### PARASOMNIAS (A AVIDAN, SECTION EDITOR)



# **Classification of Parasomnias**

Louis Kazaglis 1,2 · Michel A. Cramer Bornemann 3,4

Published online: 30 March 2016

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Abstract Parasomnias, or undesirable events accompanying sleep, encompass a broad spectrum of behaviors and experiences. Classification of parasomnias has undergone a significant transformation in the International Classification of Sleep Disorders Third Edition. Underlying this new classification is the understanding that Wake, NREM sleep, and REM sleep are not mutually exclusive states. Recent advances in neuroscience support the State Dissociation paradigm which would allow for an unstable admixture of components of these states to coexist. Parasomnias are the clinical manifestation of this state instability. This article briefly reviews the characteristics, demographics, and pathophysiology of the core parasomnias and associated disorders, with emphasis on disorders of arousal and diagnosis and prognostic significance of REM sleep behavior disorder.

Parasomnia  $\cdot$  REM sleep behavior disorder  $\cdot$  Sleep terrors  $\cdot$  State dissociation

**Keywords** Confusional arousals · Disorders of arousal ·

### Introduction

Parasomnias, or undesirable events accompanying sleep, encompass a broad spectrum of behaviors and experiences. Classification of parasomnias has undergone a significant transformation in the most recent iteration of the International Classification of Sleep Disorders (ICSD). Parasomnias can be best understood using the State Dissociation paradigm. This article briefly reviews the characteristics, demographics, and pathophysiology of the core parasomnias and associated disorders, with emphasis on Disorders of Arousal and REM sleep behavior disorder.

This article is part of the Topical Collection on Parasomnias

Michel A. Cramer Bornemann Michel9626@yahoo.com

> Louis Kazaglis Louis.Kazaglis@gmail.com

- Minnesota Regional Sleep Disorders Center, Hennepin County Medical Center, 701 Park Avenue, G8.320, Minneapolis, MN 55415, USA
- Department of Medicine, School of Medicine, University of Minnesota, Twin Cities, MN, USA
- Olmsted Medical Center, Rochester Northwest, 5067 55th Street NW, Rochester, MN 55901, USA
- Sleep Medicine Fellowship, Minnesota Regional Sleep Disorders Center, Hennepin County Medical Center, Minneapolis, MN, USA

# **Background**

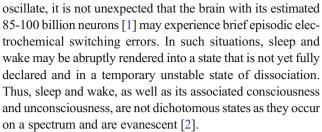
The word parasomnia derives from the Greek prefix para, meaning alongside of, combined with the Latin noun somnus for sleep, to account for the dictionary definition of events that accompany sleep. In the clinical setting, the term thereby relates to undesirable events that accompany sleep. Accordingly, parasomnias encompass a broad spectrum including dreaming, misperceptions, dysphoric emotions, abnormal sleep-related movements as well as behaviors, and dysregulated autonomic nervous system functioning. Parasomnias become clinical disorders as they may result in sleep fragmentation, adverse health effects, troublesome psychosocial effects, and even injuries. The latter may have potential forensics implications. Consequently, addressing safety is often an initial goal as the clinical impact may involve more



than just the patient, depending upon the complexity and duration of the sleep-related behaviors.

Parasomnias have long been defined in the International Classification of Sleep Disorders (ICSD) as undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousals from sleep. Furthermore, parasomnias may occur during non-rapid eye movement sleep (NREM), rapid eye movement sleep (REM), and during transitions to and from sleep. However, such a definition, though technically correct, is overly simplistic, open for misinterpretation, and vulnerable for misapplication. In an age in which an inquisitive mind may almost immediately satiate their thirst for knowledge with the stroke of a few keypads when interacting with an internet search engine, healthcare providers must remain vigilant concerning web-based information that are often uncritically accepted by patients. The general public and popular media continue to be captivated by the belief that the unconscious mind, in either a state of hypnosis or sleep, may reveal itself in words, mental images, or behaviors though its meaning is kept at a distance from the conscious mind through a barrier of repression. Various avenues for the interpretation into dreams have evolved based upon the premise that behaviors and/or experiences which arise from the platform of sleep are the result of a breakdown of psychic censorship and may thereby provide insight into the machinations of the unconscious mind. Such "Dream Theory," including that developed by Sigmund Freud, which may masquerade in subtle forms including that as "wish fulfillment," especially when applied to parasomnias has been supplanted by modern neuroscientific constructs that are driven by rigorous methodology that require hypotheses that are both testable and verifiable. As such, the human condition is now understood to be comprised of three essential states: Wake, NREM sleep, and REM sleep. It is the dynamic interplay of these three states which can account for previously difficult to explain human experiences. Nevertheless, the pseudoscience of certain aspects of "Dream Theory" continues to hold sway over the general public as supported by the everlasting success of dream interpretation manuals and the belief in the metaphorical significance of dream symbolism. Particularly in cases with legal implications, it is important to recognize when older, now discredited, paradigms for understanding human behavior remain in play.

Recent advances in neuroscience coupled with refined neurodiagnostic imaging modalities now reveal that the three states are modulated by a host of physiologic influences including the degree of aminergic and cholinergic neurochemical bias, CNS activation, and the degree of endogenous vs. exogenous input. Directly influenced by regularly recurring physiologic conditions including homeostatic drive and circadian rhythmicity, the process of state declaration is most often maintained in a stable and predictable fashion throughout a 24-h period. However, as the components of sleep frequently



The most current version of the International Classification of Sleep Disorders (ICSD third Edition) now recognizes State Dissociation as the paradigm for parasomnias [3...]. Previously, wakefulness, non-rapid eye movement sleep (NREM), and rapid eye movement sleep (REM) were thought to be the three states that were essentially mutually exclusive. Recent research has shown that combinations of one or more of these states is possible and may result in unusual unstable states that potentially manifest as parasomnias or as altered levels of awareness [4-8]. Appreciation for the State Dissociation paradigm facilitates a neurophysiologic mechanistic approach to understand parasomnias as well as a refinement of its classifications. NREM-related parasomnias are an admixture of wakefulness and NREM sleep and include confusional arousals, somnambulism, and sleep terrors. Here, the prefrontal cortex is considered to be "offline" with subsequent severe impairment, or absence, of higher executive cognitive functioning while potential for motor capacity may be retained [9, 10]. REM-related parasomnias are an admixture of the elements of REM sleep together with wakefulness. In contrast with NREM-related parasomnias, these individuals often recollect emotionally dysphoric dreams. Aside from REM sleep behavior disorder (RBD), the admixture of REM sleep and wakefulness explains the experiences of sleep paralysis, cataplexy, and hypnagogic hallucinations which are seen in narcolepsy. All three states may be present in the same individual as overlap disorders. As parasomnias arise from the platform of sleep, behaviors attributed to this condition are performed without awareness.

One should remain mindful that there are several abnormal sleep-related movements that do not adhere to the State Dissociation paradigm. These are important clinical conditions worthy of separate classification which have been placed under the heading of "Sleep Related Movement Disorders." This heading is most notable for restless legs syndrome (RLS), otherwise referred to as Willis Ekbom Disease (WED). Abnormal sleep-related movements encompass a broad range of simple movements including bruxism as well as myoclonic, rhythmic, rocking, cramping, and dyskinetic movements or tremors, which are not characteristically associated with dream mentation.

The current iteration of the ICSD third edition recognizes 10 core categories of parasomnias (Table 1). Only one of the core categories, rapid eye movement (REM) sleep behavior disorder (RBD), requires video polysomnographic



Table 1 (see REF. 3) Classification of parasomnias

NREM-related parasomnias

Disorders of arousal

Confusional arousals

Sleepwalking

Sleep terrors

Sleep-related eating disorder

REM-related parasomnias

REM sleep behavior disorder

Recurrent isolated sleep paralysis

Nightmare disorder

Other parasomnias

Exploding head syndrome

Sleep-related hallucinations

Sleep enuresis

Parasomnias due to medical disorder

Parasomnias due to medication or substance

Parasomnia, unspecified

Isolated symptom/normal variant

Sleep talking (somniloquy)

documentation as one of the essential diagnostic criteria. However, for most of the other parasomnias, polysomnographic monitoring can provide corroborative documentation in support of the clinical diagnosis. The ICSD third edition is largely based upon peer-reviewed consensus-driven clinicalbased evidence in conjunction with up-to-date pathophysiologic developments in somnology and neuroscience. Any classification system of disorders in medicine would appear to play several key roles. First, it serves as a guide for healthcare providers in the identification of specific disease states which in turn would drive focused therapeutic strategies resulting in effective clinical outcomes. One should also recognize that formal recognition of a disease state by a medical professional society also may influence future research agendas and mobilize funding subsequently improving personal and public health. Lastly, particularly, in the realm of parasomnias with its potential for sleep-related violence, formal recognition of certain conditions, including sleep-related abnormal sexual behavior (sexsomnia), can now be considered in the development of legal arguments and admissible in a court of law as these uphold the Daubert Standard in criminal cases where a sleep disorder or condition may be involved [11].

## **NREM-Related Parasomnias**

The NREM-related parasomnias arise from an admixture state of wakefulness and NREM sleep and are termed Disorders of Arousal. Confusional arousals, sleepwalking, and sleep terrors are the primary disorders of arousal. Sleep-related eating disorder (SRED) is a subset of sleepwalking while sexsomnia is a unique form of confusional arousal. Recent electromagnetic tomographic studies have demonstrated early localized arousal-related activation of the cingulate motor area preceding sleepwalking further support the State Dissociation paradigm [12].

The NREM-related parasomnias are defined by incomplete awakening, unresponsiveness, minimal cognition, and near-to-complete amnesia. They most commonly arise associated with NREM stage 3 sleep and tend to occur during the first third of the night, but are not restricted by either boundary [13]. The differential diagnosis for NREM-related parasomnias includes sleep-disordered breathing, REM-related parasomnias, nocturnal seizures, and psychogenic dissociative disorders. Formal diagnosis of NREM-related parasomnias is typically made by clinical evaluation; however, polysomnographic evaluation is vital in atypical cases due to the 40 % incidence of alternative diagnosis or precipitant [14].

#### **Confusional Arousals**

Confusional arousals present as movements and/or vocalizations confined to the bed or sleep location. The affected individual may display varying levels of confusion or sleep-drunkenness, with lesser degrees of agitation or distress. Like the other primary disorders of arousal, they are more common in children than adults, with a lifetime prevalence of 18.5 % and an adult prevalence of only 2.9–4.2 % [15–17]. Unsurprisingly, shift-workers have a two- to three-fold increased incidence of confusional arousals, possibly related to circadian misalignment of sleep or insufficient sleep intake [18].

Sleep-related abnormal sexual behaviors, popularly referred to as sexsomnia, are thought to be a variant of confusional arousals, although they may overlap with somnambulism when the sleep surface is vacated [3••]. Inappropriate sexualized behaviors that arise from the platform of sleep encompass a broad range of behaviors from profane vocalizations, inappropriate touch/fondling, masturbation, oral sex, to sexual intercourse. These behaviors are without conscious awareness and are frequently without dream mentation. They have broad clinical, social, and legal implications [19•]. It is thought to be fairly common, with a lifetime and annual prevalence of 7.1 and 2.7 %, respectively [15].

### Somnambulism (Sleepwalking)

Despite the misnomer, sleepwalking is a relative amnestic state not confined to simple ambulation and may include vocalization, manipulation of household objects, and even operation of motor vehicles. It can be associated with profound



anesthesia; in one study of patients with violent parasomnias, almost 80 % experienced anesthesia during violent and self-injurious behavior without complete awakening [20]. Sleepwalking frequently recurs; in one study, 22 % of sleepwalkers had daily episodes, and 44 % had at least weekly episodes [21]. Sleepwalking displays an even higher child-hood preponderance compared to confusional arousals, with lifetime prevalence of 22 % compared to adult prevalence of 2 % [15, 17]. Furthermore, early onset portended higher frequency of violent behaviors. Median age at sleepwalking onset is 9–10 years, although in one series, a third of adult patients with injurious sleepwalking developed sleepwalking after the age of 16 [21, 22].

Family history of sleepwalking was reported in 57 % of sleepwalkers, and the prevalence of sleepwalking was 47 % among children with one parent who had a history of sleepwalking, consistent with prior studies suggesting a genetic inheritance [21–23]. Sleepwalkers may be more sensitive to sleep deprivation; resting cerebral blood flow was decreased in sleepwalkers compared to controls following a night of sleep deprivation [24]. They also display alterations in sleep microarchitecture and more frequent NREM stage 3 arousals. Evaluations of slow-wave activity and oscillation density in sleepwalkers have demonstrated differences between behavior-associated arousals and benign arousals [25, 26].

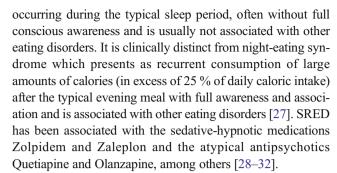
# **Sleep Terrors**

As the name implies, pavor nocturnus, or sleep terrors appear externally as terrifying experiences. Sleep terrors and sleepwalking likely exist on a spectrum, differentiated by the nature of vocalization and degree of agitation. Sleep terrors consist of screaming, extreme agitation, and prominent and sometimes violent motor activity. Despite outward appearances, and in contrast to nightmare disorder, there is no dream recall, and they are essentially amnestic for the event. Perception of the environment is minimal, and attempts to abruptly terminate the episode may provoke a vigorous unintended oppositional response.

As with other disorders of arousal, sleep terrors are more common in childhood but not rare in adulthood, with a lifetime and adulthood prevalence of 10 and 2 %, respectively [15, 17]. Sleep terrors typically occur at a much younger age, with peak at 1 1/2 years of age. There appears to be a link to sleepwalking, one study showed that approximately one third of children who had sleep terrors developed sleepwalking later in life and that parental sleepwalking predicted higher rates of childhood sleep terrors [22].

### **Sleep-Related Eating Disorder**

SRED is a type of nocturnal eating characterized by consumption of food and non-food items, not due to hunger stimulus,



At this time, it is unclear whether SRED is a disorder of arousal, a non-motor variant of RLS, an overlap syndrome between RLS and disorders of arousal, or a heterogeneous collection of disorders with similar phenotypes. SRED shares many characteristics with other disorders of arousal, including frequent amnesia, lack of awareness as evidenced by reports of consumption of non-food items, and increased NREM stage 3 arousals [15, 33]. Notably absent are the typical childhood predominance and gender equality. Supporting an association with RLS, SRED was present in 36 % of RLS patients in one series [34]. Furthermore patients with RLS and SRED experienced improvement in SRED on dopamine agonist therapy and had more frequent SRED on sedative hypnotic therapy. Whether or not the relationship is due to decreased arousals from effectively treated RLS, manifestation of sedative-hypnotics medication side effects in patients with NES causing amnestic SRED or demonstration of a nonmotor RLS phenomena waits to be seen [28, 30, 34, 35].

### **REM-Related Parasomnias**

REM-related parasomnias offer perhaps the best clinical examples of state dissociation sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy had been difficult to explain human experiences but now is regarded as the manifestation of fascinating experiments in nature in which components of REM sleep mix and temporarily coexists with wakefulness often with vividly memorable oppressive apprehensiveness. Sleep paralysis is the most common example of the state dissociation of REM sleep and wakefulness. In this condition, the muscle atonia associated with REM sleep has persisted into wakefulness and is often associated with a dysphoric emotional awareness which may be accompanied by hypnopompic hallucinations.

#### **Recurrent Isolated Sleep Paralysis**

Most cases of sleep paralysis are isolated and sporadic, with 7 % of the general population reporting at least one episode of sleep paralysis [36]. However, the condition can occur frequently, as in recurrent isolated sleep paralysis (RISP). RISP is described as repeated episodes of sleep paralysis causing



significant somniphobia or fear of initiating sleep. Despite the description as isolated, episodes of sleep paralysis are commonly accompanied by hallucinatory experiences. RISP has usually been reported in a familial pattern [37].

#### Nightmare Disorder

Nightmares, or dysphoric threatening dreams associated with prominent recall, are thought to predominantly arise from REM sleep. The prevalence of nightmares is fairly high [15] often persisting into adulthood. Nightmare disorder is defined as recurrent nightmares associated with awakening dysphoria, and accompanied by clinically significant sleep or daytime dysfunction, such as anxiety, somniphobia, cognitive impairment, daytime sleepiness, or fatigue. Nightmare disorder is fairly rare in children outside of those with severe psychosocial stressors; however, the prevalence in adults may reach 2–6% depending on estimates used [38]. The frequency is even higher in certain psychiatric subpopulations, including patients with anxiety disorders, borderline personality disorder, post-traumatic stress disorder, or psychogenic dissociative disorders.

#### **REM Sleep Behavior Disorder**

REM sleep behavior disorder (RBD) is defined as repeated episodes of vocalizations or complex behaviors during REM sleep associated with REM sleep without atonia (RWA), as defined by formal criteria established for monitoring abnormal increases in phasic or tonic muscle tone of surface EMG electrodes during REM sleep [39]. In contrast to NREM-related parasomnias, RBD often occurs with dreams that are of an emotionally dysphoric nature. Symptomatic RBD typically occurs in males starting in the sixth decade of life [40]. It is frequently described as an early precursor of neurodegenerative disorders, particularly the alpha-synucleinopathies including Parkinson's disease, dementia with Lewy Bodies, and multiple systems atrophy. In one recent series, over 80 % of patients with idiopathic RBD subsequently developed a neurodegenerative disorder after a mean interval of 14 years [41]. Despite the association with neurodegenerative disorders, RBD is most commonly seen secondary to antidepressant medication use, typically selective serotonin reuptake inhibitor (SSRIs) or tricyclic antidepressants (TCAs), with an annual prevalence approaching 4 % in psychiatric patients [42, 43]. In patients with medication-associated RBD, there is increasing gender parity and a trend towards younger patients [44,

RBD requires formal diagnosis with video polysomnography in order to confirm RWA and to differentiate it from the shared features with other disorders such as NREM-related parasomnias, seizures, or nocturnal panic attacks. Testing is typically performed with augmented EMG leads on bilateral flexor

digitorum superficialis muscles, as RWA classification based on quantification of flexor digitorum phasic activity has demonstrated the best accuracy [46, 47, 48•]. Evaluation of RWA requires painstaking review of 3-s micro-epochs and can be somewhat user-dependent; recent advances in standardized quantification and automated analysis will allow for more uniform evaluation and diagnosis [49–51].

Due to absence of widespread awareness of RBD, specific questioning for dream enactment behavior is crucial during clinical evaluation [40]. As polysomnography may be occasionally performed without formal sleep clinician evaluation in certain contexts, RWA may be seen during PSG without confirmatory history of dream enactment behavior. RWA is also commonly encountered in antidepressant-treated patients not meeting criteria for RBD diagnosis [52•, 53]. In these cases, clinical correlation is required, as the significance of isolated RWA remains yet to be determined

### Other Parasomnias

Several other parasomnias have been described in the literature, but cannot be classified distinctly into a NREM or REM-related parasomnia. The pathophysiology of sleep enuresis does not appear to adhere to the State Dissociation paradigm but does fit the historical definition of parasomnias and remains a very important disorder in pediatrics. Sleep enuresis, or chronic involuntary nocturnal voiding, is a combination of two subtypes, primary and secondary. Several different etiologies have been proposed, but the two subtypes are distinct clinical entities. This disorder is fairly uncommon outside of childhood. Sleep-related hallucinations (or hypnagogic or hypnopompic hallucinations) are most frequently a REM-related phenomenon; however, drowsy-wake states may produce similar events.

Somniloquy, or sleep talking, is not actually considered a disorder according to the ICSD third edition; rather it is considered as a normal variant or isolated symptom. It is relatively common, with a lifetime prevalence of 69 % [15] and is associated with disorders of arousal and REM sleep behavior disorder. Somniloquy may occasionally be unintelligible or utterances and should be differentiated from catathrenia (or sleep-related prolonged expiratory groaning—now categorized under sleep-related breathing disorders) or other mimics of disorders of arousal.

#### **Exploding Head Syndrome**

Exploding head syndrome (EHS) is a rare benign condition best described by its other name, episodic cranial sensory shock. Sufferers report paroxysms of sudden loud noise or flashes of light experienced in the head, without cephalalgia, occurring during sleep-wake or wake-sleep transition [54].



Polysomnographic recording of these episodes have demonstrated occurrences during wake, as well as NREM stages 1 and 2 sleep [55]. EHS has not been formally classified as a NREM-related parasomnia likely due to differences with disorders of arousal in terms of demographics and associated factors. Numerous etiologies have been postulated, including delayed deactivation of the brainstem reticular activating system on transition to sleep, middle ear dysfunction, or sensory variant of hypnic jerks [55, 56]. The benign nature of EHS likely precludes future research on the disorder.

### **Secondary Parasomnias**

Secondary parasomnias also deserve consideration, particularly given the prevalence of their underlying primary conditions and potential multiplicative implications. Theoretically, any disorder that can increase sleep pressure or cause sleep fragmentation has the potential to trigger various parasomnias. Obstructive sleep apnea (OSA) has been associated with REM-related dream enactment behavior. In this condition, known as pseudo-RBD, arousals from OSA events may trigger REM-related dream enactment behavior. This typically resolves with effective treatment of OSA with positive airway pressure delivery [57].

Sleep-related abnormal sexual behaviors and other disorders of arousal may also be precipitated by OSA-triggered arousals, with potentially disastrous consequences [58]. Similarly, sleep deprivation has been associated with disorders of arousal. In clinical settings, sleep deprivation may be used in conjunction with forced arousals to assist in the diagnosis of disorders of arousal [59]. As noted above, increased frequency of disorders of arousal have also been associated with shift work and circadian misalignment [18, 60].

Medications have been also associated with a number of parasomnias. Zolpidem has been most commonly cited in the literature [29, 61], but is not alone as other benzodiazepines and benzodiazepine receptor agonists have also been implicated [34]. Nonetheless, Zolpidem is frequently associated with a number of complex sleep-related behaviors, including sleepwalking and sleep-related eating, with a recent study putting the adult incidence at 25 % [62]. It is unclear if the proportion of medication-related parasomnias linked to Zolpidem is due to its high market share or to possible uniquely distinct pharmacokinetic properties not shared by other sedative-hypnotic agents. Lastly, the new class of Orexin-antagonist medications formulated for insomnia, including first-to-market Suvorexant, may carry a theoretical risk of inducing Narcolepsyassociated parasomnias such as RBD and cataplexy due to its manipulation of the Orexin system, although the true incidence of side effects in a clinical practice have yet to be defined [63].



The ICSD third edition recognizes 10 core categories of parasomnias. The State Dissociation paradigm allows workable conceptualization of parasomnias as changing unstable oscillatory admixtures of Wake, NREM sleep, and REM sleep. As our understanding of the neurophysiologic systems accounting for parasomnias deepens, we continue to refine the classification of these disorders. This classification allows us to identify disease states which drive therapeutic strategies for effective outcomes, define appropriate avenues for future research and public education, and guide the legal system on complex and oft-confused disorders to help determine appropriate standards [64]. Further research will hopefully continue to deepen our understanding of disorders of arousals and RBD and associated conditions with a focus on neuroprotective therapies, clarify the neurophysiologic mechanisms linking pharmacology with untoward parasomnias, and allow us to better define these behaviors across the spectrum of human existence.

**Acknowledgments** We would like to acknowledge Dr. Mark Mahowald for his contributions in the review and preparation of this manuscript.

### Compliance with Ethical standards

**Conflict of Interest** Louis Kazaglis and Michel A. Cramer Bornemann declare that they have no conflicts of interest

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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