be used for diagnostic testing. Further, the mechanisms by which a genetic predisposition for confusional arousal or other related disorders contributes to their occurrence are not known.

Onset, Course, and Complications

Confusional arousals most often appear in early childhood, around the age of two years. This childhood form of confusional arousals is typically benign but may cause concern in parents. Confusional arousals of early childhood diminish in occurrence after the age of five years.

Sleepwalking can begin as soon as a child can walk but may begin at almost any time in the life cycle, including as late as the seventh decade. Sleepwalking is often preceded by confusional arousals. Childhood sleepwalking usually disappears spontaneously around puberty but may persist into adolescence. Episodes can occur sporadically or with high frequency, such as multiple times nightly for several consecutive nights. Sleepwalking may occur for the first time in adulthood or may recur in adulthood during periods of sleep deprivation or stress. In adults with sleepwalking, 73% have reported childhood-onset sleepwalking. Violence during sleepwalking episodes was more frequent in males, with nearly half reporting self-injury and violence towards others during sleepwalking episodes. More than half of

adolescent and adult patients with sleepwalking have reported complex and bizarre interactions with the environment and violent behaviors. Stress is a reported trigger for episodes in 80% of patients.

Sleep terrors usually emerge from very early childhood to late pre-adolescence (but can also emerge in adulthood) and tend to resolve spontaneously by early adolescence, as does sleepwalking. Social embarrassment over the sleep terrors can impair social relationships in children and adults. Severe or even lethal injuries can occur.

Developmental Issues

Developmental issues are discussed in relevant sections (see *Demographics and Onset, Course, and Complications*).

Pathology and Pathophysiology

The overwhelming majority of individuals with disorders of arousal do not have neurological or psychological pathology. There are rare, reported cases of confusional arousals associated with brain lesions in areas subserving arousal, such as the posterior hypothalamus, midbrain reticular area, and periventricular gray matter. However, data from a single patient with confusional arousals suggest that they may be due to a functional abnormality in the brain that leaves some regions, such as hippocampus and frontal associative cortices, asleep, while other parts of the brain, such as motor, cingulate, insular, amygdala, and temporopolar cortices, are active or awake.

It is generally considered that disorders of arousal represent a dissociation of different regions of the brain in addition to activation of locomotor centers/central pattern generators, accompanied by sleep inertia and sleep state instability.

Objective Findings

Although not routinely indicated for the evaluation of typical, uncomplicated, and noninjurious parasomnias, polysomnographic studies demonstrate that disorders of arousal typically begin after an arousal from slow wave sleep, most commonly toward the end of the first or second episode of slow wave (N3) sleep. Occasionally, disorders of arousal can emerge from N2 sleep. Heart rate acceleration, increased muscle tone, and muscle twitching may rarely be observed before a slow wave sleep arousal. A video-polysomnographic (vPSG) study of motor patterns in adolescent and adult patients with disorders of arousal found simple arousal movements in 84% of episodes and rapid/complex arousal movements in 16% of episodes. A slow wave sleep fragmentation index (the sum of all slow-wave sleep interruptions/hour) has been developed for these disorders, with an index cutoff value of 6.8/hour demonstrating high sensitivity and specificity. In addition, an analysis of behaviors arising from N3 sleep

in patients with disorders of arousal found that two or more N3 interruptions with eye-opening and associated behaviors (such as fear, surprise, sitting up, screaming, or standing) were specific to patients with disorders of arousal.

Diagnostic polysomnography may reveal high-amplitude hypersynchronous delta waves and frequent arousals from slow wave sleep. However, these findings have low specificity and have been reported in other disorders such as OSA and asymptomatic individuals. On rare occasions, video-polysomnography can support the clinical diagnosis by documenting arousals from slow wave sleep accompanied by behaviors typical of confusional arousals. Out-of-bed behaviors are very rare in the sleep laboratory. Changes between the home and sleep laboratory environment, timing, habits, and other factors may decrease the likelihood of sleepwalking in the laboratory. Time-synchronized video-polysomnographic (vPSG) recording is essential if polysomnography (PSG) is to be used as support for the diagnosis. However, a normal v PSG does not rule out the diagnosis of a disorder of arousal. In adults in whom there are only one or two episodes per year, there is a very low likelihood of occurrence in the sleep laboratory. In addition, the sleep study may assist in ruling out disorders with similar presentations, such as RBD or nocturnal epilepsy. PSG may further be useful by identifying potential triggers, such as sleep-related breathing disorders or periodic limb movements. Provocative sleep studies using sleep deprivation and acoustic stimuli have been used for research purposes with success. However, the sensitivity and specificity of these techniques for clinical purposes are unknown.

Postarousal EEG recordings in children and adults with sleepwalking often demonstrate a partial or near-complete persistence of sleep, with diffuse, rhythmic delta activity; diffuse delta and theta activity; mixed delta, theta, alpha, and beta activity; or, at times alpha and beta activity.

A study of all-night sleep deprivation in sleepwalkers and controls revealed altered brain perfusion patterns while awake in the sleepwalkers, who had bilaterally decreased regional cerebral blood flow in the inferior temporal gyrus. Therefore, a pattern of neural dysfunction during wakefulness represents another component of the phenotype of adult sleepwalking. Another video-PSG study also found altered brain perfusion patterns in wakefulness and slow-wave sleep in sleepwalking patients.

vPSG also may help exclude the diagnosis of RBD by demonstration of normal muscle atonia in REM sleep (assuming adequate amounts of REM sleep are observed). Although the “macrostructure” of sleep (i.e., the cycling of various NREM and REM sleep stages and the relative distributions of these sleep stages) is generally preserved with sleepwalking, the “microstructure” of sleep can be perturbed. Power spectral analyses of slow wave activity in adult sleepwalkers have revealed several forms of slow wave sleep dysregulation, including significant slow wave sleep fragmentation (particularly during the first NREM-REM sleep cycle), a significant increase in delta power just before an arousal, and increased slow wave activity across all NREM sleep cycles. In a PSG study of NREM parasomnia patients utilizing high-density EEG, the findings supported the current understanding that NREM parasomnias are caused by local arousals in motor and cingulate cortices, with persistence of localized changes in neuronal excitability that predispose patients to clinical episodes. An EEG functional connectivity study found that sleepwalking episodes were preceded by the co-existence of arousal and deep sleep.

Differential Diagnosis

Disorders of arousal should be carefully distinguished from other disorders with similar presentations but different pathophysiologies, courses, and treatments. Other sleep disorders, such as *OSA*, can precipitate disorders of arousal. Therefore, a careful history must be obtained to identify other sleep disorders.

REM sleep behavior disorder typically presents as dream-enacting behaviors during the second half of the night. It is most commonly observed in middle-aged men, although it can affect women and any age group. RBD episodes rarely involve standing up and leaving the bed and usually do not involve the trunk. Because sleepwalking in adults can also present as dream-enacting behaviors that emerge during any time of night, vPSG may be necessary to distinguish sleepwalking from RBD. In contrast to disorders of arousal, signs of RBD, particularly tonic/phasic EMG activity during REM sleep, are almost always present during sleep studies. If sleepwalking (or sleep terrors) occurs with RBD in the same patient, both should be diagnosed. This co-occurrence has been referred to as a parasomnia overlap disorder.

Sleep-related epilepsy can manifest with wandering behavior or with frenzied walking or running. Manifestations of various epilepsy syndromes may mimic disorders of arousals.

Alcohol intoxication Disorders of arousal should not be diagnosed in the presence of intoxication. The behavior of the alcohol-intoxicated individual may superficially resemble that of the sleepwalker. However, the sleepwalker is typically severely cognitively impaired, with only limited motor impairment. The alcohol-intoxicated individual's level of cognitive functioning may be reduced but not absent, whereas motor behavior is often severely impaired. In alcoholic blackouts, where anterograde amnesia is, by definition, the cardinal manifestation, it is essential to note that outward motor behavior and cognitive function may not be impaired and may be perceived as normal. In addition, drug-induced automatic-amnestic behaviors need to be considered in the differential diagnosis.

Psychogenic dissociative disorders arising from sleep are typically characterized by a history of sexual, physical, or emotional trauma or abuse. Abnormal behaviors during vPSG emerge from well-established EEG wakefulness, with prolonged complex behaviors that often mimic past abuse scenarios. Most patients also have daytime dissociative episodes.

Malingering should also be considered in adult patients.

Unresolved Issues and Further Directions

With the further development of sophisticated genetic testing and neuroimaging, direct research into the causes and mechanisms of disorders or arousals is anticipated to advance. Further investigations that aid in the characterization of the pathophysiology are necessary. Development of sleep laboratory-based techniques for provoking episodes of sleepwalking would improve diagnostic accuracy. Finally, the

growing use of HD-EEG during vPSG studies is anticipated to deepen our understanding of the neurobiological substrates and mechanisms promoting disorders of arousal.

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Sleep-Related Eating Disorder

ICD-9-CM code: 327.40

ICD-10-CM code: G47.59

Alternate Names

Sleep eating

Diagnostic Criteria

Criteria A-D must be met

- A. Recurrent episodes of dysfunctional eating that occur after an arousal during the main sleep period.
- B. The presence of at least one of the following is associated with the recurrent episodes of involuntary eating.
 1. Consumption of peculiar forms or combinations of food or inedible or toxic substances.
 2. Sleep-related injurious or potentially injurious behaviors performed while in pursuit of food or while cooking food.
 3. Adverse health consequences from recurrent nocturnal eating.
- C. There is partial or complete loss of conscious awareness during the eating episode, with subsequent impaired recall.
- D. The disturbance is not better explained by another current sleep disorder, medical disorder, mental disorder, or medication/substance use.

Essential Features

SRED consists of recurrent episodes of involuntary eating and drinking during arousals from sleep associated with diminished consciousness levels, impairment of subsequent recall, and adverse consequences.

The episodes of eating always occur in an involuntary or “out of control” manner after an interval of sleep. Typically, they occur during partial arousals from sleep with subsequent partial recall. Some patients cannot easily be brought to full consciousness during an episode of eating (as is the case with sleepwalking) and may have no recall of having eaten during the night. However, other patients seemingly have considerable alertness during an episode and have substantial recall in the morning. There may be variability of awareness and subsequent recall within one night and across the evolution of the disorder

in individual patients. The recurrent episodes of involuntary eating and drinking during the main sleep period are typically associated with a feeling of lack of control over the eating.

Problematic features of recurrent sleep-related eating include consumption of peculiar forms or combinations of food or inedible or toxic substances (e.g., frozen pizzas, raw bacon, buttered cigarettes, cat food and salt sandwiches, coffee grounds, ammonia cleaning solutions) and sleep-related injury (e.g., lacerations from careless manipulation of kitchen utensils; internal or external burns from consuming or spilling hot foods or beverages; or poisoning and internal injuries from ingesting toxic substances). Adverse health consequences include dental caries and tooth chipping from biting frozen foods; weight gain; obesity (including morbid obesity resulting in bariatric surgery); and various metabolic problems, such as destabilization or precipitation of diabetes mellitus, hypertriglyceridemia, and hypercholesterolemia. Nonrestorative sleep from sleep disruption, morning anorexia, and abdominal distention may occur. SRED carries the risk of consuming foods to which one is allergic. Overnight fasting prior to next-day surgery or testing can be compromised. Secondary depressive disorders may emerge from longstanding personal dejection and a sense of failure over the inability to control the sleep-related eating. Secondary daytime food restriction, prompted by despair over not being able to stop the nocturnal eating, often occurs at some point during the course of the disorder. This food restriction may exacerbate the SRED due to inadequate caloric intake during the day. Patients may also engage in potentially hazardous (and expensive) weight-loss regimens.

Associated Features

Sleep-related eating, including multiple episodes during the main sleep period, is reported by most affected individuals. The episodes of eating occur at any time in the sleep cycle. High-caloric foods are typically preferred. The foods preferentially consumed during sleep-related eating are not typically consumed with preference during the daytime. Paradoxically, to the extent that there is recall, hunger and thirst are absent during episodes of compulsive eating with SRED. The episodes of eating are sometimes experienced as food-related enactment of a dream. Simple foods or entire hot or cold meals may be prepared and consumed. Careless food handling often occurs. Alcoholic beverages are almost never consumed. The usual response to interference during an eating episode is irritability and agitation.

Clinical or Pathophysiological Subtypes

None known.

Demographics

Females comprise 60% to 83% of SRED patients in reported series. The mean age of onset of SRED is 22-39 years. In reported series, the mean duration of SRED prior to clinical presentation ranged from four to

15 years, suggesting that SRED often is a chronic disorder with considerable diagnostic delay. Features consistent with both eating disorders and parasomnias were found in these subjects. A Japanese survey of young adults found a 2.2% prevalence of SRED-like behavior. Self-administered questionnaires produced the following prevalence rates: 16.7% in an inpatient eating disorders group; 8.7% in an outpatient eating disorders group; and 4.6% in an unselected university student group. These data indicate a high prevalence of SRED, although confirmatory studies across different clinical and nonclinical population groups are needed. In addition, an estimated lifetime prevalence of SRED in psychiatric outpatients has been reported to be 4%, while 8.4% of psychiatric outpatients taking hypnotics reported SRED.

Predisposing and Precipitating Factors

SRED can be idiopathic, but it appears to be most commonly associated with another primary sleep disorder, another clinical condition, or the use of a sedative-hypnotic medication. Sleepwalking is most commonly associated with sleep-related eating, although once eating becomes part of the behavioral repertoire, it quickly becomes the predominant, if not the exclusive, nocturnal behavior. This observation would indicate that SRED is most often a “sleepwalking variant disorder.” A history of sleepwalking during childhood appears to be a predisposing factor in many cases. A retrospective controlled study of SRED patients, sleepwalking patients, and controls found that SRED patients were mainly women with onset of the disturbance in adulthood. They typically experienced nightly episodes and had more frequent eating problems in childhood and higher current anorexia scores than sleepwalking patients or controls. They also shared commonalities with sleepwalking patients, including a high (66%) frequency of past or current sleepwalking, a similar timing of parasomnia episodes (in the first half of the night), and numerous arousals from N3 sleep. On video-polysomnography, eating episodes mainly occurred within one minute after awakening from N2 or N3 sleep. The frequencies of RLS, PLMs, and sleep apnea were similar across the three groups.

Other sleep disorders closely associated with SRED include RLS, OSA, narcolepsy, and circadian rhythm sleep-wake disorders, particularly an irregular sleep/wake pattern. In addition, multiple parasomnias in the same patient have been reported with SRED, including sexsomnia as a variant of confusional arousals, sleepwalking, and REM sleep behavior disorder. Medication-induced SRED has been reported with zolpidem, in particular, and a broad range of sedative-hypnotics, including benzodiazepines, benzodiazepine receptor agonists, mirtazapine, risperidone, quetiapine, aripiprazole, ziprasidone, sodium oxybate, lithium carbonate, anticholinergics, and various other psychotropic agents.

The onset of SRED also has been reported with cessation of cigarette smoking, cessation of alcohol and substance abuse, acute stress (usually involving major separation reactions), after daytime dieting, and with the onset of narcolepsy, autoimmune hepatitis, encephalitis, Parkinson’s disease, and other conditions. SRED can also be associated with daytime eating disorders and nocturnal dissociative disorder. The prevalence of sleep-related eating disorder is significantly increased in patients with narcolepsy type 1 and patients with RLS. The use of hypnotic medication in RLS patients further increases the risk for SRED.

Familial Pattern

A familial basis for SRED is not uncommon, including co-occurrence in fraternal twins, although detailed genetic studies have not been carried out.

Onset, Course, and Complications

The onset of SRED can be insidious and sporadic or precipitous and fulminant, with the rapid development of nightly eating episodes (related or unrelated to the start of hypnotic medication for insomnia). The course is usually unremitting. Fires can occur when the individual with SRED begins to cook food and then abandons it, returning to bed. Screening for SRED prior to bariatric surgery for morbid obesity is recommended, as SRED may complicate the postoperative course of patients undergoing bariatric surgery.

Developmental Issues

SRED can emerge in childhood, either associated or unassociated with a family history of SRED.

Pathology and Pathophysiology

The underlying pathophysiology of SRED is unclear. Despite the broad range of predisposing and precipitating factors in SRED, the relatively homogeneous set of clinical features suggests the presence of a “final common pathway” precipitated by a variety of factors. Although SRED has prominent features of both a sleep disorder and an eating disorder, its relatively homogeneous presentation supports its classification as a separate diagnostic entity. More than half of patients with SRED have a history of another parasomnia that preceded the onset of nocturnal eating, suggesting that the presence of another parasomnia is a major risk factor for SRED. However, the female predominance in SRED is more consistent with eating disorders, which are female predominant, than with sleepwalking or movement disorders (e.g., RLS) which have slight to no female bias. Thus, it appears that two basic drive states—sleeping and eating—are pathologically intertwined in SRED.

Objective Findings

Although not routinely indicated in the assessment of SRED, vPSG evaluations have often reported positive findings. The most common finding consists of multiple confusional arousals, with or without eating, arising from slow wave sleep. However, abnormal arousals have been documented from all NREM

sleep stages and occasionally from REM sleep. The level of consciousness has typically spanned the range from virtual unconsciousness to various levels of partial consciousness despite a concurrent EEG pattern that is often predominantly awake. This range suggests a dissociation between the EEG and the level of consciousness. This dissociation also can be found in adult sleepwalking without associated eating. In contrast, classic sleepwalking in childhood is usually associated with the persistence of high-voltage delta waves or the admixture of delta, theta, and alpha activity. A predominant wake pattern is rare in childhood sleepwalking. PLMs and OSA may be observed in polysomnographic monitoring of SRED patients. Investigations of the boundaries between SRED and fully conscious abnormal nocturnal eating found that 22 of 35 SRED patients had PLMs, 5 of 35 had RLS, and 29 of 35 had recurring chewing and swallowing movements during sleep associated with nearly half of the total number of EEG arousals.

Differential Diagnosis

Night eating syndrome (NES) is the most important disorder to differentiate from SRED. It is characterized by excessive eating between dinner and bedtime and during full awakenings during the sleep period. In contrast to daytime eating disorders (*bulimia nervosa*, *anorexia nervosa*), inappropriate compensatory behavior, such as self-induced vomiting, enemas, misuse of laxatives, diuretics, or other medications, or other purging activity, are not present in SRED. However, the two conditions may be comorbid. A person with a daytime eating disorder may also have a coexisting SRED associated with confusional arousals but not with purging behaviors during the night or upon arising in the morning. Patients with longstanding SRED and excessive weight gain may eventually fast during the daytime or engage in excessive exercise to prevent obesity from the SRED. Likewise, patients who otherwise fulfill the criteria for SRED may consciously eat during the prebedtime period in a futile attempt to suppress the compulsion to eat after falling asleep.

SRED appears to be considerably more female predominant than NES (which has <60% female prevalence). Mood disorders are more common with NES than with SRED. Nevertheless, SRED and NES share many overlapping features and may exist along a common spectrum of pathophysiology. SRED should also be distinguished from nocturnal (sleep-related) extensions of *bulimia nervosa*, *binge-eating disorder*, and *anorexia nervosa, binge/purge type*.

Nocturnal eating (drinking) syndrome described in the original International Classification of Sleep Disorders is primarily a disorder of infancy characterized by recurrent awakenings with the inability to resume sleep without eating or drinking.

Kleine-Levin syndrome (periodic hypersomnia) can present with inappropriate nocturnal (wakeful) eating, but its predominance in adolescent males and its hallmark symptom complex of periodic hypersomnia, hypersexuality, and hyperphagia lasting days to weeks should easily distinguish it from SRED.

Medical and neurologic disorders associated with abnormal recurrent eating during the main sleep period (usually with full or near full alertness) should also be excluded. These include *hypoglycemic states, peptic ulcer disease, reflux esophagitis, and Kluver-Bucy syndrome*.

Unresolved Issues and Future Directions

The extent of overlap and divergence between SRED and NES needs to be further elucidated. The increasing availability and use of HD (high density) EEG during vPSG studies should further elaborate the underlying brain mechanisms promoting abnormal eating behaviors in SRED and NES. The underlying brain mechanisms revealing the extent of overlap and divergence of SRED and disorders of arousal need to be elucidated.

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REM-Related Parasomnias

REM Sleep Behavior Disorder

ICD-9-CM code: 327.42

ICD-10-CM code: G47.52

Alternate Names

None.

Diagnostic Criteria

Criteria A-D must be met

- A. Repeated episodes of sleep-related vocalization or complex motor behaviors.^{1,2}
- B. These behaviors are documented by video-polysomnography to occur during REM sleep or, based on clinical history of dream enactment, are presumed to occur during REM sleep.
- C. Polysomnographic recording demonstrates REM sleep without atonia (RWA)³
- D. The disturbance is not better explained by another current sleep disorder or mental disorder.

Notes

1. This criterion can be fulfilled by observing repetitive episodes during a single night of video polysomnography.
2. The observed vocalizations or behaviors often correlate with simultaneously occurring dream mentation, leading to the frequent report of “acting out one’s dreams.”
3. As defined by the guidelines for scoring PSG features of RBD in the most recent version of the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events. The scoring manual does not identify the frequency of REM epochs without atonia required to establish a diagnosis of RBD. The reader is referred to the discussion of this issue in the Objective Findings section.
4. The individual is typically awake, alert, coherent, and oriented upon awakening.
5. On occasion, there may be patients with a typical clinical history of RBD with dream-enacting behaviors, who also exhibit typical RBD behaviors during vPSG, but do not demonstrate sufficient RWA, based on the current evidence-based data, to satisfy the PSG criteria for diagnosing RBD. RBD may be provisionally diagnosed in such patients based on clinical judgment. The same rule applies when vPSG is not readily available.
6. RBD may be diagnosed in the presence of CNS-acting medications. Certain antidepressant medications may contribute to RWA on polysomnography without dream enactment behavior

and RBD. Medication (antidepressant)-induced RBD may signal and unmask an underlying neurodegenerative disorder. Therefore, medication-induced RBD should be diagnosed as RBD, pending future longitudinal studies.

Essential Features

RBD is characterized by abnormal behaviors and EMG abnormalities during REM sleep. The EMG demonstrates an excess of muscle tone during REM sleep or an excess of phasic EMG activity during REM sleep, known as REM sleep without atonia (RWA or RSWA), the neurophysiologic signature of RBD.

Behaviors in RBD usually manifest as excessive jerks and complex vocal or motor behaviors with the enactment of unpleasant, action-filled, and often violent dreams in which the individual is being confronted, attacked, or chased by unfamiliar people or animals. Typically, the individual awakens quickly, becomes rapidly alert, and reports a dream with a coherent story, when questioned immediately at the end of an episode. Later (e.g., next day) dream recall is variable. The dream action corresponds closely to the observed sleep behaviors.

Sleep and dream-related behaviors reported by history and documented during vPSG include both violent and (less commonly) nonviolent behaviors: talking (including giving speeches), smiling, laughing, singing, whistling, shouting, swearing profanities, crying, chewing, gesturing, reaching, grabbing, arm flailing, clapping, slapping, punching, kicking, sitting up, leaping from bed, crawling, running, or dancing. Walking, however, is relatively uncommon with RBD, and leaving the room is especially rare. There can be rare occurrences of smoking a fictive cigarette, masturbation-like behavior, pelvic thrusting, and mimics of eating, drinking, urinating, and defecating. The eyes usually remain closed during an RBD episode.

Associated Features

A complaint of sleep-related injury is common with RBD. Medical attention is often only sought after a sleep-related injury to either the person or the bed partner and less frequently due to sleep disruption. Because RBD occurs during REM sleep, it usually appears at least 90 minutes after sleep onset, unless there is coexisting narcolepsy, in which case RBD can emerge shortly after sleep onset during a sleep-onset rapid eye movement period (SOREMP). In addition, RBD may emerge during intense REM sleep rebound states, such as during withdrawal from alcohol and sedative-hypnotic agents, or in association with certain medication use, drug intoxication, or relapsing multiple sclerosis.

Daytime tiredness or sleepiness is uncommon as a presenting feature of RBD unless narcolepsy is also present. There is typically no history of irritable, aggressive, or violent behavior during the day. PLMs during NREM and REM sleep are very common with RBD. Studies have suggested that the presence of RBD in patients with Parkinson's disease is associated with more significant cognitive decline.

Clinical or Pathophysiological Subtypes

Isolated RBD is a condition characterized by dream enactment and polysomnographic RWA, without other associated overt neurological symptoms or signs. Isolated RBD, nevertheless, confers a high risk for the eventual development of a neurodegenerative disease, including Parkinson's disease (PD), dementia with Lewy bodies (DLB), or multiple system atrophy (MSA). When one of these diseases is already present at the time of RBD diagnosis, the subtype, **Secondary RBD**, should be employed. While alpha synucleinopathies such as PD, DLB, MSA, and pure autonomic failure are the most frequent causes of secondary RBD, other causes include narcolepsy, autoimmune encephalopathy, or brainstem lesions.

Parasomnia overlap disorder is a condition in which patients have both RBD and either a disorder of arousal, sleep-related eating disorder, or rhythmic movement disorder. This condition is male predominant but less so than isolated RBD. Most cases begin during childhood or adolescence. Virtually all age groups can be affected. It can be idiopathic or symptomatic of a broad set of disorders, including narcolepsy, multiple sclerosis, brain tumor, rhombencephalitis (right pontine tegmentum/medulla lesion), brain trauma, Moebius syndrome, agrypnia excitata, Machado-Joseph disease, various psychiatric disorders and their pharmacotherapies, and substance abuse disorders and withdrawal states.

Status dissociatus can be classified as a subtype of RBD that manifests as an extreme form of state dissociation without identifiable sleep stages but with sleep and dream-related behaviors that closely resemble RBD. Status dissociatus represents a significant breakdown of the polysomnographic markers for REM sleep, NREM sleep, and wakefulness, with admixtures of these states being present. In this condition, conventional sleep stages are not identifiable during polysomnographic monitoring. An abnormal behavioral release can be associated with disturbed dreaming, strongly suggesting dream-enacting behaviors closely resembling RBD. Not uncommonly, individuals think they are awake when observers presume that they are asleep and acting out a dream, or vice versa. An underlying neurologic or medical condition, spanning a broad range of pathology, is almost always present.

Dream enactment (“oneirism”) that is REM sleep-related or related to a dissociated REM sleep-wakefulness state can be a core feature of a pathologic condition called agrypnia excitata, characterized by generalized motor overactivity, impaired ability to initiate and maintain sleep (with “wakeful dreaming”), loss of slow wave sleep, and marked motor and autonomic sympathetic activation. Agrypnia excitata is found with such diverse conditions as delirium tremens, Morvan syndrome, and fatal familial insomnia. Thus, agrypnia excitata manifests as both a severe parasomnia and severe insomnia.

Demographics

Isolated RBD (iRBD) is a predominantly male disorder that usually emerges after age 50. However, cases of RBD from early childhood up to age 88 years have been reported. RBD emerging in adults before age 50 tends to have different demographics and associated features, including greater sex parity and increased rates of parasomnia overlap disorder (POD), comorbid narcolepsy, antidepressant medication use, and possibly autoimmune diseases. In addition, the clinical presentation of RBD in younger adults

differs from that in older adults. It is characterized by less aggressive and violent behavior, possibly due to greater female representation and higher rates of comorbid narcolepsy (which manifests with milder RBD behaviors).

RBD associated with neurologic disorders and other symptomatic forms of RBD is as male predominant as iRBD, except for narcolepsy (as described below) and multiple system atrophy. RBD may not be the presenting complaint to a sleep disorders center. RBD in children is virtually never isolated and is usually associated with narcolepsy (at times emerging months before the emergence of narcoleptic symptoms), brainstem tumors, antidepressant medications, neurodevelopmental disorders, and various rare conditions.

Recent estimates of the prevalence of vPSG-verified iRBD in the middle-aged to elderly general population were approximately 1.06 - 1.34%.

Predisposing and Precipitating Factors

The major predisposing factors are male sex, age 50 years or older, and an underlying neurological disorder, particularly dementia with Lewy bodies, Parkinson's disease, multiple system atrophy, narcolepsy, or stroke. A recent multicenter case-control study of environmental risk factors of RBD found that smoking, head injury, pesticide exposure, and farming were significant risk factors. Medications, particularly the antidepressants venlafaxine, serotonin-specific reuptake inhibitors (SSRIs), mirtazapine, tricyclic antidepressants, monoamine oxidase inhibitors, selegiline, and other antidepressant agents, are increasingly recognized precipitating factors. Beta-blockers (bisoprolol, atenolol) and cholinergic agents have been implicated as triggering agents. Likewise, excessive caffeine and withdrawal from cocaine, amphetamine, alcohol, barbiturate have been associated with causing or unmasking RBD. The disorder may also be precipitated or worsened by the pharmacologic treatment of cataplexy. RBD may also be associated with posttraumatic stress disorder.

Although many factors may precipitate RBD, the more specific diagnosis of REM sleep behavior disorder should be made when diagnostic criteria for RBD are met.

Familial Pattern

A recent multicenter controlled study revealed a significantly increased positive family history of dream enactment, raising the possibility of a genetic contribution to RBD.

Onset, Course, and Complications

The onset of RBD can be gradual or rapid, and the course is often progressive. Complications include sleep-related injuries to self or bed partner that can be life-threatening and disruption of the bed partner's

sleep, which can be severe. Marital discord due to the RBD is uncommon but can be severe when present due to repeated injury or disruption of the bed partner's sleep.

Delayed emergence of a neurodegenerative disorder, often more than a decade after the onset of iRBD, is very common in men 50 years of age and older. These disorders include alpha-synucleinopathies – Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy (MSA). The largest multicenter study of patients diagnosed with iRBD recently reported a 73.5% eventual conversion rate from iRBD to an overt neurodegenerative syndrome of parkinsonism/dementia. Some previous, smaller single-center cohorts with longer follow-up have reported even higher phenocconversion rates of 81-91%. Of a substantial number of patients with RBD who underwent post-mortem examination, 94% demonstrated alpha-synucleinopathy. Moreover, other synuclein-related neurodegeneration biomarkers are common in patients with long-standing iRBD (long-standing non-converters). Conversely, RBD is present in > 90% of reported cases of MSA, in approximately 80% of reported cases of DLB, and up to 60% of reported patients with PD.

There may be a longstanding prodromal history of sleeptalking, yelling, limb twitching, and jerking during sleep (that may or may not be dream related) or isolated RWA without accompanying clinical behaviors, found only as an incidental finding during polysomnography. This phase preceding full-blown RBD has been named prodromal RBD.

Developmental Issues

As stated previously, RBD can emerge in children, usually in association with narcolepsy type 1, brainstem tumors, antidepressant medications, or neurodevelopmental disorders.

Pathology and Pathophysiology

Current evidence suggests a specific association between RBD and *neurodegenerative disorders*. The synucleinopathies comprise a set of neurodegenerative disorders that share a common pathologic lesion composed of aggregates of insoluble α -synuclein protein in selectively vulnerable populations of neurons and glial cells. These pathologic aggregates appear to be closely linked to the onset and progression of clinical symptoms and the degeneration of affected brain regions in neurodegenerative disorders. The major synucleinopathies include PD, DLB, and MSA.

RBD is also linked with *narcolepsy* (almost always narcolepsy type 1), which represents another form of REM sleep motor-behavioral dyscontrol. RBD associated with narcolepsy is now considered a distinct RBD phenotype, characterized by less complex and more elementary movements in REM sleep, less violent behavior, earlier age of onset, and hypocretin deficiency. The presence of RBD in pediatric patients may be an initial manifestation of narcolepsy type 1.

Other reported etiologic associations of RBD with *neurologic disorders* include ischemic or hemorrhagic cerebrovascular disease, autoimmune encephalopathies including autoantibodies associated with the voltage-gated potassium channel complex (i.e., LGI1, Caspr2) and IgLON5, multiple sclerosis, progressive supranuclear palsy, chronic traumatic encephalopathy, Guillain-Barré syndrome, brainstem neoplasms (including cerebellopontine angle tumors), Machado-Joseph disease (spinocerebellar ataxia type 3), mitochondrial encephalomyopathy, normal pressure hydrocephalus, Tourette syndrome, group A xeroderma, and autism.

The pathophysiology of human RBD is presumed to correspond to the findings from animal models of RBD with respect to lesioning or dysfunction of the REM atonia pathways, especially involving the sublaterodorsal nucleus/subcoeruleus or disinhibition of brainstem motor pattern generators.

Objective Findings

Polysomnography demonstrates an excessive amount of sustained or intermittent loss of REM atonia or excessive phasic muscle activity of the chin or limb EMGs during REM sleep. Some patients have almost exclusively arm and hand behaviors during REM sleep, indicating the need for both upper and lower extremity EMG monitoring in evaluating for possible RBD. Simultaneous video recording is highly recommended to document the associated behaviors.

Although specific diagnostic criteria for RBD (above) and scoring guidelines for RSWA (see the AASM Manual for the Scoring of Sleep and Associated Events and the published guidelines by the International RBD Study Group) are critical to establishing the diagnosis, the frequency of REM sleep epochs without atonia that is necessary to confirm the diagnosis is not well-defined. No definitive cut-off has been established and the RSWA quantity/percentage requirement may vary depending on the clinical circumstances of the patient and the surface EMG leads used in a sleep study. Nevertheless, the following information is provided in part to assist clinicians in making this determination.

Some patients preserve most of their REM atonia but have excessive EMG phasic motor activity during REM sleep. Several studies indicate that specific cut-offs of muscle tone (enhanced during more than 50% of an epoch) adequately differentiate RBD patients from healthy controls, although this depends on the muscles used for the analysis (the upper arms muscles being the more specific). For example, enhancement of the chin muscle tone (phasically or tonically) during more than 9% of REM sleep epochs represents a *sensitive* cutoff, although a more *specific* cutoff is 18%. Likewise, enhancement of the chin + flexor digitorum superficial muscle tone during more than 27% and the chin + tibialis anterior muscle tone during more than 36-45% of REM sleep epochs are proposed cutoffs.

Autonomic nervous system activation (such as tachycardia) is uncommon during REM sleep motor activation in RBD, in contrast to the disorders of arousal. Increased percentages of slow wave sleep and increased delta power in RBD have been found in controlled and uncontrolled studies, but this can be a highly variable finding in RBD, depending on the clinical population. Sleep architecture and the customary

cycling among REM and NREM sleep stages are usually preserved in RBD, although some patients show a shift toward N1 sleep.

Several validated RBD screening questionnaires that can assist in the process of screening for RBD are currently available. However, their diagnostic value outside the context of validation studies has been shown to be low.

Differential Diagnosis

RBD is one of several disorders that can manifest as complex, injurious, and violent sleep-related and dream-related behaviors in adults.

Other disorders that can mimic RBD in adults or children include *sleepwalking, sleep terrors, OSA, sleep-related hypermotor epilepsy (SHE, formerly known as nocturnal frontal lobe epilepsy; nocturnal focal seizures); rhythmic movement disorder, dissociative disorders arising from sleep, frightening hypnopompic hallucinations, and posttraumatic stress disorder*. In general, RBD involves the enactment of unpleasant, aggressive dreams that usually occurs two or more hours after sleep onset, with rapid awakening from an episode. In contrast, sleepwalking and sleep terror episodes often emerge within two hours after sleep onset, are not usually associated with rapid alertness, and are rarely associated with dreaming in children. Adults can have dreams associated with disorders of arousal, but they are often more fragmentary and limited than RBD dreams. Sleep-related seizures usually present with repetitive, stereotypical behaviors.

Parasomnia overlap disorder can be distinguished from *status dissociatus* in several ways. If there is an awakening after an episode of RBD, sleepwalking, or sleep terror, there is the realization of having just been asleep; *status dissociatus*, however, is more likely to manifest with confusion over whether one is asleep, awake, or dreaming. vPSG in overlap conditions shows the typical findings for both RBD and disorders of arousal, whereas with *status dissociatus*, there is an inability to discern sleep stages. In addition, patients with *status dissociatus* do not walk far during an episode, and their behavioral repertoire more closely resembles that of RBD than that of the disorders of arousal.

Unresolved Issues and Future Directions

Numerous questions related to the vPSG evaluation of RBD remain unresolved. These include issues of defining and quantifying RWA and RBD activity: (1) What is the minimum REM sleep percentage of total sleep time (and minimum absolute REM sleep time) needed to diagnose or rule out RWA? (2) What is the minimum number of REM sleep epochs and minimum duration of REM sleep epochs necessary to identify or rule out RWA? (3) What guidelines can be developed to identify RWA in the setting of disrupted REM sleep continuity due to obstructive sleep apnea or medications? (4) What are the minimal amounts of RBD behaviors documented by vPSG to identify RBD in patients without sufficient RWA? (5) What amounts of RWA or movements during REM sleep define prodromal RBD patients at risk for developing RBD or a defined neurodegenerative disease?

The male predominance of RBD reported in earlier studies may be at least in part due to underdetection in women. It is unknown if specific RBD subgroups are at increased risk for the development of parkinsonism or dementia. These subgroups include patients younger than 50 with antidepressant medication-induced RBD or underlying neuropsychiatric disorders such as post-traumatic stress disorder (PTSD). New antidepressants or other psychotropic agents being developed for clinical use should be assessed for their immediate and long-term effects on REM atonia, REM phasic activity, REM sleep behavioral release, and proclivity to precipitate dream-enacting behaviors.

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Recurrent Isolated Sleep Paralysis

ICD-9-CM code: 327.43

ICD-10-CM code: G47.51

Alternate Names

Hypnagogic and hypnopompic paralysis, predormital and postdormital paralysis, kanashibari (Japan).

Diagnostic Criteria

Criteria A-D must be met

- A. A recurrent inability to move the trunk and all of the limbs at sleep onset or upon awakening from sleep.
- B. Each episode lasts seconds to a few minutes.
- C. The episodes cause clinically significant distress, including bedtime anxiety or fear of sleep.
- D. The disturbance is not better explained by another current sleep disorder (especially narcolepsy), medical disorder, mental disorder, or medication/substance use.

Essential Features

Recurrent isolated sleep paralysis is characterized by an inability to initiate voluntary movements at sleep onset (hypnagogic or predormital form) or on waking from sleep (hypnopompic or postdormital form) in the absence of a diagnosis of narcolepsy. The event consists of an inability to speak or to move the limbs, trunk, and head. A feeling of suffocation is sometimes described by patients, probably due to involvement of the accessory respiratory muscles, although respiration is unaffected. Awareness is preserved, and full recall is present. An episode of sleep paralysis lasts seconds to minutes. It usually resolves spontaneously but can be aborted by sensory stimulation, such as being touched or spoken to, or by the patient making intense efforts to move.

Associated Features

At least during the initial episodes, intense anxiety is usually present. Hallucinatory experiences accompany the paralysis in about 25% to 75% of patients. These may include auditory, visual, or tactile hallucinations, or the sense of a presence or intruder in the room. Some patients experience predormital or postdormital hallucinations at times separate from episodes of sleep paralysis.

Clinical or Pathophysiological Subtypes

A familial form of sleep paralysis has been described (see below).

Demographics

Estimates of the prevalence of sleep paralysis vary widely due to differences in the definition used, the age of the population sampled, and possibly cultural and ethnic factors. Most prevalence studies of sleep paralysis (usually of students younger than 30 years) have investigated the occurrence of one or more episodes without requirement of recurrence or distress. The most extensive systematic review of sleep paralysis analyzing 35 studies found an average reported prevalence of 20.8% for at least one lifetime episode of sleep paralysis across all studies. However, the frequency varied across different populations, as there was only a 7.5% general population prevalence for sleep paralysis, yet up to 28.3% in student populations. An even higher frequency was found among psychiatric patients (31.9%), rising to 34.6% in those with a history of panic disorder. Lifetime sleep paralysis episodes appear to be higher in those of Hispanic, African, and Asian descent than in those of European descent. No consistent sex differences have emerged from multiple studies, although the systematic review reported a slightly higher lifetime sleep paralysis frequency among women (18.9%) than in men (15.9%). The mean age of onset is 14 to 17 years, although onset earlier and later in life has been reported.

Predisposing and Precipitating Factors

Sleep deprivation and irregular sleep-wake schedules have been identified as predisposing factors to episodes of sleep paralysis. Mental stress has been reported as a precipitating factor in some but not other studies. Sleep paralysis appears to be more common during sleep in the supine position. Personality factors have not been shown to play a significant role, although one study found a higher score on the paranoia scale of the Minnesota Multiphasic Personality Inventory in patients with sleep paralysis compared to controls. Other factors that have been noted to be associated with sleep paralysis include the use of anxiolytic medication, alcohol use, shift work, insufficient sleep syndrome, obstructive sleep apnea, exploding head syndrome, sleep-related leg cramps, bipolar disorder, hypertension, idiopathic hypersomnia, and Wilson's disease.

Familial Pattern

Two families with apparent familial sleep paralysis occurring over three and four generations have been reported. A maternal form of transmission has been postulated.

Onset, Course, and Complications

Onset is usually in adolescence. Most events appear to occur in the second and third decades but may continue later in life. There are no known complications, apart from anxiety over the episodes.

Developmental Issues

Although sleep paralysis may be present as part of the narcolepsy tetrad in children, there is no current information about childhood presentation of recurrent isolated sleep paralysis.

Pathology and Pathophysiology

Episodes of sleep paralysis elicited by awakening patients from nocturnal sleep appear to arise from REM sleep. Sleep paralysis is an example of state dissociation with elements of REM sleep persisting into wakefulness. Early-onset REM sleep after forced awakenings predisposes an individual to sleep paralysis. It may be that subjects with less tolerance to sleep disruption are more likely to experience the phenomenon.

Objective Findings

Analysis of sleep paralysis during PSG studies reveals the event to be a dissociated state with the persistence of REM-related electromyographic atonia and predominant theta EEG rhythms. The findings

suggest that sleep paralysis represents either an intermediate state between wakefulness and REM sleep or possibly an atypical REM sleep dreaming state.

Differential Diagnosis

Cataplexy produces similar generalized paralysis of skeletal muscles but occurs during wakefulness and is precipitated by emotion.

Atonic seizures occur during wakefulness.

Nocturnal panic attacks are not usually associated with paralysis.

Familial periodic paralysis syndromes, especially *hypokalemic periodic paralysis*, may occur at rest and on awakening. However, the episodes usually last hours, may be associated with carbohydrate intake, and are usually accompanied by hypokalemia. There are also *hyperkalemic and normokalemic periodic paralysis syndromes*.

Unresolved Issues and Further Directions

Not applicable or known.

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Nightmare Disorder

ICD-9-CM code: 307.47

ICD-10-CM code: F51.5

Alternate Names

Nightmares, REM nightmares, recurrent nightmares, dream anxiety disorder, anxiety dreams.

Diagnostic Criteria

Criteria A-C must be met

- A. Repeated occurrences of extended, extremely dysphoric, and well-remembered dreams that usually involve threats to survival, security, or physical integrity.
- B. On awakening from the dysphoric dreams, the person rapidly becomes oriented and alert.
- C. The dream experience, or the sleep disturbance produced by awakening from it, causes clinically significant distress or impairment in social, occupational, or other important areas of functioning as indicated by the report of at least one of the following:
 1. Mood disturbance (e.g., persistence of nightmare affect, anxiety, dysphoria).
 2. Sleep resistance (e.g., bedtime anxiety, fear of sleep/subsequent nightmares).
 3. Negative impact on caregiver or family functioning (e.g., nighttime disruption).
 4. Behavioral problems (e.g., bedtime avoidance, fear of the dark).
 5. Daytime sleepiness.
 6. Fatigue or low energy.
 7. Impaired occupational or educational function.
 8. Impaired interpersonal/social function

Notes

1. Nightmares that occur intermittently during the course of *ASD* or *PTSD* are an expected symptom of those mental disorders and do not always require independent coding as nightmare disorder. However, when the frequency or severity of posttraumatic nightmares is such that they require independent clinical attention, then a diagnosis of nightmare disorder should be applied. In some cases, other symptoms of *PTSD* may have largely resolved while the nightmares persist. Nightmare disorder should be coded in these cases as well.

Essential Features

Nightmare disorder is characterized by recurrent, highly disturbing dreams that generally occur during REM sleep and often result in awakening. Given that these experiences are most often associated with REM sleep, the episodes have a greater tendency to occur during the second half of the major sleep episode when the REM pressure is most pronounced. Nightmares involve an internally generated conscious experience or dream sequence that seems vivid and real. They tend to become increasingly more disturbing as they unfold. Emotions are characteristically negative and most frequently involve anxiety, fear, or terror but may also involve anger, rage, embarrassment, and disgust. Nightmare content most often focuses on imminent physical danger to the individual but may also involve other distressing themes. The ability to detail the nightmare's contents upon awakening is common in nightmare disorder. Multiple nightmares within a single sleep episode may occur and bear similar themes. Nightmare disorder does not involve the simultaneous enactment of the nightmares, as with REM sleep behavior disorder.

Nightmares are prevalent in children. They typically occur in the last third of the night and result in complete awakening, after which the child can often provide a detailed description of the frightening scenario. However, distinguishing nightmares from confusional arousals and sleep terrors in young children is often impossible. Nightmare disorder in children is most likely to occur in those exposed to severe psychosocial stressors. Because childhood nightmares often resolve spontaneously, the diagnosis should only be given if there is persistent distress or impairment. The dream content during nightmares is often that of being chased or attacked or witnessing violence and aggression, including the injury or death of family, friends, or others. Uncommon themes, such as suicide, are of unique importance in light of their predictive value of future psychopathology.

Post-awakening anxiety and difficulty returning to sleep may be present. Nightmares are more common in those with higher levels of anxiety. Additionally, nightmares are commonly seen in those who have been physically or sexually abused and in those suffering from posttraumatic stress disorder. Posttraumatic nightmares may take the form of a realistic reliving of a traumatic event or may depict only some of its elements or emotional content.

Clinical or Pathophysiological Subtypes

Nightmares may be further classified into two key subtypes:

Idiopathic: Nightmares without evidence of comorbid psychopathology or

Comorbid: Nightmares associated with comorbidities such as PTSD, borderline personality, substance use/abuse, schizophrenia-spectrum disorders, depression, and insomnia. Indeed, both depression and insomnia symptoms are strong predictors of frequent nightmares.

Recent data implicate a novel individual risk variant for nightmares involving the gene encoding PTPRJ, a specific locus previously implicated in sleep duration and short sleep, thus highlighting a possible effect of variation at the PTPRJ locus on sleep and nightmares. The data highlight a putative mechanism for associating the genetic risk for nightmares with unique sleep traits, particularly insomnia.

Demographics

The true prevalence of nightmares is uncertain due to inconsistent terminologies and diagnostic criteria. Data indicate that clinicians may not inquire about nightmares, despite their clinical relevance; therefore, they may be underreported. Furthermore, nightmare sufferers do not typically discuss their nightmares with clinicians, contributing to their underdiagnosis.

Occasional nightmares are very common in children, occurring in 60% to 75%, beginning as young as 2.5 years. The occurrence of occasional nightmares in children does not constitute a nightmare disorder. However, frequent nightmares are uncommon, occurring in 1% to 5% of preadolescent children. It is estimated that 10-50% of children aged three to five years have at least occasional nightmares severe enough to disturb their parents. Nightmares appear to be a trait-like characteristic that persists over time during childhood. Females report more frequent occurrences of nightmares than males during adolescence and young adulthood at a ratio of 1.5 to 1. However, children and older adults did not demonstrate this gender difference. Population studies have revealed that the prevalence and frequency of nightmares increases through childhood into adolescence.

About 85% of adults report at least one nightmare a year, but 2-6% report more regular weekly episodes. Approximately 2% to 8% of the general population has a current problem with nightmares, and this frequency is higher in individuals with mental disorders. The best predictor of recurrent nightmares at an older age is recurrent nightmares in childhood.

Recent data from the Korean Genome and Epidemiology Study indicates that in the age group over 70, nightmare prevalence was 6.3% and was associated with attributes such as bereavement, unemployment, and low family income.

Trauma-related nightmares are the most consistent sleep-related symptom reported by patients with PTSD. Nightmares beginning within three months of a trauma are present in up to 80% of patients with PTSD. Although approximately 50% of PTSD cases resolve within three months, posttraumatic nightmares may persist throughout life. In a large epidemiologic study, 4.8% of females and 3.5% of males reported frequent nightmares, with prevalence increasing with age, especially in men. War veterans reported significantly more frequent nightmares. Assessment of nightmares in an active-duty military population

identified that 31.2% of individuals met the criteria for nightmare disorder, although only a small fraction (3.9%) were referred for evaluation of the nightmares.

Predisposing and Precipitating Factors

Frequent nightmares are associated with enduring personality characteristics and psychopathologies and are inversely correlated with measures of well-being. Measures of nightmare distress are more robustly associated with psychopathology than are measures of nightmare frequency. Data confirm a distinct risk for nightmares in adults and adolescents with psychopathology, but research on children is largely absent, other than in those with PTSD. Nightmares and sleep disturbance are significantly more frequent in children and adolescents with PTSD than in normal pediatric populations.

The clinical use of pharmacologic agents affecting the neurotransmitters norepinephrine, serotonin, and dopamine is associated with the complaint of nightmares. A majority of these agents are antidepressants, antihypertensives, and dopamine-receptor agonists. Agents affecting the neurotransmitters gamma-aminobutyric acid (GABA), acetylcholine, and histamine, and the withdrawal of REM sleep suppressive agents also can be associated with the complaint of nightmares. Nightmares are especially common with varenicline, an agent that blocks α -4- β -2 nicotinic acetylcholine receptors. Antidepressant medication may significantly reduce dream recall, likely due to REM-suppressing effects. In addition, SSRI/SNRI use intensified dreaming with the potential to cause nightmares. Withdrawal from these medications and TCAs and MAOIs may also significantly intensify dreaming and cause nightmares, presumably from REM-rebound. Nightmares associated with short half-life hypnotics (e.g., triazolam, zolpidem) may emerge late in the sleep cycle.

Respiratory-related nightmare content (e.g., suffocating or drowning) is rarely present in untreated obstructive sleep apnea (OSA) patients. The severity of the OSA can predict the severity of the disturbed dreaming. Among patients with OSA, those with a higher AHI, specifically in REM sleep, have more nightmares. Patients who have both nightmares and OSA report a reduction in nightmares after starting positive airway pressure therapy.

Respiratory events and leg movements due to sleep apnea may precipitate nightmare episodes as demonstrated by home sleep apnea testing in individuals with PTSD.

Familial Pattern

Twin-based studies have identified a persistent genetic predisposition to nightmares in childhood (reported retrospectively by adults) and adulthood, as well as genetic influences on the co-occurrence of nightmares and other parasomnias, such as sleepwalking (somniloquy). Data indicate that nightmare frequency has a heritability of 36- 51%, supporting the role of genetic factors underlying predisposition to nightmares.

This genetic predisposition accounts for 45-51% of the phenotypic variance in childhood nightmares, and about 37% in adult nightmares. Furthermore, the presence of nightmares throughout childhood, adolescence, and adulthood correlate significantly, indicating that a predisposition to nightmares may be a stable and persistent trait.

Onset, Course, and Complications

Nightmares usually start between ages three years and six years. The proportion of children reporting nightmares reaches a peak between six and ten years of age and decreases thereafter. However, a subgroup of children continues to have nightmares into adolescence or adulthood and may become lifelong nightmare sufferers. Nightmares generally diminish in frequency and intensity over decades, but some patients still describe frequent episodes at 60 or 70 years. Nightmare disorder can lead to sleep avoidance and deprivation, predisposing to more intense nightmares and insomnia.

Autism spectrum and PTSD-associated nightmares can develop at any age after physical or emotional trauma. However, it is not known to what extent nightmares contribute to PTSD complications such as mood disorders, social and employment consequences, self-destructive and impulsive behavior, and substance abuse.

Developmental Issues

Developmental aspects of nightmares are discussed in the *Demographics* section above.

Pathology and Pathophysiology

A disruption of processes that regulate the expression or memory of fear is implicated in the pathophysiology of nightmare disorder. Nightmares, however, may also represent an innate adaptive response. Increasing evidence links nightmares with a specific personality trait characterized by heightened sensitivity to environmental stimuli and processing of the environment. While several functional theories of nightmares implicate its role in emotional regulation, the evidence remains controversial.

Not applicable or known.

Objective Findings

PSG recordings during actual nightmares are few, but when recorded, some have shown abrupt awakenings from REM sleep in the last third of the night, preceded by accelerated heart and respiratory rates. NREM sleep microstructure is altered with reduced amounts of Cyclic Alternating Pattern (CAP) A1

phase and increased A2 and A3 phases, highlighting abnormal arousal processes. Spectral power analysis found that nightmare sufferers had increased fast frequency EEG power within the beta and gamma ranges. Other research found that patients with nightmares spent significantly less time in N3 sleep than controls. In addition, highly disturbing dream content frequently contrasts with only minor autonomic changes.

PSG recordings of sleep in patients with PTSD have provided widely variable results. There are few PSG recordings during posttraumatic nightmares. These have demonstrated nightmares during both REM and NREM sleep. Nightmares arising either immediately following a trauma (acute stress disorder [ASD]) or one month or more after a trauma (PTSD) have been observed during NREM sleep. Nightmares associated with PTSD are equally likely to manifest during N1, N2 and REM sleep and, therefore, may occur both early and late in the sleep period.

PSG evaluation is not routinely performed but may be indicated in some circumstances to exclude other parasomnias such as RBD, disorders of arousal, and sleep-associated seizures. A PSG is particularly appropriate if patients report nightmares in conjunction with sleep behaviors that are repetitive or stereotyped or are injurious to self or others.

Differential Diagnosis

Nightmare disorder must be distinguished from dream disturbances associated with certain other neurological and sleep disorders. Nightmares encompass heterogeneous experiential phenomena ranging from abrupt awakenings from threat dreams to dream experiences of interpersonal conflicts, injury, or death of loved ones.

Several other types of dream experiences need to be differentiated from nightmares. The absence of clinically significant anxiety, distress, mood disturbances, sleep resistance, cognitive impairments, daytime sleepiness, and impairment of family, occupational, educational, and interpersonal/social function further helps distinguish these from nightmares.

Normal dreams are described as hallucinatory visual images or mentation that arise during sleep in which visual images, cognitive and sensory experiences, are organized in a story-like manner and range from sensible to bizarre.

Sleep-related hallucinations are perceptual visual phenomena that manifest in the absence of external physical counterpart and typically occur at the transition from wakefulness to sleep (hypnagogic hallucination) or upon awakening (hypnopompic hallucination).

Lucid dreams are characterized by the dreamer realizing that they are dreaming while remaining asleep.

Epic dreams consist of unrelenting, repetitive dreaming throughout the night associated with the absence of distress

Other conditions that may present with dream-like experiences include:

Seizures Rare cases of *seizures* presenting only as “nightmares” have been reported and should be considered in the differential diagnosis, particularly in patients with a history of central nervous system disease. PSG or continuous video EEG may be necessary to identify nightmares associated with nocturnal seizures.

Sleep terrors Nightmares differ from *sleep terrors* in that nightmares include a detailed recollection of dreaming, in contrast to fragments of dreams or no dream recall typical of sleep terrors. Unlike sleep terrors, nightmares are not usually associated with overt movement or the degree of autonomic arousal observed with terrors. Nightmares generally occur late in the night, most often arising from REM sleep, and are followed by rapid awakening and difficulty returning to sleep.

REM sleep behavior disorder (RBD) occurs more often in late middle-aged men and, unlike nightmares, is often associated with violent explosive movements and a history of nocturnal injuries. The dream disturbance of RBD usually involves being threatened or attacked by unfamiliar people or animals. Unlike RBD, which is seen predominantly in older age groups, nightmares occur at any age.

Sleep paralysis Anxiety may accompany episodes of *sleep paralysis* occurring either at sleep onset (hypnagogic) or offset (hypnopompic), when the individual feels conscious but unable to move, speak, and, at times, breathe properly. Anxiety may be further worsened if disturbing *hypnagogic hallucinations* or dream sequences accompany the paralysis.

Nocturnal panic attacks occur either during or immediately after nocturnal awakenings from NREM sleep, usually during transition from N2 to N3 in the first four hours of the sleep episode. Although frequency of panic attacks is correlated with frequency of nightmares and many patients report that dysphoric dreams precede their attacks, there may be no dream recall reported on awakening with a panic attack.

Sleep-related dissociative disorders (SRDD) comprise a sleep-related variant of the dissociative disorders as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (DSM-V). These include dissociative identity disorder (formerly called multiple personality disorder). In sleep-related dissociative disorders, individuals meeting waking criteria for these diagnoses may at times experience the recall of actual physical or emotional trauma as a “dream” during periods of EEG-documented nocturnal waking.

Unresolved Issues and Further Directions

Basic pathophysiologic studies are still needed, especially studies contrasting “idiopathic” nightmare disorder and nightmares associated with PTSD. In particular, whether posttraumatic nightmares arise from sleep or primarily from wakefulness is an important distinction, particularly when determining effective clinical interventions. In addition, the PSG correlates of nightmare disorder and posttraumatic nightmares, as well as the variables affecting dream mentation and recall, require further definition and delineation.

The distinction between nightmares and sleep terrors is difficult when assessed only by questionnaires. It remains unclear to what degree and level of complexity sleep mentation is associated with sleep terrors. The topic of NREM sleep dream disturbances (other than disturbed mentation that may occur with sleep terrors) also needs formal investigation, including whether the term NREM sleep nightmare should be utilized.

The optimal methods for assessing nightmare frequency and nightmare distress are still unclear. Standardized scales assessing nightmare distress should be developed and utilized. Retrospective questionnaire-based evaluations of nightmares are problematic since they underestimate nightmare frequencies relative to home logs, whereas home logs may selectively increase recall of nightmares.

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Other Parasomnias

Exploding Head Syndrome

ICD-9-CM code: 327.49

ICD-10-CM code: G47.59

Alternate Names

Sensory sleep starts; episodic cranial sensory shock

Diagnostic Criteria

Criteria A-C must be met

- A. There is a complaint of a sudden, loud noise or sense of explosion in the head either at the wake-sleep transition or upon waking during the night.
- B. The individual experiences abrupt arousal following the event, often with a sense of fright.
- C. The experience is not associated with significant complaints of pain.

Essential Features

Exploding head syndrome is characterized by a sudden, loud imagined noise or sense of a violent explosion in the head occurring as the patient is falling asleep or waking during the night.

The event is variously described as a painless loud bang, an explosion, a clash of cymbals, or a bomb exploding, but occasionally may be a less alarming sound. It is usually associated with a sense of fright, and many patients believe they are having a stroke. In a minority of cases a flash of light or myoclonic jerk may accompany the event. The abnormal sensation lasts a few seconds and may recur during further attempts at sleeping. The number of attacks varies—from many on a single night to infrequent—with some patients reporting clustering of attacks over several nights followed by a gap of weeks to months. A high level of clinical distress can be associated with recurrent attacks, particularly concern about their underlying cause. Although the condition generally appears to be more common in headache patients, its occurrence is usually not associated with head pain.

Associated Features

A flash of light may accompany the sound, and a myoclonic jerk may occur. Although the event is typically painless, a simultaneous stab of pain in the head has occasionally been reported. Tachycardia and sense of fear are commonly associated features. Sleep paralysis and other experiences of dissociation, such as lucid dreaming, are frequent concomitants. Complaints of poor sleep are also common in exploding head syndrome,

Clinical or Pathophysiological Subtypes

None known.

Demographics

Exploding Head Syndrome was initially described as more common in older adults (ages 50 and above). Although small clinical case series generally confirm this, it is now evident that many younger people report having had at least one experience resembling exploding head syndrome in their lifetime. Although

clinical case series suggest female predominance, surveys indicate an approximately equal prevalence across men and women. The episodes are often associated with psychological distress.

Predisposing and Precipitating Factors

Case reports typically have emphasized anxiety and depression in association with Exploding Head Syndrome, but large-scale surveys have not confirmed these as risk factors. Similarly, case reports have suggested associations with migraine aura, brainstem lesions, seizures, cardiac abnormalities (sick sinus syndrome), and medication withdrawal (both benzodiazepine and selective serotonin-reuptake inhibitors), but large-scale population-based surveys indicate that these comorbid factors are infrequent, relative to the reported frequency of the phenomenon generally.

Familial Pattern

Occasional cases of exploding head syndrome occurring in the same family have been reported, although it is not clear whether this represents a true familial pattern.

Onset, Course, and Complication

Exploding Head Syndrome has long been considered a normal sleep variant, akin to and sometimes sharing the phenomenology of sleep starts. It can be associated with insomnia. Patients may catastrophically misinterpret it as evidence of a more serious neurologic disorder. This usually can be discounted, although rare case histories suggesting focal neurologic or cardiac origins of the condition have been reported, and a completely benign origin should not be assumed. The exceptionally high prevalence of individuals who have experienced the phenomenon in their life on at least one occasion (exceeding 50% in some online surveys) indicates that the experience of an episodic cranial sensory shock is not rare. In many patients, the symptoms appear to remit spontaneously over some years.

Developmental Issues

Not known or applicable.

Exploding Head Syndrome has not been described in children. However, population-based surveys that include college-aged individuals indicate that many endorse the experience of an episodic cranial sensory shock at some point in their lifetimes, though seldom to the point of seeking help from a health care professional.

Pathology and Pathophysiology

The events occur most frequently during a period of drowsiness preceding sleep. However, some events are reported to occur upon waking during the night or during re-initiation of sleep. The condition may be a sensory variant of the better-known transient motor phenomenon of sleep starts or hypnic jerks occurring at wake-sleep transition. The neurophysiologic mechanisms underlying these hypnagogic phenomena are unknown. Speculation has focused on middle ear or eustachian tube dysfunction. Sounds are most typically noted as occurring bilaterally in population-based studies, though some case reports have documented lateralizing presentation. Sensations of perceived heat, often epigastric, are noted in about one-third of the episodes. There is no consistent association with chronotype.

Objective Findings

VPSG in a small sample of patients found that events arose from early drowsiness with predominant alpha rhythm interspersed with some theta activity. Events occurring in the N1/N2 to wake transition have been recorded during both nocturnal vPSG and MSLTs. Slow eye movements were present in the only tracing reproduced in the report of a patient with exploding head syndrome emerging during wake to N1 sleep transition. Arousals occurred immediately following the episodes. Abnormal ictal EEG activity is rare but has been noted. At least one case series documented episodic cranial sensory shock arising during periods of PSG-confirmed wakefulness during the night.

Differential Diagnosis

Headache syndromes EHS is not typically described as involving pain. Nonetheless, EHS often presents in patients in headache clinics and their condition should be distinguished from *sudden onset-headache syndromes*. “*Idiopathic stabbing headache*” (*ice-pick headache*) is a benign syndrome of brief stabs of pain on the side of the head. Although they can occur at sleep onset, they are more common during wakefulness. “*Thunderclap headache*” is a very severe sudden onset headache characteristic of subarachnoid hemorrhage that may also result from other causes or occur as a benign symptom. It does not usually occur at sleep onset. “*Hypnic headache syndrome*” affects older people who regularly awaken 4-6 hours after sleep onset, with a diffuse headache lasting 30-60 minutes and often with nausea but no autonomic symptoms. Other conditions to be considered include *sleep-related migraines*, *cluster headaches*, and *nocturnal paroxysmal hemicrania*. In contrast to headache syndromes, exploding head syndrome is usually painless.

Simple partial seizures can present with sensory phenomena but do not usually occur predominantly at sleep onset.

Nocturnal panic attacks can waken a person from sleep but are not usually associated with a sense of noise or explosion.

Recurrent nightmares are characterized by recall of more complex and longer-lasting visual imagery but may bear resemblance, particularly in the context of combat-associated experiences (e.g., gunfire) associated with Post-Traumatic Stress Disorder (PTSD).

Sleep starts occur at wake-sleep transition but are predominantly a motor phenomenon with sudden myoclonic jerks rather than an emphasis on sensory symptoms.

Unresolved Issues and Future Directions

The neurophysiologic basis of these events requires further study.

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Sleep-related Hallucinations

ICD-9-CM code: 368.16

ICD-10-CM code: H53.16

Alternate Names

Hypnagogic hallucinations, hypnopompic hallucinations, complex nocturnal visual hallucinations.

Diagnostic Criteria

Criteria A-C must be met

- A. There is a complaint of recurrent hallucinations that are experienced just prior to sleep onset or upon awakening during the night or in the morning.
- B. The hallucinations are predominantly visual.
- C. The disturbance is not better explained by another current sleep disorder (especially narcolepsy), medical disorder, mental disorder, or medication/substance use.

Notes

1. Sleep-related hallucinations that occasionally occur in isolation and are not the subject of distress do not require independent coding as sleep-related hallucinations. However, when the frequency or severity of the events is such that they require independent clinical attention, then a diagnosis of sleep-related hallucinations should be applied.
2. Sleep-related hallucinations may occur in isolation or as a manifestation of another medical, neurological, or substance-related disorder. When a comorbid condition is the cause of the hallucinations, and the hallucinations are the subject of independent clinical attention, clinicians are advised to use the specific diagnosis of sleep-related hallucination rather than the more general diagnosis of parasomnia due to a medical disorder. The comorbid condition should be coded separately as well.

Essential Features

Sleep-related hallucinations (SRH) are hallucinatory experiences that occur at sleep onset or upon awakening from sleep. Sleep-related hallucinations are predominantly visual but may include olfactory (smell of perfume, gasoline, smoke), gustatory (metallic taste), auditory (hearing voices, steps), somatic (body distortions, entities climbing over the body), emotional (severe, unpleasant and frightening), tactile (a sensation of being touched), or kinetic (involving movement, floating sensation, levitation, flying, jumping, falling, out-of-body experiences) phenomena. The hallucinatory episode may be single or multisensory. These hallucinations may remain present for many minutes but usually disappear if ambient illumination increases. Patients are clearly awake but often initially perceive the hallucinations as real and frightening. Hallucinations on waking in the morning (*hypnopompic hallucinations*) may arise from a period of REM sleep, and patients may also be uncertain whether they represent waking or dream-related experiences.

Associated Features

Sleep-related hallucinations may be associated with episodes of sleep paralysis, either at the same time or on different nights. Patients with complex nocturnal visual hallucinations may jump out of bed in terror, sometimes injuring themselves. Some may experience other parasomnias, such as sleep talking or sleepwalking, independent of the hallucinations; others may also experience similar complex hallucinations during the day, unassociated with sleep. Sleep paralysis episodes may present with an extensive range of surreal, bizarre, and often terrifying hallucinations that may be classified and fall into three categories: 1) Intruder hallucinations which consist of a sense of evil presence in the room, along with vivid multisensory, hallucinations of a bedroom intruder; 2) Incubus hallucinations which consist of a sense of pressure on the chest, often associated with sensations of being choked or suffocated; and 3) vestibular-motor (V-M) hallucinations involving illusory feelings of movement, out-of-body feelings, and out-of-body autoscapy.

Clinical and Pathophysiological Subtypes

Complex nocturnal visual hallucinations may represent a distinct form of sleep-related hallucinations. They typically occur following a sudden awakening without recalling a preceding dream. They usually take the form of complex, vivid, relatively immobile images of people or animals, sometimes distorted in shape or size.

Dream-like hypnagogic and hypnopompic hallucinations appear to differ in clinical features and pathogenesis from complex nocturnal visual hallucinations arising in wakefulness after sudden arousals during the night. Sleep-related hallucinations are common in narcolepsy and also occur as occasional phenomena in a high percentage of the general population. In contrast, complex nocturnal visual hallucinations appear to be rare and occur in the setting of a range of neurologic and visual disorders (see

Differential Diagnosis) as well as in an idiopathic form. However, further work is needed to establish whether or not these forms of hallucinations represent truly different entities.

Demographics

In large European population studies, the prevalence of sleep-related hallucinations was 25% to 37% for hypnagogic hallucinations, whereas the equivalent reported prevalence for hypnopompic hallucinations is 7% to 13%. Both hypnagogic and hypnopompic hallucinations are more common in younger persons and occur slightly more frequently in women than in men.

Predisposing and Precipitating Factors

Multivariate analyses in population studies have suggested that sleep-related hallucinations are associated with younger age, current drug use, past alcohol use, anxiety, mood disorder, sleep onset insomnia, and perceived insufficient sleep. In addition, β -adrenergic receptor-blocking agents have been cited as possible triggers of sleep-related hallucinations.

Familial Pattern

Not applicable or known.

Onset, Course, and Complications

Sleep-related hallucinations appear to be more common in adolescence and early adulthood. In many patients, the frequency appears to decrease with age. The natural history of complex nocturnal visual hallucinations depends on the underlying cause.

Developmental Issues

Not known or applicable.

Pathology and Pathophysiology

It is presumed that most sleep-related hallucinations are due to dream ideation of REM sleep intruding into wakefulness, but this has not been firmly established. Infrequent hallucinations of this type may be within the limits of normal sleep-wake transition. In some cases, complex nocturnal visual hallucinations

may be release phenomena in which loss of visual input or decreased reticular activating system activity results in the visual cortex generating aberrant images.

Neuroanatomical and neurophysiological data suggest that mental events follow a gradual evolution. Hallucinatory events may begin with thoughts during the waking period that progress to hallucinatory experiences at sleep onset (hypnagogic hallucinations). Likewise, dream experiences may conclude with hallucinatory experiences at the onset of wakefulness (hypnopompic hallucinations).

Objective Findings

Hypnagogic hallucinations appear to arise predominantly from sleep onset REM periods. However, the very few polysomnography reports of complex nocturnal visual hallucinations suggest an onset from NREM sleep.

Differential Diagnosis

Hallucinations are the perception of an object or event in the absence of an external stimulus. Hallucinations can manifest themselves in isolation, as well as in *narcolepsy and mental disorders* such as *schizophrenia*. While kinetic and visual hallucinations are more strongly associated with sleep than schizophrenia, auditory hallucinations are more commonly seen in schizophrenia and occur more frequently (≥ 3 /week). Hallucinations at sleep onset (*hypnagogic hallucinations*) may be difficult to differentiate from sleep onset dreaming.

Numerous sleep-related phenomena may mimic or be confused with sleep-related hallucinations.

Visual illusions (Optical illusions) are brief misperceptions of living things or objects that differ from objective reality. These are more common as sleep-related phenomena than in schizophrenia.

Nightmares are frightening dreams awakening the patient from sleep. They are clearly recognized as dreams and do not persist into wakefulness.

Exploding head syndrome consists of a sudden sensation of an explosion in the head, usually at sleep onset and sometimes accompanied by a noise or flash of light. It does not involve complex visual imagery and lasts only seconds.

Complex nocturnal hallucinations: characterize a state of dream mentation that occurs at sleep onset or offset. They are typically described as visual, vivid, usually multicolored, and distorted. They occur in wakefulness after sudden arousal from sleep and occur in the setting of idiopathic hypersomnia, dementia with Lewy Bodies, B-blockers, anxiety, and macular degeneration.

REM Sleep Behavior Disorder (RBD) In *RBD*, the patient acts out dreams during REM sleep with mostly preserved recollection of dream content.

Oneiric stupor occurs in the setting of *agrypnia excitata*, a syndrome characterized by loss of sleep and permanent motor and autonomic hyperactivation. Oneiric stupor consists of repetitive, stereotyped gestures mimicking simple daily life activities. Conditions presenting with oneiric stupor include fatal familial insomnia (FFI), Morvan syndrome (MS), and delirium tremens (DT).

Sleepwalking may occasionally be associated with transient imagery and dream ideation, initially perceived as real, but the patient recognizes that the dream occurred during sleep.

Sleep-related Epilepsy (SRE) Visual hallucinations may occur in the setting of occipital epilepsy but are usually brief, stereotyped, and fragmentary in such cases.

Migraine Headaches with Visual Aura Occasionally, complex visual hallucinations may be associated with *migraine* but are usually followed by a headache.

Narcolepsy Complex nocturnal visual hallucinations in the form of hypnagogic or hypnopompic hallucinations at the wake-sleep transition are observed in patients with narcolepsy. Sleep-related hallucinations are differentiated from narcolepsy by the absence of hypersomnia and objectively verifiable indicators of narcolepsy.

Visual hallucinations in the setting of α -Synucleinopathies Patients with Parkinson's disease (PD) and dementia with Lewy bodies (DLB) are more likely to experience visual hallucination than those with cortico-basal degeneration (CBD) and progressive supranuclear palsy (PSP). The hallucinatory events are perceived as real and unpleasant, but they are typically not frightening.

Hallucinations in PD and dementia with Lewy bodies (DLB) are typically expressed as visual mostly of persons or animals, associated with flickering lights and illusionary misconception.

Hallucinations tend to be more common among patients with longer disease duration who experience more cognitive disturbances and are on chronic dopamine replacement therapy. These patients are more likely to present with disturbances of visuospatial orientation and facial recognition problems.

Hallucinations in PD may be accompanied by confusion and delusions encountered in "indeterminate sleep," a state characterized by continuous slow waves or continuous alpha rhythm

Hallucination in the setting of PD may shed more light on disease progression, which corresponds to standard clinical measures of disease severity.

Visual Hallucinations in the setting of CNS injury may involve key structures with well-defined syndromes. *Peduncular hallucinosis* (PH) represents complex, realistic visual hallucinations secondary to lesions of the midbrain or the thalamus. The hallucinations are described as complex, vivid, colorful, but realistic, often in the setting of dynamic scenes involving familiar people or places lasting several minutes. Patients have difficulty distinguishing their hallucinations from reality but have preserved insight into the hallucinations.

Medications-induced β -adrenergic receptor-blocking medications may precipitate hallucinations.

Medication-withdrawal Hallucinations and violent dream enactment may be encountered in alcohol abusers following withdrawal from alcohol (delirium tremens). Alcohol withdrawal hallucinations are differentiated based on additional symptoms, including insomnia, anxiety, nausea, tremors, motor and autonomic activation with agitation.

Psychiatric conditions While patients with schizophrenia may report visual hallucinations, most report primarily auditory or tactile hallucinations.

Charles Bonnet Hallucinations consist of true visual hallucinations resulting from damage along the visual pathway. The episodes are bizarre but are seldom disturbing. Patients maintain partial or complete insight that the hallucinations are not real while maintaining intact intellectual functioning. Percepts consist of familiar or unfamiliar images of patterns, inanimate objects, animals, and people.

Lucid dreams are dream experiences in which individuals are aware that they are dreaming but may have the capacity to gain control over a part of the dream plot and scenery.

Unresolved Issues and Further Directions

In contrast to the extensive study of sleep paralysis, little work has been reported on sleep-related hallucinations. It is uncertain whether they represent normal variants or pathological entities. It is unclear whether they are always associated with REM sleep intruding into wakefulness. It is uncertain how frequently complex nocturnal visual hallucinations are an independent entity, as opposed to representing a final common pathway of a range of other disorders. Further work is needed to determine from which stages of sleep they arise. MRI scans of the brain, PSG, EEG, and neuropsychological testing may help in the differential diagnosis and in identifying underlying disorders.

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Sleep-related Urologic Dysfunction

Alternate Names

Enuresis nocturna; nocturnal bedwetting; primary, familial, functional, idiopathic, monosymptomatic, or essential enuresis; night wetting; sleep-related enuresis.

Diagnostic Criteria

Sleep Enuresis

- A. The patient exhibits recurrent involuntary voiding during sleep, occurring at least once per month.
- B. The condition has been present for at least three months.
- C. The patient is older than five years.

Nocturia

- A. The patient exhibits three or more nightly episodes of urination arising from sleep.
- B. Each episode of urination is followed by sleep or the intention to sleep.
- C. The condition has been present for at least three months.
- D. The patient is older than five years.

Nocturnal Urinary Urge Incontinence

- A. The patient or care provider reports or observes urinary urgency and leakage after arising from sleep.¹
- B. Sleep-related wetness episodes must occur at least once per week.
- C. The condition has been present for at least three months.

Notes

1. Leakage is defined as wetting bedding, bedclothes, or undergarments.

Essential Features

Sleep enuresis (SE) is characterized by recurrent involuntary voiding during the physiologic sleep state. SE is distinguished from voluntary voiding associated with awakenings from sleep, which is referred to as nocturia. SE is also differentiated from nocturnal urinary urge incontinence (UUI), which is incontinence occurring after an awakening from sleep with inability to reach the bathroom before micturition occurs.

Historically, SE was referred to as secondary for children who have had a dry period for > 6 months; otherwise, the condition was referred to as primary. The International Children's Continence Society

(ICCS) currently differentiates between frequent (> 4 episodes per week) versus infrequent (< 4 episodes per week). When SE occurs with no other lower urinary tract symptoms, the condition is referred to as monosymptomatic. When SE occurs with other lower urinary tract symptoms, such as bowel dysfunction, daytime incontinence or underactive bladder (evidenced by straining to urinate), the condition is referred to as non-monosymptomatic.

Both monosymptomatic and non-monosymptomatic SE share the common symptom of voiding during physiologic sleep. Excess urine production during sleep (nocturnal polyuria) may be seen in both.

The International Continence Society (ICS) defines nocturia as the number of voids occurring during the sleep period with specification that each urination must be followed by sleep or the intention to sleep. Conflicting evidence exists on the number of voids considered to be clinically meaningful. Some studies suggest a minimum threshold of two, three, or even four or more voids per sleep period.

Urinary Urge Incontinence (UUI) (typically a nocturnal event for individuals sleeping at night) occurs when an individual awakens from sleep with urinary urgency and cannot reach the bathroom before an episode of incontinence occurs.

Associated Features

SE is associated with difficulty arousing from sleep in response to an urge to urinate and may occur during any sleep stage. Sleep disorders that fragment sleep, such as sleep-related breathing disorder (SRBD), periodic limb movement disorder (PLMD), or restless legs syndrome (RLS), can be associated with SE. In children, treatment of SRBD may cure or reduce SE incidence. In adults, studies have shown mixed evidence regarding whether SE, nocturia, or nocturnal UUI can be effectively treated by addressing the primary sleep disorder.

Urinary incontinence during wakefulness may be associated with SE and nocturnal UUI and may indicate a physiological etiology. Psychosocial problems are considered a relatively rare cause in SE, though it does occur more commonly in children with attention-deficit/hyperactivity disorder and children living in disorganized families. The onset of SE following a dry period of six months or longer is seen more commonly in children who have recently experienced significant psychosocial stress, such as parental divorce, physical or sexual abuse, or neglect. Chronic constipation and encopresis (fecal soiling) can be associated with non-monosymptomatic SE and nocturnal UUI.

SE, nocturia and nocturnal UUI can be associated with diabetes and urinary tract infection. In addition, they may occur in individuals with nocturnal epilepsy. Among older adults, SE, nocturia, and nocturnal UUI may be associated with symptoms of congestive heart failure, OSA, depression, and dementia. In dementia, some cases of apparent SE are likely to represent nocturnal UUI, particularly if transfer for toileting is difficult. In men, nocturia can be associated with bladder outlet obstruction reflecting prostate hypertrophy, but in both men and women, nocturia can also be associated with detrusor overactivity (overactive bladder) and excess urine production at night (nocturnal polyuria).

Nocturia has been associated with both falls and mortality risk, the latter association noted even when other medical comorbidities are taken into account, suggesting that sleep loss may be a mediator. UUI has been well-established as a risk factor for falls both during daytime and nighttime hours.

SRBD is reported in 8% to 47% of children with SE, compared to an overall prevalence of 1% to 2%. PLMD has been reported in patients with refractory SE. RLS has been associated with nocturia, an association robust in women. A large epidemiology study of children aged 6-10 years found that a current complaint of SE was significantly associated with increased odds ratios (2.7-3.4) for subjectively high arousal threshold, night terrors, nocturia, and confusion when awakened from sleep. Other studies have found mouth breathing, nasal congestion, snoring, and restless sleep highly related to SE in children.

Recent studies have demonstrated that patients with SE are subjectively sleepier than normal controls. The sleepiness may result from fragmented nocturnal sleep, consistent with a large body of sleep research in other areas.

Clinical and Pathophysiological Subtypes

The most important distinction is between monosymptomatic and non-monosymptomatic SE. Excess urine production at night may reflect free water and solute-driven clearance and may have implications for treatment.

Demographics

SE occurs in 15% to 20% of 5-year-olds. It is three times more common in boys than in girls. SE is reported by 2.1% of community-dwelling older adults and is more common among women than men, but this figure likely reflects both SE and nocturnal UUI. The prevalence of nocturia, when defined as two or more voids per night, occurs in about 11 to 12% of men and women in their 20's and about 42% to 45% of men and women in their 70's. When defined as 3 or more voids per night, nocturia occurs in about 2% to 3% of men and women in their 20's and about 17% to 19% of men and women in their 70's. Nocturnal UUI has been estimated to occur in about a third of individuals over the age of 65 with nocturia.

Predisposing and Precipitating Factors

The etiology of voiding dysfunction during the sleep period is complex. Precipitating factors on a particular night and at a particular time remain unknown. One model hypothesizes that voiding dysfunction during the sleep period consists of three interrelated factors: large nocturnal urine volume production, nocturnal bladder overactivity, and difficulty arousing from sleep. Children with SE are often described by their families as “deep sleepers” and very difficult to arouse. A high arousal threshold has been objectively confirmed in these children.

Sleep disorders causing sleep fragmentation, such as SRBD and PLMS, have been previously reported to be proximal triggers for disorders of arousal—sleepwalking, confusional arousals, and night terrors. Successful treatment of SRBD in these disorders has been reported to reduce or eliminate disorders of arousal. Similarly, surgical treatment of obstructive sleep apnea SRBD by adenotonsillectomy has been reported to cure SE in 60% or more of pediatric patients, although this is not a consistent result. Several studies have noted the presence of SRBD in > 40% of SE patients studied. However, not all sleep studies have noted a high percentage of SRBD in patients with SE. Those without SRBD were still found to have a high arousal threshold from sleep.

SE occurs when an individual fails to arouse from sleep in response to bladder sensations or fails to inhibit a bladder contraction. These are developmentally acquired skills, and, as such, there is a range in the ages of their acquisition. Nocturnal polyuria (excess of urine production during sleep) underlies not only SE but also nocturia and nocturnal UUI. Voiding dysfunction also can be caused by, or be associated with, any one of the following identifiable problems: (1) an inability to concentrate urine due to diabetes mellitus, diabetes insipidus, nephrogenic diabetes insipidus (idiopathic or pharmacologic [e.g., secondary to the use of lithium carbonate]), or sickle cell disease; (2) increased urine production secondary to the ingestion of caffeine, diuretics, or other agents; (3) urinary tract pathology, such as urinary tract infections, irritable bladder, malformations of the genitourinary tract (e.g., ectopic ureter); (4) chronic constipation and encopresis; (5) neurological pathology, such as dementia, seizures or neurogenic bladder; or (6) psychosocial stressors, such as parental divorce, neglect, physical or sexual abuse, and institutionalization.

Familial Patterns

Hereditary factors are suspected in children with SE. There is often a high prevalence among the parents, siblings, and other relatives of the child. The reported prevalence is 77% when both parents were enuretic as children and 44% when one parent has a history of enuresis. Recent linkage studies support the hypothesis of genetic and phenotypic heterogeneity of SE. A putative linkage to a region on chromosomes 22q, 13q, and 12q across different families has been reported.

Onset, Course, and Complications

Voiding is a spinal reflex during wakefulness and sleep in infants until about 18 months. Between 18 months and three years of age, the child can delay voiding with a full bladder, first during wakefulness and at a later age during sleep. The primary determinant of the age at which this skill is acquired is developmental maturation. Somewhat arbitrarily, SE is defined as a problem if it persists beyond five years of age. The spontaneous cure rate is 15% per year. The primary adverse effect of SE is on the child's self-esteem. The response of the child's family to the symptom is an important determinant of whether complications develop.

Nocturia and UUI have been implicated in falls and hip fractures. Nocturnal UUI puts elderly patients at risk for decubitus ulcers.

Developmental Issues

The developmental pattern of SE in children is discussed above (see *Onset, Course, and Complications*). It is similar to NREM parasomnias, although onset in adulthood is uncommon. In cases of adult-onset, SE is likely preceded by nocturia or nocturnal UUI.

Pathology and Pathophysiology

Voiding dysfunctions are heterogeneous disorders with various underlying pathophysiological mechanisms, resulting in a mismatch between nocturnal bladder capacity and the amount of urine produced during sleep, in association with a simultaneous failure of arousal from sleep in response to the sensation of bladder fullness. SE can be seen in association with sleep fragmentation disorders including SRBD, PLMD and RLS (in adults).

Objective Findings

SE can occur in all sleep stages. The relative composition of sleep stages is not different on nights when enuresis occurs versus nights on which it does not occur. The results of polysomnographic studies of children with SE compared to normal controls have been inconsistent. A power analysis of sleep EEG data suggested an increase in delta power, whereas most other studies have reported no differences. However, a recent study found that those aged 6-14 years had elevated N1 sleep and reduced N3 sleep and REM sleep compared to normal controls. In addition, the population with SE had a significantly elevated arousal index.

SRBD has been reported in 8% to 47% of children with SE. SE and SRBD are highly correlated with an increasing prevalence of enuresis as the respiratory disturbance index (RDI) increases. In addition to SRBD, PLMS (range of 3.9 to 38.6 per hour of sleep) have been reported in a group of children with treatment-resistant SE.

Differential Diagnosis

Urologic dysfunctions may be caused by a variety of medical or neurological disorders such as *diabetes mellitus, diabetes insipidus, epilepsy, sickle cell disease, bowel or bladder dysfunction, anatomical abnormalities or infection of the urinary tract, heart failure, neurological/developmental disorders or other sleep disorders, especially SRBD*. Organic pathology of the urinary tract is more prevalent in children with

sleep enuresis who also exhibit daytime enuresis, abnormalities in the initiation of micturition, or abnormal urinary flow.

A sleep study should be conducted when signs and symptoms of SRBD, such as mouth breathing, snoring, adenotonsillar hypertrophy, daytime sleepiness, and hyperactivity are present—.

Unresolved Issues and Further Directions

Further work is necessary to understand the genetic and clinical aspects of voiding dysfunction. Current research suggests that all forms of sleep-related urologic dysfunction may involve overlapping components of overproduction of urine, storage issues (including bladder capacity, detrusor overactivity or underactivity) and impaired arousal. Many patients have all three components to varying degrees.

Studies of the causal relationships of sleep, sleep disorders, and sleep fragmentation to voiding dysfunctions have been inconsistent. This is likely due to different definitions and varying research methodologies. Further sophisticated sleep laboratory research studies are necessary to elucidate the relationship. In particular, the proximal trigger for episodes of voiding dysfunctions has not been determined, although limited data with simultaneous cystography and polysomnography have suggested bladder contractions may occur prior to micturition and prior to awakenings. Other polysomnographic studies have suggested that negative pressure breathing during apneic episodes may result in episodes of micturition during the breathing obstruction.

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Parasomnia Due to a Medical Disorder

ICD-9-CM code: 327.44

ICD-10-CM code: G47.54

This diagnosis is intended for parasomnias that do not meet the criteria for a specific disorder listed above and are temporally attributable to and explained by an underlying medical or neurological disorder. For example, REM sleep behavior disorder is the parasomnia most commonly associated with an underlying neurological condition (“symptomatic RBD”). However, if the diagnostic criteria for RBD are met, the more specific diagnosis of REM sleep behavior disorder should be made, in addition to the underlying neurological diagnosis when applicable. Similarly, complex nocturnal sleep-related (hypnagogic and hypnopompic) visual hallucinations that occur with neurological disorders such as *PD*, *DLB*, *visual loss (Charles Bonnet hallucinations)*, and *midbrain and diencephalic pathology (peduncular hallucinosis)* should be diagnosed as a sleep-related hallucination if the criteria are met.

In some cases, this diagnosis is temporary, given when a sleep-related diagnosis is required before the underlying medical or neurological condition, or the specific nature of the parasomnia is determined. However, once the underlying condition and a specific parasomnia are identified, the more specific parasomnia (e.g., RBD or sleep-related hallucination) becomes the diagnosis, accompanied by notation of any associated medical or neurological disorder.

Parasomnia Due to a Medication or Substance

ICD-9-CM code: 292.85 (drug-induced); 291.82 (alcohol-induced)

ICD-10-CM code: F11-F19 (see table in Appendix B for detailed coding instructions)

This diagnosis is intended for parasomnias that do not meet the criteria for a specific disorder listed above and are temporally attributable to and explained by the use of or withdrawal from a medication or substance. For example, the onset of REM sleep behavior disorder may occur following the initiation of a selective serotonin reuptake inhibitor. However, if the diagnostic criteria for RBD are met, the more specific diagnosis of REM sleep behavior disorder should be made.

Parasomnia, Unspecified

ICD-9-CM code: 327.40

ICD-10-CM code: G47.50

This diagnosis is intended for parasomnias that cannot be classified elsewhere or for cases in which the clinician has a suspicion of a parasomnia but is unable to establish a specific diagnosis. In many cases, “parasomnia, unspecified” will be a temporary diagnosis. However, in other patients, an underlying condition may not ever be established, and in those patients, “parasomnia, unspecified” should remain an ongoing diagnosis.

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Isolated Symptoms and Normal Variants

Sleep Talking

Alternate Names

Somniloquy.

The essential feature is talking, with varying degrees of comprehensibility, during sleep. Sleep talking may occur during REM or NREM sleep. Sleep talking can be idiopathic or associated with parasomnias such as

RBD or disorders of arousal such as confusional arousal. Sleep talking may follow arousals from sleep or, more rarely, cause them. Sleep talking is highly prevalent. A recent cross-sectional epidemiologic study found the lifetime prevalence of sleep talking to be 66% and the current prevalence—in the past three months—to be 17%. There are no consistent sex differences. The onset and course are unknown.

Complications usually arise when sleep talking is very frequent or loud or if the content is objectionable to others. Utterances that do not explicitly involve speech (humming, mumbling, laughter) are commonly reported. Sleep talking is usually reported by the bed partner or someone sleeping in the same room or sleeping area as the affected individual. Sleep talking can disrupt the sleep of a bed partner, roommate, or others in a group-sleeping situation (such as college dormitories, military barracks, fire stations, or a tent while camping). The content of sleep talking has not been shown to reflect actual prior waking behavior or memories, although substantial syntactical and semantic structure reminiscent of waking speech is often preserved. The sleep talker is rarely aware of their sleep talking.

Nocturnal vocalization, including frank sleep talking, is often seen in patients with RBD and isolated REM-without-atonia. The vocalizations of RBD may be loud, emotional, profane, and associated with behaviors that correlate with remembered dream mentation. Vocalizations arising from NREM sleep yielded word counts comparable to those seen in REM. Nocturnal seizures may be associated with vocalization that tends to be stereotypic. The vocalizations associated with sleep terrors are emotionally laden and associated with intense arousal and agitated behavior. Increased vocalizations during sleep have been described in PTSD.

Differential Diagnosis

Sleep talking should be differentiated from *catathrenia*, which is defined as a sleep-related breathing disorder, typically characterized by moaning during sleep. Catathrenia has been described as an expiratory noise. It is more common in REM sleep than NREM sleep. Because some somniloquy episodes have been described in similar terms (e.g., groaning) by both patients and researchers, there is potential for confusion between catathrenia and somniloquy. Recent acoustic analyses indicate that episodes identified as catathrenia have complex harmonic components, consistent with vocal cord abduction/adduction compatible with human speech. The presence of sustained vocal cord activity and its presence during REM suggest catathrenia. Catathrenia is 10-fold more likely in competitive swimmers than in the general population, suggesting plasticity in sensorimotor pathways may be involved.

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