Dreaming

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History of the Study of Dreams
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Glossary
Activation-synthesis theory: Hobson and McCarley theory that dreams are initially random images that acquire meaning following arousal.
Atonia: Abrupt loss of muscle tone at the onset of rapid eye movement (REM) sleep.
Dream: A hallucinatory experience during sleep consisting of visual images related in a story-like structure, which are accepted as reality at the time.
EMs: Eye movements during a REM period, which vary in speed and density. These may relate to the visual content of the dream.

Imagery rehearsal therapy: A treatment program for the control of nightmares through practice during waking of pleasant visual images.
Incorporation: Inclusion in the dream report of an external stimulus.
Mood regulation function: Dream reports are initially negative in emotion and progressively become more positive at the end of the night.
Nightmares: Strongly unpleasant dreams that awaken the dreamer with full recall of the dream story.

The Early History of Laboratory Investigation of Dreams

Dreams have been a source of interest throughout human history. However, much of this literature does not meet the criteria of being a ‘study.’ This article will cover only investigations that test a hypothesis. Such studies began in the mid-1950s when laboratory-monitored sleep proved dreams could be elicited reliably by awakening sleepers from a specific neurophysiological state known as rapid eye movement (REM) sleep. This established that REM sleep is typically free of body movements and that their presence interferes with dream continuity. This study led to the addition of a chin muscle monitor, in recognition that loss of muscle tone is a reliable signal of the onset of REM sleep and thus the likely presence of dreaming.

Hypothesis: Dreams are Related to REM Sleep Characteristics

Early sleep studies, and more recent brain imaging work, hypothesized that REM sleep determines the psychological characteristics of dreams. The first such study hypothesized that body movement within a REM period would disrupt the continuity of the reported dream story. REM periods were divided into those that were continuous and those that were interrupted by a body movement. The dream reports from these episodes were judged as being either a continuous narrative or one with an abrupt change to another story. The data analysis showed that REM periods, free of body movement, yield continuous dream reports while those with one or more body movements were associated with reports of unrelated dreams. This established that REM sleep is typically free of body movements and that their presence interferes with dream continuity. This study led to the addition of a chin muscle monitor, in recognition that loss of muscle tone is a reliable signal of the onset of REM sleep and thus the likely presence of dreaming.

Another hypothesis tested whether the reported dream is related to the type of eye movements (EMs) that precede the awakening. The EMs were divided into those that were large (high amplitude) and dense (occurring in bursts) versus those that were slower and sparser. A significant association was found between the activity of the EMs and a dream story in which the
Hypothesis: Dreams Relate to Each Other Within the Night

Testing the relation of dreams to each other found these were not obviously similar within the night nor did all the dreams of a night make up one continuous story. The conclusion was that dreams are independent stories but with some elements in common, and that those that were similar were not always found in reports from adjacent REM periods. Since in only a few cases was the same theme expressed throughout all the dreams of a night, it was concluded that, at the level of the manifest content, dreams are not related to each other. This raised the question of whether the experimental awakenings were disrupting a natural continuity of the dreams. Further study showed the amount of time spent awake for the sleeper to report their dream was negatively related to the continuity between that dream and the report from the next REM awakening. The longer the time awake, the less the continuity was.

Although awakenings from REM yielded a report of dreaming 80% of the time, those from nonrapid eye movement (NREM) sleep yielded widely varied percentages of dream reports. The highest percent was found at sleep onset. More typically, NREM reports differed in quality from REM reports. They were described as less imagistic and more thought-like, less emotional and more pleasant than the highly emotional, unpleasant reports from REM. To test whether the failure to find continuity between dreams of the same night was because the dream theme was set prior to the first REM, the next investigation collected samples from both NREM and REM sleep, sampling all Electroencephalography (EEG) stages of sleep. Sleepers were awakened either 30 or 90 min following sleep onset by a coin toss. The coin toss was repeated following each report to determine the timing of the next awakening. This resulted in 6–9 reports each night in random sequences of various sleep stages. The reports were examined for repeated images or themes in the manifest content. Sometimes, the initial report was from a NREM stage before any REM had occurred. Repeated elements were found in different sequences of sleep stages. Testing continuity of the sleeping mind using this random awakening schedule presents a real difficulty: repeated elements may be present but missed if the random protocol skipped a time when reports were most connected.

In conclusion, there were nights with little or no repeated elements and others when these were plentiful in both NREM and REM sleep. During nights when these were frequent, they were also the most vivid and memorable of the reported dream but were disrupted by on-going unconscious (latent) dream thoughts. The conclusion was that there is an interaction of preconscious and unconscious streams of thought throughout sleep but that the methods used to analyze dreams were not appropriate to identify these.
the influence of the emotional state of the participants before they fell asleep. It was clear that there was also a need for more subtle and more systematic methods to measure dream content. The most comprehensive and influential of the scales developed were those of Hall and Van de Castle. These allowed studies to compare dream reports of various groups on standardized measures. Differences were found between the dreams of men and women, older and younger age groups, ethnic groups, and many clinical groups such as alcoholics and nondrinkers. Studies of the relation between the prior waking psychological state and the dreams of the night began to use the Hall and Van de Castle scales for standardizing the dream content and various personality tests for measuring waking traits and states. The presleep emotional state of the volunteer was then manipulated using stimuli chosen to be emotion invoking or bland, and reports from the following dreams were analyzed using the new content scales. One study used two episodes of a TV series, one very violent and the other a comedy. The order of these was counterbalanced on two sleep nights. Reports were collected from both REM and NREM sleep episodes to explore the differences in the influence of these movies on the different sleep stages, as well as the relation to the waking personality characteristics. The aggressive film produced longer and more imaginative, more vivid, and emotional REM reports than did the comedy movie. However, these film differences were not found between the reports collected from NREM sleep. The correlation of dream characteristics and the waking personality tests showed an extremely consistent pattern of correlations between the clinically oriented scales and dream-like features of the reports. The imaginativeness of the person in waking was highly correlated with that aspect of the dream reports. There were no significant direct incorporations of either film into the sleep reports. Why the aggressive film had a clear impact on REM reports but not on those from NREM and why, despite the increase in vivid, imaginative, emotional REM dreams after the violent film, were the dreams not more violent or unpleasant? The explanation offered was that the violent film had a general effect and not a specific one, and that the general emotional arousal stimulated the viewers’ personal emotional memories to be displayed during REM sleep.

To focus the waking attention to a specific drive, the next study included a physiological measure of sexual arousal during the exposure to a pornographic film. This study examined the effects of this on the dreams of adult men over five nights of REM collections. The first night was a control to assess the baseline rate of sexual dreams. The following day, the participants wore a penile strain gauge to measure their response to the movie shown before their second night. The dream reports were analyzed using the Hall and Van de Castle norms for the frequency of common words in the dream reports of a similar sample of adult men. Judges first rated these words for symbolic sexual reference, for example, balls, nuts, shaft, and fountain. The judges agreed on ten words as having symbolic sexual meaning and ten others were chosen to refer to the laboratory setting. There was a marked increase in the symbolic words in the dream reports over the rate expected from the norms. That this might represent a latent response to the sexual film was supported by a significant increase in ‘No recall’ reports on Night 2, and an increase in number of dreams with one character, indicating a possible suppression response to two-person interactions. On the final night, Night 5, the recall rate returned to the baseline control level and the number of dreams with two characters was significantly higher than on the control night.

In summary, the findings of an immediate increase in failure to recall from REM awakenings and lack of any direct incorporation into dreams of the arousing movie suggested an inhibiting effect possibly related to the presleep interactions with the laboratory personnel, two attractive female technicians, with whom they had some bodily contact during the application of the electrodes. This appears to have raised anxiety about having, or reporting, explicit dreams leading to both a dampening of recall and increased number of dreams with only one character. The conclusion was that although the sexual movie produced an immediate physiological arousal response in waking, it was inhibited from direct expression in sleep on Night 2. On the following Night 3, the number of symbolic sexual words in the dream reports hit the highest peak. Over the next three nights, there was a gradual return to the baseline recall rate. The laboratory situation appeared to have a powerful inhibiting effect on the drive aroused by watching the movie.

Finding that the planned effect of experimental stimuli often had a minimal effect and that the social context may have a more powerful, unanticipated effect on dream content, there was a shift in research strategy toward more naturalistic studies. Dreams following natural disasters, such as the 9/11 terrorist attack, the holocaust, bereavement, divorce, kidnapping, rape, and living under missile attacks, have all been studied. The landmark study of this kind chose an inherently emotion arousing event, elective surgery, to study the effect on dreams. Patients were recorded for four nights before and three nights after surgery. Rating scales were constructed for analyzing the dreams including degree of recall, anxiety, and involvement. The general conclusion was that the surgeries meant different things to different patients. The initial dreams never dealt with the surgery directly but as has been seen before there were many transformations to represent this event symbolically. Most apparent was that the dreams demonstrated the participant’s attempts to integrate the present stressful event into their individual adaptive strategies that had worked for them in the past. If this has a learning effect on future coping, longer follow up would be needed.

**Hypothesis: Dreams Effect Postsleep Psychological Functioning**

Studies of the effect of dreams on changing the waking mood have examined both healthy persons and those with clinical diagnoses. One study of a healthy, high functioning sample used the Profile of Mood States (POMS) test before and after sleep for two nights with REM interruptions for collecting dreams on the second night. The sleepers rated the emotional quality of each dream immediately following their report as positive/pleasant, neutral, or negative/unpleasant. The sample was divided on the presleep mood score into those who had little or no elevation on the Depression Mood Scale and those who had a mild elevation of this negative mood. The Not Depressed (ND) group had twice as many positive dreams as negative and the Mildly Depressed (MD) had an equal number of positive and negative dreams. To test whether dreams regulate mood within sleep, the average ratings of dream affect in the first nights.
half of the night was compared to the average of those in the second. The ND had more positive than negative dreams in both halves. The MD had a high proportion of negative dreams in the first half-night, with a marked decrease in the last half and the opposite pattern for positive dreams; with few at the beginning of the night and a high proportion at the end of the night.

The conclusion that sleep generally improves morning mood was confirmed by a lower depression score following both nights. Whether this effect is related to the intervening dreams was supported by the finding that the affect in first dreams of the night was significantly correlated to the previous waking mood. Even when this mood was only mildly unhappy, negative dreams dominate in the first dream reports and then decrease in the second half-night. The natural sequence appears to be that the emotional state before sleep is continued into sleep onset, stimulating a network of memories associated with similar feeling. The varied dream scenarios or ‘contexts’ appear to dissipate the negative mood, which in turn accounts for the improved morning mood in healthy persons. If this is a natural function in well-adjusted adults, do dreams display dysfunctions in those not emotionally fit?

**Hypothesis: Dreams Differ in Psychiatric Patients**

The ‘naturalistic’ studies, particularly of sleep during or after traumatic events, brought attention to the study of nightmares. These fear-inducing dreams lead to an interruption of sleep, an awakening with full recall of the dream. These are the most disturbing symptom of posttraumatic stress disorder (PTSD), the most long-lasting symptom and the one most difficult to treat. The PTSD diagnosis includes not only distressing dreams but in some exact replications of the traumatic event. Treatments that train patients to control their dreams have become the behavioral treatment of choice. To test whether dreamers are capable of controlling their dreams, Imagery Rehearsal Therapy, a brief clinical program, was developed. This begins by training nightmare patients to rehearse a positive image of their choice during waking. Next step is to write out their nightmare but to change the ending to one they prefer. That this trains nightmare control is being reported in some studies based on self-report.

Dreams have also been studied in major depression since these patients show abnormalities of REM sleep and dream reports that are both brief and bland in feeling when the depression is severe. Moderate depression is characterized by dreams with negative feelings, which fail to reduce, in fact increase, in frequency within the night. Those whose within-sleep pattern of dream affect resembles that of healthy samples, with decreasing negative and increasing positive dreams within the night, are more likely to remit without treatment within a year. This finding has been confirmed in several studies leading to the first verified function of dreams: dreaming performs a mood regulatory function.

**The Future of Dream Research**

As reviewed here, studies of the last 60 years have freed dreams of being seen as meaningless accompaniments of REM sleep. Partly, this is due to recent studies of patients with brain injuries, seizure disorders, and psychosurgeries who report changes in their dreaming. Solms reported almost 1000 cases experiencing a cessation of dreaming following a focal forebrain lesion. Many of these were confirmed as ‘dreamless’ by the REM awakening method. In these cases, the pontine brain stem was completely spared and REM sleep was intact. Further, he found that dreaming can be initiated by a forebrain mechanism independent of the REM state in those with nocturnal seizures occurring in NREM sleep, which are experienced as nightmares. Comparing a large sample of patients who reported changes in their dream experience and a healthy control sample, Solms identified the brain areas that had been damaged or surgically removed and the patients’ experience of changes in their dreams, to map the structures responsible for specific characteristics of dreams, for example, the presence of color or of people. This led him to conclude that dreaming and REM sleep are controlled by different mechanisms; with REM initiated from the pons and dreaming from the forebrain. What is common is that dreaming occurs not only in sleep when the brain is highly activated as it is in REM but also in the transitions between waking and sleep; at sleep onset in NREM and at the end of the sleep cycle just prior to waking. This allows clinical intervention for control of nightmares, to target sleep onset.

The other major conclusion from this review is that dreams are strongly influenced by the waking emotional state, which is not expressed directly but in sensory images drawn from associated memory networks. These will be displayed in a sequence of dreams that function to down-regulate negative mood. Given these studies, it should be possible to estimate the health of this function by collecting only two samples: the first from sleep onset and the second from the end of sleep. This would avoid disrupting the sleep with REM awakenings and minimize the laboratory effect.

**Further Reading**


Sleepwalking

**Glossary**

**Parasomnias**: Undesirable movements and behaviors that occur during entry into sleep, within sleep, or in the setting of arousals from sleep.

**Sleep diaries**: Records kept by the patient or family member/partner that indicate sleep onset and offset times, including naps and awakenings overnight; these data are often helpful in determining whether parasomnia episodes are triggered by relative sleep deprivation.

**Sleepwalking**: Complex behaviors usually initiated during arousals from sleep culminating in ambulation during an altered state of consciousness and impaired judgment; also referred to as somnambulism.

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**Description**

Sleepwalking is characterized by complex behaviors that are typically initiated during arousals from sleep and result in ambulation. The activity can vary from simple events such as sitting up in bed to more complex movements such as walking or even ‘bolting’ from the room. These episodes can last from a few seconds to several minutes long. Patients are generally difficult to arouse during these periods, and if they are able to be awakened, patients are often in a confused state. Many patients typically have their eyes open and have a ‘glassy-eyed’ appearance during sleepwalking episodes. As these events typically occur because of arousals from slow-wave sleep, they generally occur during the first half of the sleep period.

While some patients may have little memory of the event, most patients generally have no memory of the event the following morning. Patients may be able to recall emotions or impressions from the event. Symptoms of tachycardia, sweating, or the expression of fear is generally not displayed in patients during an episode. The absence of autonomic symptoms and screaming is what can differentiate a sleepwalking episode from sleep terrors.

Sleepwalking is a subset of a larger group of parasomnias. Parasomnias are undesirable movements and behaviors that occur during entry into sleep, during sleep, or with arousals from sleep. Parasomnias are subdivided into several categories: (1) disorders of arousal from non-REM sleep, (2) parasomnias associated with REM sleep, and (3) other parasomnias. The disorders of arousal include confusional arousals, sleepwalking, and sleep terrors. The disorders of arousal tend to occur in stage N3 sleep and therefore typically occur in the first third of the night.

**Risk Factors**

There are a number of factors that may predispose a patient to sleepwalking. There is a strong genetic influence in the development of sleepwalking. Generally, if one or both parents have had a history of sleepwalking, the child is at a significantly increased risk of developing sleepwalking episodes as well. The Finnish Twin Cohort study published by Hublin et al. reported a concordance rate of 55% for monozygotic and 35% for dizygotic twins for sleepwalking in childhood. Bakwin et al. also published a twin study that reported a six-time greater concordance for sleepwalking among monozygotic twins than in dizygotic twins.

Factors such as sleep deprivation, fever, head injury, alcohol abuse, hyperthyroidism, and other conditions have also been shown to induce sleepwalking. The use of certain medications, including lithium, tricyclic antidepressants (TCAs), phenothiazines, zolpidem, and other benzodiazepine receptor agonists, can also precipitate these events. Studies have also shown that sleep-disordered breathing in children, that is, obstructive sleep apnea (OSA), may trigger sleepwalking due to the frequent arousals associated with respiratory events. Effective treatment of OSA may reduce the frequency of sleepwalking episodes in some patients.

Overall, sleepwalking has been reported to have a 2% prevalence in the general population. Sleepwalking tends to be more prevalent in childhood, peaking around age 8, and generally resolves with puberty although episodes have been described in adults. While de novo sleepwalking can occur in adulthood, many adults who sleepwalk first exhibited sleepwalking behavior in childhood. The persistence of sleepwalking into adulthood has been associated with underlying psychopathology in a significant number of patients.

**Diagnosis and Differential Diagnosis**

The most important initial approach to diagnosing sleepwalking is to obtain a careful and detailed history from the patient and their bed partner, parent, or caregiver. Information regarding the frequency, timing, and duration of the episodes should be obtained. It may be helpful to have patients keep a sleep diary to document this information. Detailed descriptions of any motor behavior should be obtained and the patient should be questioned about sensory symptoms. The clinician should pay particular attention to the patient’s past medical history, family history, and medication list to look for any precipitating factors outlined above. If the patient relays a history of associated snoring or apnea, they should also be evaluated for underlying sleep-disordered breathing.

While not required for a diagnosis, overnight polysomnography (PSG) can also be a valuable tool in the evaluation of sleepwalking. Although rare, the occurrence of a complex
behavior during PSG can support the diagnosis. While not pathognomonic for sleepwalking, several PSG findings have been thought to be associated with disorders of arousals. Patients with sleepwalking have been found to have an increased number of arousals from slow-wave sleep when compared to matched controls. It has also been suggested that patients with a higher percentage of slow-wave sleep are at higher risk for disorders of arousals. However, studies of sleepwalkers have revealed that many have the same if not lower slow-wave sleep activity when compared to matched controls. Also, arousals during slow-wave sleep can be seen in disorders other than sleepwalking such as OSA and periodic limb movements in sleep (PLMS). Hypersynchronous delta (HSD) activity has been documented just before sleepwalking episodes in several studies. HSD waves consist of two or more high amplitude delta frequency waves that precede an arousal or complex behavior during sleep. Although sleepwalkers have been found to have higher ratios of HSD during slow-wave sleep, this finding has not been confirmed in more recent studies. Finally, as sleep-disordered breathing has been postulated as a possible trigger for sleepwalking, evidence of OSA on PSG should prompt treatment with nasal continuous positive airway pressure (nCPAP), as successful treatment has been reported to decrease or eliminate the occurrence of sleepwalking.

The differential diagnosis of sleepwalking includes other NREM parasomnias such as confusional arousals and night terrors and other sleep disorders, including nightmare disorders, rapid eye movement sleep behavior disorder (RBD), nocturnal seizure activity, epileptic events, and sleep-related panic attacks. Sleepwalking can be differentiated from sleep terrors by the lack of autonomic hyperactivity and loud screaming during nocturnal episodes. Nightmare disorder and RBD both occur within REM sleep and are more common in the second half of the night. Also, children who are aroused from a nightmare generally become alert quickly and may often provide a detailed description of their dream content. If there is concern regarding epileptic activity, nocturnal PSG should be performed with an expanded seizure montage. Patients with sleep-related panic attacks typically develop autonomic activation following arousal from sleep and lack the confusion and amnesia seen in sleepwalkers.

Management

Management of sleepwalking should focus on both attempting to eliminate the occurrence of the events and mitigating the adverse effects of a potential episode. Patients with other sleep, medical, or psychiatric disorders should obtain appropriate treatment for the underlying disorder. Next, patients should be provided reassurance and counseling regarding safety precautions in the home. Patients and their parents, bed partners, or caregivers should be reassured that many arousal disorders decline in frequency, as a child enters adolescence. The clinician should ensure that counseling regarding environmental protection is provided. Safety measures include locks on doors and windows, sleeping on the first level of the home, gates across stairs, removing sharp objects from the bedroom, avoiding bunk beds, and placing padding or mattresses next to the bed. Emphasis should also be placed on sleep hygiene, as sleep deprivation, irregular sleep schedules, and unfamiliar sleep environments can increase sleepwalking episodes. If inciting agents are noted on the medication list, the precipitating agent should be avoided and the patient should be provided with a therapeutic alternative. If sleepwalking activity remains problematic, pharmacologic therapy with benzodiazepines, TCAs, and selective serotonin reuptake inhibitors may provide benefit. Clonazepam at a dose of 0.5–2.0 mg administered at bedtime has been successful at controlling sleepwalking activity.

Conclusion

In conclusion, sleepwalking is a common parasomnia that is most prevalent in children. There is a strong genetic influence, and many factors can precipitate sleepwalking episodes. The diagnosis can be obtained from a careful and detailed history. In more complicated cases, PSG may be used. Clinical suspicion of any underlying etiology warrants appropriate evaluation and treatment. The management of sleepwalking is typically straightforward with reassurance and counseling on safety precautions. Finally, in refractory cases, pharmacotherapy may be warranted.

See also: Descriptions of Parasomnias: Confusional Arousals; Parasomnias in Children; Sleep Terrors.

Further Reading


Gender Differences in Sleep-Related Movement Disorders

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Glossary

Periodic limb movements (PLMs): Stereotyped and repetitive limb movements that occur during sleep.

Periodic limb movement disorder (PLMD): A sleep disorder characterized by stereotyped and repetitive limb movements that occur during sleep at the rate of more than 15 times per hour in adults (or more than five times per hour in children) and is associated with sleep disturbance and/or daytime fatigue or sleepiness.

Sleep-disordered breathing (SDB): This describes a group of disorders characterized by abnormalities of respiratory pattern (pauses in breathing) or the quantity of ventilation during sleep.

Restless Legs Syndrome

Clinical Features

Restless legs syndrome (RLS) is a sleep-related movement disorder whose cardinal feature is unpleasant leg sensations, typically occurring at night, that interfere with sleep. The sensation is probably most aptly described as a powerful urge to move the legs; it is rarely described as painful, and the possibility of neuropathy should be considered when the discomfort presents primarily as pain. There is a circadian variation in symptoms, with greatest intensity typically occurring between 10 p.m. and 2 a.m. Symptoms are worse at rest and improve with movement or stimulation, including walking, rubbing, and stretching. The distressing sensations most typically involve the legs, but can also occur in the arms. Because of the nature and timing of RLS symptoms, patients with RLS may present with sleep-onset insomnia.

Diagnosis

The diagnosis of RLS is made by history and physical examination based on criteria listed in Table 1.

Thus, the diagnosis is based on subjective criteria alone, and polysomnography (PSG) is not generally necessary. The specificity of these criteria is not ideal, but careful application of the first four features, accompanied by a physical examination (to rule out neuropathy and vascular disease), is fairly specific for RLS. The differential diagnosis includes cramps, positional discomfort, vascular leg disease, and neuropathy. Adding response to dopaminergic medication to the essential criteria improves diagnostic accuracy.

Epidemiology

In population-based surveys, typically conducted by phone, the prevalence of any degree of RLS symptoms is estimated to be somewhere between 10% and 15% for all adults, with lower rates in the young and higher in the elderly. However, the prevalence of RLS varies considerably with different criteria for frequency and severity. For example, in the restless legs syndrome prevalence and impact Restless Legs Epidemiology Symptoms and Treatment (REST) study, RLS symptoms were endorsed by 7.2% of the survey population. However, symptoms occurring at least twice per week were reported by only 5% of the subjects and were moderately or severely distressing in only 2.7%.

The rate of RLS may be lower in Asian than in European populations, but the prevalence in African Americans is similar to that of Caucasians.
**Gender Differences for RLS**

RLS affects women disproportionately. A consistent finding in the literature about RLS is that women are 1.5–2 times as likely as men are to report RLS symptoms. Studies in both children and adolescents have demonstrated that this difference does not usually develop until the second or third decade of life. However, after the third decade, women are about twice as likely as men to endorse RLS symptoms, and the likelihood of having RLS may be related to pregnancy. Pregnancy is an important risk factor for RLS, both during the pregnancy and in subsequent years. About a fourth of pregnant women experience RLS symptoms, which typically peak in severity in the third trimester and resolve promptly after delivery. Lower hemoglobin, mean corpuscular volumes, and serum folate levels appear to be risk factors for RLS in pregnancy. With aging, the risk of RLS is fairly level for men, but it increases for women, proportionate to parity. In one study, nulliparous women had the same risk for RLS as did men up to the age of 64. However, for women who had borne children, the risk of RLS increased with the number of children. A woman with one child had twice the risk of RLS as a nulliparous woman and the risk increased with additional children. Indeed, a recent publication by Pantaleo et al. indicated that pregnancy accounts for almost all of the gender differences reported in overall RLS prevalence.

The gender difference in RLS symptoms appears to be present for both primary and secondary RLS. In a large cross-sectional study of patients with end-stage renal disease (ESRD), women were much more likely than men were to endorse RLS symptoms. Other associated factors for RLS in ESRD include lower hemoglobin, worse subjective and objective sleep quality, excessive daytime sleepiness, use of sleeping pills, depressive symptoms, and higher risk of both obstructive sleep apnea and hypertension.

RLS is frequently reported to occur with antidepressant use. It appears likely that the association between RLS and antidepressant use varies by gender and by type of antidepressant. Indeed, antidepressants were more strongly associated with RLS for men than for women in one study. But analyses of individual agents showed that fluoxetine was more strongly associated with RLS in women than in men, whereas use of paroxetine, citalopram, and amitriptyline was more likely to be associated with RLS symptoms in men.

Augmentation (worsening of symptoms despite treatment) occurs in a large percentage of patients treated with levodopa. Data on the prevalence of augmentation with dopamine agonists are still scant, but this phenomenon has been documented to occur with these agents. One study reported a prevalence rate of about 12% with dopamine agonists, with low ferritin being the primary associated risk. In that study, there were no gender differences in the rate of augmentation.

**Associative, Predisposing, and Precipitating Factors**

Two recent genome-wide association studies have reported positive association with sequence variants in or around specific genes on chromosomes 6p, 2p, and 15q and having symptoms of RLS (and periodic limb movements). Serum ferritin levels are lower in those with the genetic variant that predisposes to RLS, which supports the hypothesis that iron depletion or dysfunction is somehow involved in the pathogenesis of the disease. Dopamine deficiency or dysfunction is also in the pathophysiology of RLS, and one unifying hypothesis is that impairment of dopamine transport or function in the central nervous system due to reduced iron may contribute to the development of this disorder.

Primary RLS occurs without a known predisposing or exacerbating condition, is more likely to have earlier age of onset, and is likely to be familial. RLS can also be ‘secondary’ to another condition, including especially iron deficiency, pregnancy, and renal failure.

A large group of conditions has now been reported to be associated with RLS. Many of these conditions and disorders also lack objective diagnostic criteria, such as attention deficit hyperactivity disorder, depression, and fibromyalgia, and many occur with increased frequency in women.

**Complications and consequences**

Individuals with RLS are at increased risk for mood disturbance, according to cross-sectional studies. This is not necessarily a causal relationship; mood disturbance could contribute to endorsement of RLS symptoms. Like RLS, depression occurs with increased frequency in women compared to men and could partly account for the increased prevalence of RLS symptoms in women. The effects of RLS symptoms on daytime function are not clear. RLS has variously been reported to be associated with daytime sleepiness as well as not to impair daytime sleepiness and alertness. It does, however, appear to adversely affect quality and quantity of nocturnal sleep. RLS appears to be associated with many significant medical conditions and may be a marker for poor overall health. Indeed, one study has reported an increased risk of death in individuals with RLS.

**Management**

**Nonpharmacologic treatment**

Elimination of factors that may cause or contribute to RLS may make a difference. Several medications have been linked to both RLS and periodic limb movements, and the data are particularly strong for the association between RLS and antidepressants. Lifestyle relates to RLS symptoms: increased

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**Table 1** Diagnostic criteria for RLS in adults

| A. | The patient reports an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs. |
| B. | The urge to move or the unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting. |
| C. | The urge to move or the unpleasant sensations are partially or totally relieved by movement, such as walking and stretching, or at least as long as the activity continues. |
| D. | The urge to move or the unpleasant sensations are worse, or only occur, in the evening or night. |
| E. | The condition is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder. |

weight, caffeine intake, and smoking have been associated with increased likelihood of endorsing RLS symptoms. RLS is also associated with earning a lower income, sedentary lifestyle, and reduced alcohol consumption. Nonpharmacologic measures therefore should include education, moderate exercise, smoking cessation, caffeine reduction or elimination, and discontinuation of exacerbating medications if it is safe to do so. Some have found that working at night and sleeping in the day has helped. Iron supplementation should be given to those who are iron deficient.

**Pharmacologic treatment**

Dopamine receptor agonists are the first-line treatment and are the only agents that are Food and Drug Administration (FDA)-approved for RLS. The two dopamine receptor agonists available for this purpose in the United States are ropinirole and pramipexole; both are FDA-approved. Pramipexole is renally excreted, and the dose is 0.125–0.75 mg day\(^{-1}\) in single or divided doses, averaging 0.25 mg day\(^{-1}\). Ropinirole is hepati- 

cally excreted, and the effective dose is in the range of 1.5–6 mg day\(^{-1}\) in single or divided doses, averaging about 2 mg day\(^{-1}\). The main side effects of these agents are nausea, vomiting, orthostasis, dizziness, sleepiness, insomnia, and compulsive behavior. Because of delays in absorption, these agents work best if given at least an hour before symptom onset typically occurs.

Use of other agents is off-label and not clearly supported by the literature. As mentioned, RLS is a particular issue in pregnancy. None of the medications commonly used to treat RLS is safe in pregnancy. For pregnant women, folic acid has been reported to improve symptoms in those who are folate deficient. Iron replacement may also reduce or eliminate symp-

toms in patients who have serum ferritin levels below 45 \(\mu\)g/l. Recently, pneumatic compression devices have been shown to relieve symptoms in a randomized, double-blinded, sham-controlled trial.

One consideration in the pharmacologic treatment of RLS is the rather large placebo effect, which has been reported to be about 40%. Another consideration in the pharmacologic management of RLS is the appearance of augmentation. The International Restless Legs Study Group has established diagnostic standards for the dopaminergic augmentation of RLS, based on usual time of RLS symptom onset each day, number of body parts with RLS symptoms, latency to symptoms at rest, severity of the symptoms, time of occurrence, and effects of dopami-

nergic medication on symptoms. In brief, augmentation may be said to have occurred if the symptoms have spread to other body parts (e.g., from calves to thighs), occur earlier in the evening than originally, or increase in severity. Augmenta-

tion occurs frequently with the (off-label) regular use of carbidopa; it also occurs, but much less frequently, with ropinirole and pramipexole. Evidence-based recommendations for management of augmentation are lacking, but some suggested strategies are to take the dose earlier in the day and split the existing dose into early evening and bedtime doses. Augmenta-

tion and progression of the disease are difficult, if not impossible, to distinguish. This, coupled with the large placebo effect associated with any treatment for this condition, results in the lack of a clear-cut approach to the management of augmentation.

**Periodic Limb Movements**

RLS and periodic limb movements frequently coexist, which has resulted in much confusion about periodic limb movements. Periodic limb movements of sleep (PLMS), originally called nocturnal myoclonus, are rhythmical kicking of the lower extremities. They increase with age and are most commonly identified in association with other sleep disorders. While an overwhelming majority (>80%) of RLS patients have periodic limb movements, only a fraction of those individuals who have limb movements during sleep have RLS. PLMS have also been included in the obstructive sleep apnea hypopnea syndrome (see Figure 1), the upper airway resistance syndrome, narcolepsy, and REM sleep behavior disorder. PLMS are also frequently seen in patients who are taking antidepressants and probably represent a serotonergic phenomenon. When patients with complaints of insomnia or hypersomnia have PLMS and no other sleep disorder or relevant (e.g., antidepressant) medication use is present, they may be diagnosed with periodic limb movement disorder (PLMD). Such patients are probably rare. Patients with PLMS associated with RLS symptoms should be treated for RLS, but there is no evidence to support pharmacologic treatment of PLMS/PLMD, and there is no agent FDA-approved for this indication. The revised diagnostic criteria for PLMD take into account the coexistence of leg jerks with many medical conditions and medications, and also ‘raise the bar’ for the ‘abnormal’ number of periodic limb movements from 5 to 15 for adults (Table 2).

**Gender Differences in Periodic Limb Movements**

Women may be more likely to have periodic limb movements than are men because they are more likely to be diagnosed with depression and to be taking antidepressants. In addition, they are more likely to have subtle or occult sleep-disordered breathing (e.g., upper airways resistance syndrome) than are men, and the resulting arousal-associated leg jerks may be misdiagnosed as PLMD.

**Bruxism**

Sleep-related bruxism is characterized by repetitive clenching or grinding of the teeth during sleep. The primary consequences of this are tooth wear and jaw pain. Bruxism probably has a prevalence of about 15% and is highest in childhood. Bruxism tends to occur in families. Anecdotally, bruxism is thought to be associated with anxiety, stress, tooth malocclusion, or a side effect of medications such as antidepressants. It has also been reported with sleep apnea, Huntington’s disease, and Parkinson’s disease. Use of splints or tooth guards, made by a dentist, is the most common form of treatment, but behavioral therapy, biofeedback, botulinum toxin, and correction of misaligned teeth may also be effective.

There are no reported gender differences in the prevalence, manifestations, or treatment of bruxism.
Other Sleep-Related Movement Disorders

Other sleep-related movement disorders include leg cramps and movement disorders due to drugs or medical conditions. Data about gender differences in these conditions are lacking.

### Table 2 Diagnostic Criteria for Periodic Limb Movement Disorder

<table>
<thead>
<tr>
<th>A. Polysomnography demonstrates repetitive, highly stereotyped, limb movements that are:</th>
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</thead>
<tbody>
<tr>
<td>1. 0.5–5 s</td>
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<tr>
<td>2. Of amplitude &gt;25% of toe dorsiflexion during calibration</td>
</tr>
<tr>
<td>3. In a sequence of four or more movements</td>
</tr>
<tr>
<td>4. Separated by an interval of more than 5 s (from limb-movement onset) and less than 90 s (typically an interval of 20–40 s)</td>
</tr>
</tbody>
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| B. The PLMS index exceeds 5 per hour in children and 15 per hour in most adult cases |
| C. There is clinical sleep disturbance or a complaint of daytime fatigue |
| D. The PLMS are not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or a substance use disorder |

Note: If PLMS are present without clinical sleep disturbance, the PLMS can be noted as a polysomnographic finding, but criteria are not met for a diagnosis of PLMD.


### Further Reading


Relevant Websites
http://www.cdc.gov/sleep/ — The Center for Disease Control’s Public Education site for sleep and its disorders.


http://www.rls.org — The Restless Legs Syndrome Foundation Website.