# Part 13

# Systems Disorders

# Sleep Disorders

# 83

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| Abbreviations | |
|---|---|
| AASM | American Academy of Sleep Medicine |
| AHI | Apnea/hypopnea index |
| CRSD ASP | Circadian rhythm sleep disorders, advanced sleep phase type |
| CRSD DSP | Circadian rhythm sleep disorders, delayed sleep phase type |
| CRSD | Circadian rhythm sleep disorders |
| CSA | Central sleep apnea |
| CSF | Cerebrospinal fluid |
| EDS | Excessive daytime sleepiness |
| EEG | Electroencephalography |
| EMG | Electromyography |
| GABA | Hypothalamic γ-aminobutyric acid |
| HLA | Human leukocyte antigen |
| KLS | Kleine-Levin syndrome |
| MSLT | Mean sleep latency test |
| NREM | Nonrapid eye movement |
| OSA | Obstructive sleep apnea |
| $PaCO_2$ | Arterial carbon dioxide tension |
| PET | Positron emission tomography |
| PLMD | Periodic limb movement disorder |
| PLMS | Periodic limb movement in sleep |
| PSG | Polysomnograph |

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| | |
|---|---|
| PTSD | Posttraumatic stress disorder |
| RBD | Rapid eye movement sleep behavior disorder |
| REM | Rapid eye movement |
| RLS | Restless legs syndrome |
| SOREMP | Sleep-onset rapid eye movement period |
| SWS | Slow-wave sleep |
| VLPO | Ventrolateral preoptic |

## Brief History

This chapter describes the major classes of sleep disorders in the adult population. There are medical conditions and an extensive list of medications and substances that may lead to any of the following sleep disorders. Refer to the suggested reading list for details on pediatric sleep disorders; sleep disorders due to medical condition, medication, or substance use; as well as the treatment of sleep disorders.

## History of Sleep Medicine

A basic understanding of sleep disorders was known in ancient times, but specific sleep disorders, such as narcolepsy, began to be recognized only in the late nineteenth century. Differentiation between causes of sleepiness and insomnia and the recognition of abnormal events that occur during sleep has reached a peak within the last 50 years since the development of sophisticated technology for the investigation of sleep.

Sleep research resulted in the establishment in the early 1970s of clinical sleep disorder centers for the diagnosis and treatment of patients. In 1976, the first sleep disorder center was established at Stanford University in California by William Dement M.D. An accreditation process for sleep disorders centers was established and the first to be accredited in 1977 was the Sleep-Wake Disorders Unit, headed by Elliot Weitzman M.D., at Montefiore Medical Center in New York.

The American Academy of Sleep Medicine (AASM), the profession's clinical association, produces the scientific medical journal SLEEP, created to present research and clinical articles on sleep. In 1979, a complete issue of SLEEP was devoted to the first modern diagnostic classification of sleep and arousal disorders. Through international cooperation, The International Classification of Sleep Disorders manual was produced in 1990.

Clinicians trained in sleep medicine in the USA were first able to take a certification examination in 1978 developed by the AASM, and in 2005, a fellowship training program was approved by the American College of Graduate Medical Education for eligibility to take a board certification examination in sleep medicine. This examination of the Board on Internal Medicine is open to physicians who have been board-certified by one of the specialty boards of the American Board of Psychiatry and Neurology, the Board of Internal Medicine,

the American Board of Pediatrics, American Academy of Family Physicians, or the American Board of Otolaryngology. The first examination was held in 2007. A board examination was also developed in behavioral sleep medicine in 2003 for clinicians, mainly psychologists, but also physicians.

The practice of sleep medicine and sleep research has rapidly expanded around the world with most countries now having professional associations and specialized centers for the evaluation, diagnosis, and treatment of sleep disorders.

## Insomnia

Insomnia is one of the most frequent sleep complaints and is defined as a repeated difficulty with sleep initiation, maintenance, duration, or subjective quality that occurs despite adequate time and opportunity for sleep and results in some form of daytime impairment. Population surveys estimate one third of all adults have one or more episodes each year. Insomnia complaints typically include difficulty initiating and/or maintaining sleep, and extended periods of nocturnal wakefulness and/or insufficient amounts of nocturnal sleep usually accompany these complaints. Occasionally, insomnia complaints are characterized by the perception of poor-quality or "nonrestorative" sleep, even when the amount and quality of the usual sleep episode is perceived to be "normal" or adequate. In addition to nighttime restlessness, insomnia also leads to daytime sequelae, including depressed mood, anxiety, daytime fatigue, irritability, reduced concentration, and memory complaints. Daytime functioning impairment often results in low quality of life and difficulty with relationships and work.

In the US population, the prevalence of insomnia is 10–15%. Women are 1.4 times more likely than men to report insomnia, and the prevalence of insomnia is also greater in the elderly population and in patients with chronic medical conditions. Psychiatric illnesses are more highly associated with insomnia than any other medical disorder, and epidemiologic studies of the general population show that one third to one half of the patients with insomnia meet the criteria for primary psychiatric disorders, especially mood and anxiety disorders.

Insomnia is often divided into transient insomnia lasting less than 1 week, short-term insomnia lasting 1–4 weeks, and chronic insomnia lasting more than 1 month. Chronic insomnia can be divided into two types: primary or secondary. Primary insomnia is insomnia that can have both intrinsic and extrinsic factors involved in the etiology, but primary insomnia is not regarded as being secondary to other disorders. Secondary insomnia can occur when insomnia is a symptom of a medical or psychiatric illness, other sleep disorders, or substance abuse. In recent years, a new term, "comorbid insomnia," has been recommended. This term was introduced due to the inability to draw firm conclusions about the nature of the secondary associations or the direction of causality in secondary insomnia. In addition, the use of the term "secondary" was believed to trivialize the importance of comorbid insomnia and potentially promote undertreatment. Comorbid insomnia is the most prevalent form of chronic insomnia.

There are three subtypes of adult primary insomnia.

## Psychophysiologic Insomnia

Psychophysiologic insomnia is a common form of insomnia that is present for at least 1 month and characterized by a heightened level of arousal with learned sleep-preventing associations. There is an overconcern with the inability to sleep. Patients associate the bedroom with arousal rather than sleep, and attempts at sleep are met with increased mental arousal and somatic tension. Often, the condition arises from a period of acute stress-related insomnia with the precipitant factors resolving but the sleeplessness persisting. Paradoxical insomnia is a complaint of severe insomnia that occurs without evidence of objective sleep disturbance and without daytime impairment of the extent that would be suggested by the amount of sleep disturbance reported. The patient often reports little or no sleep on most nights, despite polysomnography (PSG) or wrist actigraphy that demonstrates relatively normal sleep. It is thought to occur in up to 5% of insomnia patients. Idiopathic insomnia is a long-standing form of insomnia that appears to date from childhood and has an insidious onset. Typically, there are no factors associated with the onset of the insomnia, which is persistent without periods of remission.

## Secondary Insomnia

Secondary or comorbid insomnia has five major subtypes. Adjustment sleep disorder is insomnia that is associated with a specific stressor. The stressor can be psychological, physiologic, environmental, or physical. This disorder exists for a short period of time, usually days to weeks, and usually resolves when the stressor is no longer present. Insomnia due to a mental disorder is insomnia caused by an underlying psychiatric disorder, such as mood, anxiety, or somatoform disorders. The insomnia typically begins with the onset of the causative mental disorder and waxes and wanes in unison with the other symptoms of this condition. Insomnia due to mental disorder is diagnosed only when insomnia is a predominant, or at least severe enough, complaint to warrant independent clinical attention.

## Inadequate Sleep Hygiene

Inadequate sleep hygiene is a disorder associated with common daily activities that are inconsistent with good-quality sleep and full daytime alertness. Such activities include irregular sleep onset and wake times; stimulating and alerting activities before bedtime; substances ingested around sleep, including alcohol or caffeine; and smoking cigarettes. Insomnia due to a drug or substance is diagnosed when there is dependence on or excessive use of a substance such as alcohol,

a recreational drug, or caffeine that is associated with the occurrence of the insomnia. Caffeine ingestion in the form of coffee or soda can produce a disorder of inadequate sleep hygiene if the intake is normal and within the limits of common use but the timing of ingestion is inappropriate, whereas caffeine ingestion that is considered excessive or abnormal by normal standards can lead to a diagnosis of insomnia due to a drug or substance.

The most accepted model for primary insomnia postulates a state of physiologic hyperarousal. In comparison with control subjects, patients with insomnia have an increased 24-h metabolic rate, increased secretion of adrenocorticotropic hormone and cortisol, increased electroencephalographic (EEG) fast activity and reduced theta and delta activity during sleep, and increased cerebral glucose metabolism on positron emission tomography (PET) scans both while awake and asleep. It has been suggested that wake-sleep transition may be explained by the presence of a neuronal circuit consisting of two mutually inhibitory elements. The hypothalamic γ-aminobutyric acid (GABA)-ergic ventrolateral preoptic (VLPO) nucleus is the major generator of NREM sleep, while monoaminergic ascending neurons in the pontine tegmentum cause arousal. These two systems mutually inhibit each other, resulting in a flip-flop switch. One might postulate that primary insomnia is caused by switch failure. Excessive sympathetic activity would manifest as stimulation of monoaminergic neurons resulting in inhibition of the VLPO nucleus at a time when the switch would normally be changing from wake to sleep. Reduced discharge of VLPO neurons would in turn disinhibit the monoaminergic neurons, further perpetuating the pathologic arousal state.

From a psychophysiologic point of view, chronic insomnia may be explained by the popularized "3P" model. In this model, *predisposing* factors (presumably genetic traits) provide the soil for the later development of insomnia. *Precipitating* factors, such as life stressors, initiate the process, while *perpetuating* factors in the form of maladaptive coping responses cause insomnia to persist.

The diagnosis of insomnia is achieved largely by taking a careful history of sleep and wakefulness. This should include a detailed account of the patient's night and day with special emphasis on periods of sleeplessness, the perceived causes, and the patient's responses. Psychosocial factors, medication and substance use, physical illnesses, occupation, and degree of exercise should all be determined. In addition, asking a patient to keep a sleep log for 7–14 days is very helpful and presents an in-depth view of the patient's sleep pattern. In selected cases where paradoxical insomnia is suspected, this can be confirmed objectively by having the patient wear a wrist actigraphy monitor, which records body movement as a surrogate marker of wake and sleep. Overnight PSG in a sleep laboratory is rarely required to establish the diagnosis of insomnia unless paradoxical insomnia, sleep-disordered breathing, or periodic limb movement disorder is suspected or the patient has failed to respond to conventional therapies.

**Table 83.1** Obstructive versus central apnea

| Obstructive apnea | Central apnea |
|---|---|
| *Weight* | |
| Commonly obese | Normal to obese |
| *Clinical presentation* | |
| Daytime sleepiness | Daytime sleepiness |
| Prominent snoring | Mild snoring |
| Witnessed apnea or gasping | Frequent awakenings |
| | Insomnia |
| *PSG findings* | |
| No airflow resulting in apnea | No airflow resulting in apnea |
| Obvious ventilatory effort present | No ventilatory effort |

## Sleep-Related Breathing Disorders

Sleep-related breathing disorders are a group of conditions characterized by disordered ventilation during sleep. The two major types are obstructive sleep apnea (OSA) syndrome and central sleep apnea (CSA) syndromes. While OSA syndrome describes a disorder of repeated mechanical obstruction of the airway, CSA syndromes are characterized by an absence of ventilatory effort (Table 83.1).

## Obstructive Sleep Apnea Syndrome

Adult OSA consists of repetitive episodes of complete (apnea) or partial (hypopnea) upper airway obstruction despite persistent respiratory effort occurring during sleep (Fig. 83.1). Based on PSG findings, apnea is defined as cessation of airflow for a minimum of 10 s with a reduction in blood oxygen saturation. Hypopnea is a 30–50% reduction in airflow for a minimum of 10 s with either polysomnographic arousal or a reduction in blood oxygen saturation of at least 4%. During either an apnea or a hypopnea episode, ventilatory effort should persist, as demonstrated by continued movement of the ribcage and abdomen.

Clinically, patients with OSA usually present with both nocturnal and daytime symptoms. Snoring between apneas is typically reported by bed partners, as are witnessed episodes of gasping or choking and frequent movements that disrupt sleep. Most patients awaken in the morning feeling tired and unrefreshed regardless of the duration of their time in bed. Consequently, excessive daytime sleepiness (EDS) becomes a major daytime complaint. With extreme sleepiness, the patient may fall asleep while conversing, eating, walking, or driving. Daytime symptoms also include headaches, impaired concentration, cognitive deficits, and increased irritability. As a result, the patient's quality of life can be adversely affected.

The diagnosis of OSA is established by PSG recording of five or more respiratory events (apneas or hypopneas) per hour with evidence of ventilatory effort during each respiratory event, plus at least one of the nocturnal or daytime symptoms described above. An apnea/hypopnea index (AHI: number of apnea or hypopnea events per

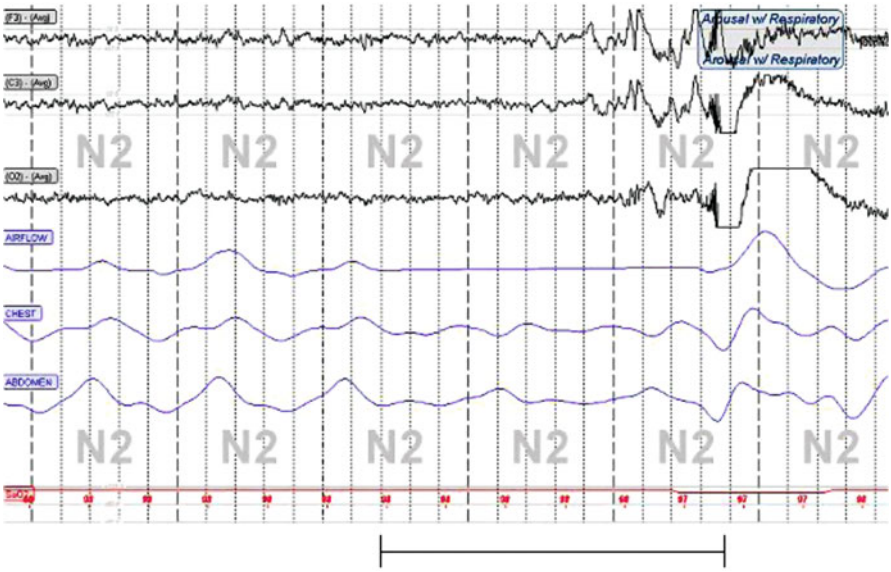


**Fig. 83.1** Obstructive sleep apnea. There is a 12-s cessation of airflow (bracket) with persistent chest and abdomen signals indicating persistent ventilatory effort

hour) of 5–15 is consistent with mild OSA, between 15 and 30 is moderate OSA, and greater than 30 is usually considered severe OSA. However, the AHI correlates poorly with the degree of sleep fragmentation and the severity of daytime symptoms; therefore, a thorough history intake is – as always – essential.

The pathophysiology underlying OSA is likely multifactorial. Patients with OSA have reduced cross-sectional area of the upper airway lumen due to either excessive bulk of soft tissues or craniofacial anatomy. Enlarged tonsils and adenoids, a long or edematous uvula, a large tongue base, and a limited space between the epiglottis and laryngeal vestibule can all contribute to limitation of airflow. Upper airway patency is dependent on pharyngeal dilating muscles, the activity of which decreases with sleep onset. There is a further reduction in tone and phasic activity of pharyngeal dilating muscles during rapid eye movement (REM) sleep, which likely contributes to apnea and hypopneas that are longer and more pronounced. Repetitive apneas and hypopneas lead to pressure changes that may lead to enlargement of upper airway tissues. The narrowing of the airway further exacerbates OSA. An increase in respiratory effort results in arousals, which occur repeatedly throughout the night, fragment sleep and lead to excessive daytime sleepiness.

Initially discovered in obese patients with Pickwickian syndrome (obesity-induced hypercapnia) in 1956, OSA has now been demonstrated in all age groups, regardless of the body habitus. Epidemiologic studies indicate that 2–5% of the population meets the criteria for OSA. Men are twice as likely to have sleep apnea as premenopausal women; however, the incidence in women increases after menopause. Obesity (body mass index greater than 30 $kg/m^2$) and increased age are two

of the greatest risk factors in OSA. Family history of OSA also plays a role, possibly due to similarities in craniofacial structure that may predispose the family members to upper airway collapse. Other risk factors for OSA include sleep deprivation, sleep in the supine position, smoking, the use of alcohol or sedatives, and certain ethnicities. African Americans and Asians have been shown to have a greater frequency of OSA than Caucasians.

Although OSA was only first recognized as a significant health problem in the 1970s, it is now known to be closely associated with many serious medical disorders. Most significantly, OSA is an independent risk factor for development of systemic hypertension. Patients with severe OSA may be at increased risk for developing pulmonary hypertension as well. Other medical disorders associated with OSA include diabetes mellitus, arrhythmias, coronary artery disease, and stroke. Finally, studies have found a two to three times greater risk of motor vehicle accidents in untreated patients with OSA. It appears that the presence of sleep apnea plus a history of a previous accident or frequent falling asleep at the wheel identifies a group of patients with especially high risk. Clearly, both medical and lifestyle issues that are known to increase the risk of complications associated with OSA should be addressed in detail with every patient.

## Central Sleep Apnea

In contrast to OSA, CSA syndromes are characterized by a lack of airflow and diminished or absent respiratory effort (Fig. 83.2). Before describing the individual syndromes, some basic knowledge of normal ventilatory control mechanisms should be explained to help appreciate the mechanism of CSA.

During wakefulness, signals from cortical areas of the brain influence ventilation, a process termed behavioral control. Many nonmetabolic stimuli, which include pulmonary mechanoreceptors and behavioral or awake stimulation, are known to modulate this phenomenon. During sleep, behavioral control is lost, and ventilation becomes critically dependent on the metabolic control system that regulates the pattern of breathing by processing information from various brain stem neurons and peripheral chemoreceptors, which in turn monitor the arterial carbon dioxide tension ($PaCO_2$). Sleep is characterized by elevation of $PaCO_2$ and a higher $PaCO_2$ apneic threshold, the $PaCO_2$ set point below which ventilation ceases. Reduction of $PaCO_2$ just a few mm Hg below the $PaCO_2$ apneic threshold can result in apneas. Central apnea events commonly occur during the transition between wake and sleep, a period during which the $PaCO_2$ set point is undergoing frequent adjustments. This is often observed in normal individuals but, once a stable sleep stage is reached, ventilation should become regular under stable metabolic control.

CSA syndromes can be broken down into the idiopathic form and those with defined underlying pathologic or environmental causes, such as Cheyne-Stokes breathing pattern or high-altitude periodic breathing. The idiopathic form is termed primary CSA, which is characterized on PSG by recurrent cessation and resumption

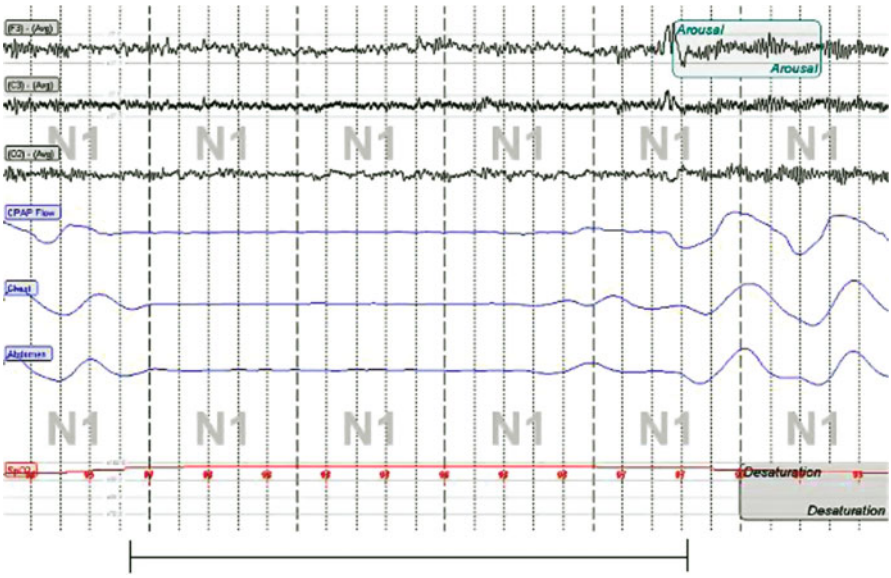


**Fig. 83.2** Central sleep apnea. There is a 20-s cessation of airflow (bracket) with no chest and abdomen signals indicating absence of ventilatory effort

of ventilation during sleep with the apnea having no associated ventilatory effort. This often leads to sleep fragmentation, EDS, or insomnia.

In comparison to normal individuals, patients with primary CSA tend to have an elevated ventilatory responsiveness to $CO_2$. They hyperventilate more in response to small increases in arterial $PaCO_2$, consequently driving the $PaCO_2$ below the apneic threshold and producing unstable ventilation. Recurrent apneas are propagated because arousals at the termination of apneas cause an abrupt lowering of the apneic threshold. At the same time, reinstitution of the wakefulness drive (behavioral control) to breathe stimulates hyperventilation, causing ventilatory overshoot and a resultant fall in the $PaCO_2$ below the apneic threshold.

CSA due to Cheyne-Stokes breathing pattern is characterized by recurrent apneas and/or hypopneas alternating with prolonged hyperpneas in which ventilation waxes and wanes in a crescendo-decrescendo pattern. At least ten cycles of apneas and hyperpneas per hour of sleep are required for diagnosis. This recurrent cessation of breathing leads to repetitive hypoxic dips which, combined with the effort of breathing upon resumption of respiration, can result in sleep fragmentation and frequent wake-sleep state changes. Clinically, patients may present with EDS, insomnia, or episodic nocturnal dyspnea.

Cheyne-Stokes breathing pattern typically occurs at the transition from wakefulness to NREM sleep and during stages 1 and 2 of NREM sleep. It tends to disappear in NREM stage 3 and in REM sleep. The hallmark crescendo-decrescendo pattern of breathing may result from prolonged lung-to-chemoreceptor

circulatory delay such that changes in $PaCO_2$ in the lungs are transmitted very slowly to the chemoreceptors, resulting in a gradual buildup and fall off ventilatory stimulation. The length of the cycle is directly proportional to lung-to-chemoreceptor circulation time and inversely proportional to cardiac output. Accordingly, Cheyne-Stokes breathing pattern is most frequently observed after the development of congestive heart failure, with a prevalence rate of 25–40%. Male sex, age older than 60 years, and the presence of atrial fibrillation are all risk factors for developing Cheyne-Stokes breathing pattern during sleep. In turn, this pattern of breathing is associated with a poor prognosis within the heart failure population, as indicated by an increased frequency of cardiac transplantation and risk of death independent of other known risk factors. Cheyne-Stokes breathing pattern is also seen in patients with cerebrovascular disorders or renal failure, but its clinical significance in those settings remains uncertain.

CSA due to high-altitude periodic breathing is characterized by cycling periods of apnea and hyperpnea with the apnea being associated with no ventilatory effort. The cycle length is typically between 12 and 34 s. Like primary CSA, five or more central apneas per hour of sleep are required to make the diagnosis. While virtually everyone will demonstrate this ventilatory pattern at elevations greater than 7,600 m, some may develop it at altitude just higher than 4,000 m.

High-altitude periodic breathing is believed to be a product of the hyperventilation induced by the hypoxia encountered at altitude. Individuals with brisk hypoxic responses are more likely to demonstrate this breathing pattern. Over the course of the apnea, the arterial oxygen tension ($PaO_2$) falls and $PaCO_2$ rises, eventually stimulating a resumption of ventilation. However, after several large breaths, the $PaCO_2$ again falls below the apnea threshold, initiating another pause in breathing. This cycle is repeated over the course of the night. Similar to primary CSA and CSA due to Cheyne-Stokes breathing pattern, the ventilatory pattern is often improved during REM sleep. This is likely due to the decreased hypoxic and hypercapnic responsiveness characteristic of REM sleep.

High-altitude periodic breathing is present most often on the first night after ascent to altitude. The major complication is frequent awakenings, often with shortness of breath or suffocation, that may lead to fatigue or sleepiness the following day. There is no clear association between high-altitude periodic breathing and other altitude syndromes. In fact, periodic breathing is a marker of high hypoxic responsiveness, which generally yields improved oxygenation at altitude and a reduced frequency of the maladaptive syndromes.

## Hypersomnias of Central Origin

Excessive daytime sleepiness (EDS) predisposes an individual to developing serious performance decrements in multiple areas of social function, as well as to potentially life-threatening domestic, work-related, and driving accidents. The hypersomnia disorders are those in which EDS is the primary complaint and the

cause is not disturbed nocturnal sleep or misaligned circadian rhythms. The three major types of hypersomnias are narcolepsy (with or without cataplexy), idiopathic hypersomnia (with or without long sleep time), and recurrent hypersomnia.

## Narcolepsy

First described in 1880 by French physician Jean Gelineau, narcolepsy is a neurologic disorder associated with EDS, sleep fragmentation, and REM sleep-related phenomena such as hypnagogic hallucinations (visual or auditory hallucination that occur at sleep onset), sleep paralysis (muscle paralysis that occurs upon awakening from sleep), and cataplexy. Considered the most specific symptom of narcolepsy, cataplexy is characterized by a sudden loss of bilateral muscle tone provoked by strong emotions that are usually positive, such as laughter, pride, elation, or surprise. Negative emotions such as anger may also occasionally be a trigger. The loss of muscle tone ranges from a mild sensation of weakness – with head drop, facial sagging, jaw weakness, slurred speech, and buckling of the knees – to complete postural collapse. The diaphragm and ocular muscles are unaffected. During a cataplexy attack, which may range from a few seconds to several minutes, the patients remain awake, aware of their surroundings, and able to remember the details of the event although they may fall asleep if the attack is prolonged.

Narcolepsy is a relatively rare disorder, affecting approximately 1 in 2,000 people in the USA. It affects men and women equally, but its prevalence varies between different ethnicities, from a low of 0.002% among Israeli Jews to a high of 0.15% among the Japanese. Disease onset can begin in infancy or as late as old age, but most commonly before age 25, and usually in the first two decades of life. The prevalence of cataplexy among patients with narcolepsy varies widely, with estimates ranging from 60% to 90%.

Most cases of narcolepsy with cataplexy are associated with an 85–95% loss in hypothalamic neurons containing the neuropeptide hypocretin, which is believed to increase muscle tone through activation of a motor facilitatory system in the brainstem. In the absence of sufficient levels of hypocretin, the motor facilitatory system is inhibited and results in decreased muscle tone and symptoms of cataplexy. The lack of hypocretin can be assessed by measuring the level in the cerebral spinal fluid (CSF). Using this test, approximately 90% of patients with narcolepsy with cataplexy have dramatically decreased CSF level of hypocretin. In addition, the histocompatability antigen human leukocyte antigen (HLA) DQB1*0602 is positive in approximately 85% of patients with narcolepsy with cataplexy, prompting the hypothesis that the cause of most cases is an autoimmune destruction of hypocretin cells that generally occurs during adolescence.

The cause of most cases of narcolepsy without cataplexy is unknown. A minority of patients have been found to have decreased CSF levels of hypocretin or increased HLA DQB1*0602 positivity. In most cases, however, the CSF hypocretin is normal.

Narcolepsy with cataplexy requires the documentation of a definite history of cataplexy. This diagnosis may be confirmed by nocturnal PSG followed by a multiple

**Table 83.2** Diagnostic criteria for narcolepsy and idiopathic hypersomnia

| Condition | Narcolepsy with cataplexy | Narcolepsy without cataplexy | Idiopathic hypersomnia with long sleep time | Idiopathic hypersomnia without long sleep time |
|---|---|---|---|---|
| Symptoms | EDS, definitive history of cataplexy | EDS, no definitive history of cataplexy | EDS, nocturnal sleep time >10 h | EDS, nocturnal sleep time >6 h and <10 h |
| Duration | ≥3 months | ≥3 months | ≥3 months | ≥3 months |
| PSG results | Sleep latency <10 min, SOREMP, sleep fragmentation | Sleep latency <10 min, SOREMP, sleep fragmentation | Sleep period >10 h | Sleep period >6 h and <10 h |
| MSLT results | Sleep latency ≤8 min and ≥2 SOREMPs, or CSF hypocretin <110 pg/ml | Sleep latency ≤8 min and ≥2 SOREMPs | Sleep latency <8 min and <2 SOREMPs | Sleep latency >6 h and <10 h |

sleep latency test (MSLT). The MSLT is a series of four to five 20-min nap opportunities, under conditions conductive to sleep, in which latency to sleep is recorded. Comparing with normal individuals, patients with narcolepsy with cataplexy will have a mean sleep latency of ≤8 min and two or more sleep-onset REM periods (SOREMPs). Alternatively, CSF hypocretin levels of ≤110 pg/ml can be used as supportive evidence. A diagnosis of narcolepsy without cataplexy is made when cataplexy is not present but when there is sleep paralysis, hypnagogic hallucinations, and supportive evidence in the form of a positive MSLT.

## Idiopathic Hypersomnia

Idiopathic hypersomnia with long sleep time is characterized by constant and severe excessive sleepiness with prolonged but unrefreshing naps of up to 3 or 4 h, a prolonged major sleep episode of at least 10 h with few or no awakenings, and great difficulty waking up in the morning or at the end of a nap. In contrast, idiopathic hypersomnia without long sleep time has very similar complaints but with either normal or slightly prolonged (less than 10 h) of nighttime sleep episode. In both disorders, post-awakening confusion is often reported. Other commonly associated symptoms include headaches, orthostatic hypotension, and peripheral vascular complaints (e.g., cold hands and feet). Onset of symptoms usually occurs before 25 years of age. Once established, the disorder is stable in severity and long lasting, although spontaneous improvement has been reported in a few subjects. Complications are mostly social and professional, including poor work or school performance. In both disorders, the excessive sleepiness should not be better explained by another sleep, medical, mental, or neurological disorder, or medication or substance use disorder. Table 83.2 lists the diagnostic criteria for narcolepsy and idiopathic hypersomnia.

## Recurrent Hypersomnia

Recurrent hypersomnia consists of two subtypes: Kleine-Levin syndrome (KLS) and menstrual-related hypersomnia. KLS is a rare condition in which prolonged episodes of excessive sleepiness are separated by periods of normal alertness and function. During an episode, patients may sleep as long as 16–18 h per day, getting up only to eat and void. Episodes usually last a few days to several weeks and appear one to ten times a year. Associated cognitive or behavioral abnormalities may occur, including confusion, hallucination, binge eating, hypersexuality, or mood changes. Complications are mainly social and occupational. Amnesia, transient dysphoria, or elation with insomnia may signal the termination of an episode. Between episodes, the patient is completely normal with regular behavior and sleep pattern.

In KLS, the usual age of onset is early adolescence, with a male to female ratio of approximately 4:1. The course of disease is typically benign, with episodes lessening in duration severity and frequency over 1 to several years. No specific etiology has been established for KLS, but intermittent hypothalamic dysfunction or autoimmune etiologies have been postulated.

Menstrual-related hypersomnia is characterized by episodic sleepiness that coincides with the menstrual cycle. The condition occurs within the first months after menarche. Episodes generally last 1 week, with rapid resolution at the time of menses. Hormone imbalance may be an explanation for the hypersomnia since oral contraceptives will usually lead to prolonged remission.

## Circadian Rhythm Sleep Disorder

Circadian (from the Latin for *about a day*) rhythms are present in almost all eukaryotic organisms from single-celled algae to humans. It is an internal timing system that allows animals to keep time in the absence of external environmental cues, the strongest of which is light. From an evolutionary point of view, circadian rhythms are crucial in allowing animals to anticipate and synchronize brain and body functions so they occur at optimal times with the external world. Many physiologic variables demonstrate endogenous circadian rhythms, including heart rate, blood pressure, blood glucose levels, hormone secretion, brain metabolism, psychomotor performance, and, of course, sleep propensity.

For optimal sleep, the desired sleep time should match the timing of the circadian rhythm of sleep and wake propensity. In circadian rhythm sleep disorders (CRSDs), there is a persistent or recurrent misalignment between the patient's sleep pattern and the pattern that is desired or regarded as the societal norm. The patient cannot sleep when sleep is needed or expected. The wake episodes can occur at undesired times as a result of sleep episodes that occur at inappropriate times; therefore, the patient may complain of insomnia or excessive sleepiness. While the exact pathophysiology of CRSD is unknown, there is almost certainly an abnormal interaction between the endogenous circadian rhythm and the sleep homeostatic process that regulates sleep and wakefulness.

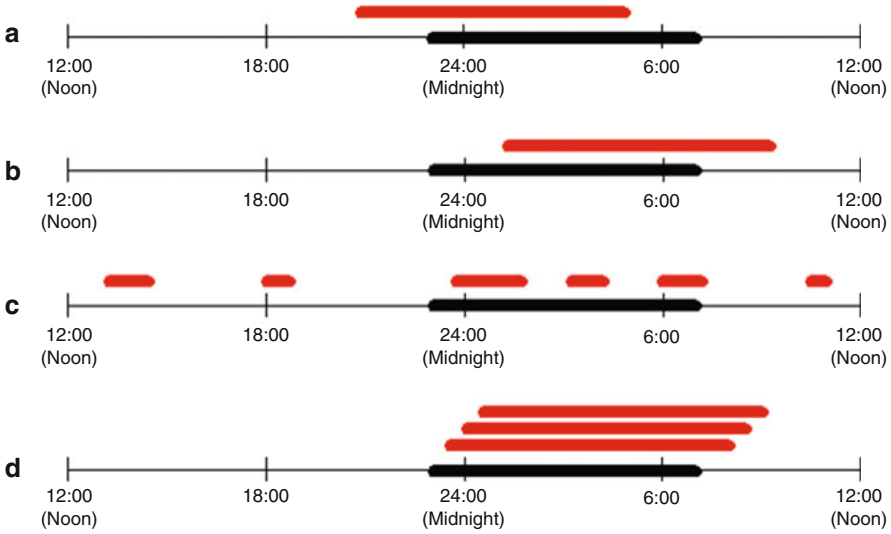


**Fig. 83.3** Schematic representation of the four major types of circadian rhythm sleep disorders. (**a**) Advanced sleep phase type. (**b**) Delayed sleep phase type. (**c**) Irregular sleep-wake type. (**d**) Free-running type. *Black bars* represent a typical sleep time (11:00 PM–7:00 AM) and red bars represent sleep times of different disorders

There are six major types of circadian rhythm sleep disorder, all of which share the following general criteria. The presentation and severity of each condition can be influenced by physiological and environmental factors, as well as maladaptive behaviors.

## General Diagnostic Criteria for CRSD

1. There is a persistent or recurrent pattern of sleep disturbance due to one of the following:
   (a) Alterations of the circadian timekeeping system
   (b) Misalignment between the endogenous circadian rhythm and exogenous factors that affect the timing or duration of sleep
2. The circadian-related sleep disruption leads to insomnia, EDS, or both.
3. The sleep disturbance is associated with impairment of social, occupational, or other areas of functioning.

### Advanced Sleep Phase Type

CRSD, advanced sleep phase type (ASP, Fig. 83.3a), is a chronic condition characterized by habitual sleep onset and wake-up times that are several hours earlier relative to conventional times. Patients usually complain of sleepiness in the late afternoon or early evening, early sleep onset, and spontaneous early morning

awakening. Attempts to stay asleep during the early morning hours may result in the development of secondary conditioned insomnia. When patients are allowed to choose their preferred schedule, sleep quality and duration are normal with an advanced, but stable, circadian phase of sleep. The prevalence of ASP is about 1% in middle-aged and older adults and increases with age. Although treatment such as behavioral approaches and bright light can delay the timing of sleep, there is usually a continual tendency and preference for earlier sleep hours.

### Delayed Sleep Phase Type

CRSD, delayed sleep phase type (DSP, Fig. 83.3b) is characterized by habitual sleep-wake times that are delayed, usually more than 2 h, relative to conventional times. A typical patient has difficulty initiating sleep and prefers late wake-up times. When allowed to follow his or her preferred schedule, the patient's circadian phase of sleep is delayed but otherwise relatively stable. Environmental factors, including decreased exposure to light in the morning or exposure to bright light late in the evening, may exacerbate the delayed circadian phase. Maladjustment to changes in work and social schedules, travel across time zones, and shift work can precipitate this disorder. The use of caffeine and other stimulants may further delay sleep onset and exacerbate the delayed sleep time. DSP is more common among adolescents and young adults, with a reported prevalence of 7–16%. Without treatment, DSP is a chronic condition that lasts into late life. However, with increasing age, the timing of the sleep-wake cycle may advance, thereby decreasing the phase delay.

### Irregular Sleep-Wake Type

CRSD, irregular sleep-wake type (Fig. 83.3c), is characterized by lack of a clearly defined circadian rhythm of sleep and wakefulness. Napping is prevalent, and sleep log or actigraphy monitoring demonstrates multiple irregular sleep bouts during a 24-h period. Total sleep time, however, is essentially normal for age. Patients may have symptoms of insomnia or excessive sleepiness, depending on the time of day. Irregular sleep-wake type is most often seen in the institutionalized elderly and is associated with a lack of synchronizing agents such as light, activity, and social activities.

### Free Running Type

The intrinsic period of the human circadian pacemaker is usually longer than 24 h and requires regular input from the environment to maintain synchrony to the 24-h day. In CRSD, free-running type (Fig. 83.3d), there is a lack of entrainment to the 24-h period and a sleep pattern that relies solely on the longer-than-24-h endogenous circadian pacemaker. Sleep log or actigraphy monitoring demonstrates sleep and wake times that typically delay with each day, resulting in a sequential shift in the sleep pattern. Because the light-dark cycle is the most important environmental time cue, a lack of photic input to the circadian pacemaker will most likely produce the free-running rhythm. Hence, most patients with free-running type are completely blind, and it is thought that over 50% of the completely blind population

has this condition. Onset may occur at any age, and in congenitally blind children, onset can occur at birth. Patients usually present with insomnia or excessive sleepiness. If left untreated, the course is chronic.

### Jet Lag Type

CRSD, jet lag type, is a temporary condition in which there is a mismatch between the timing of the sleep-wake cycle generated by the endogenous circadian clock and the common sleep-wake schedule of the new time zone. The desynchronization and consequent sleep loss can lead to decreased alertness and impaired daytime function. Associated symptoms may include general malaise and gastrointestinal symptoms. The duration and severity of symptoms are usually in proportion to the number of time zones traveled and the direction of travel. It is estimated that it takes 1 day per time zone for circadian rhythms to adjust to the local time. However, if traveling more than six time zones, circadian rhythms may shift in the opposite direction of the direction of travel, resulting in prolonged duration and severity of symptoms. In addition, eastward travel (requiring advancing circadian rhythms and sleep-wake hours) is usually more difficult to adjust than westward travel. Finally, while jet lag type affects all age groups, symptoms may be more pronounced in the elderly, and the rate of recovery may be more prolonged.

### Shift Work Type

CRSD, shift work type, is characterized by complaints of insomnia or excessive sleepiness that occur in relation to work hours that are scheduled during the usual sleep period. With an estimated 20% of the workforce in industrialized countries employed in a job that requires shift work, this condition has an approximate prevalence rate of 5%. Night and early morning shift workers are most commonly affected. These patients typically complain of insomnia during the scheduled sleep time and excessive sleepiness at work. Total sleep time is usually shortened by 15–20%, and sleep quality is perceived as unsatisfactory. Reduced alertness may lead to impairment of work performance as well as personal and public safety issues. Furthermore, circadian adaptation to the work schedule is often counteracted by exposure to light at the wrong time of the day and the tendency of most workers to resume full daytime activities and nighttime sleep during weekends and vacations. While shift work type usually persists only for the duration of the work-shift period, the condition may lead to chronic sleep disturbances in some individuals.

## Parasomnias

Parasomnias are undesirable physical events or sensory experiences that occur during entry into sleep, within sleep, or during arousals from sleep. These events may include abnormal sleep-related movements, behaviors, emotions, dreaming, and autonomic activity. They are usually manifestations of central nervous system activation transmitted into skeletal muscle and autonomic nervous system. The most common explanation for parasomnias is that sleep and wakefulness are

not mutually exclusive states and the overlap or intrusion of these states into one another causes these abnormalities. Parasomnias often occur in conjunction with other sleep disorders, and it is not uncommon for several parasomnias to occur in a single patient.

There are two major types of parasomnias: disorders of arousal and parasomnias associated with REM sleep. Disorders of arousal are defined by incomplete arousal from NREM sleep resulting in wakeful behaviors while asleep. The three subtypes of this condition are confusional arousals, sleepwalking, and sleep terrors. While each has its own defining characteristics, they do share some common features and clinically represent a continuum of behaviors. The general pathophysiology involves slow-wave sleep (SWS) instability with disordered arousals early in the sleep period. Clinically, disorders of arousal tend to occur in the first half of the night, last seconds to minutes, and rarely occur as multiple episodes during a single night. Patients usually have total or near-total amnesia for these events. Children are most often affected but symptoms usually improve with age. There is also a strong genetic predisposition. For example, first-degree relatives of patients with sleepwalking have a tenfold greater incidence of sleepwalking, and identical twins have a six times greater incidence of events than fraternal twins. Furthermore, all these events can be exacerbated or precipitated by the same risk factors.

## Risk Factors Exacerbating or Precipitating Disorders of Arousal

- Sleep deprivation
- Sleep disruption
- Fever or infections
- Sleep disorders (OSA and CRSDs in particular)
- Mental disorders
- Stress
- Anxiety
- Psychotropic medication
- Alcohol consumption
- Drug abuse

### Confusional Arousals

Confusional arousals consist of mental confusion or confusional behavior during or following arousal from sleep. They typically occur from SWS in the first part of the night but may also happen upon attempted awakening from sleep in the morning. The patient is disoriented in time and space, with slow speech, diminished mentation, and blunted response to commands or questions. During forced awakenings, the patient's behavior may be very inappropriate, highly resistive or even violent.

Confusional arousals are very common in children, with a prevalence rate of 17% in children 3–13 years of age. The condition is typically benign and diminishes in occurrence after the age of 5 years. In adults older than 15 years of age, the prevalence rate is 3–4%. The adult form usually persists on a long-term basis

without remission and may be associated with a number of serious complications, including sleep-related injury and violence, suboptimal performance at school or at work, and interpersonal difficulties.

### Sleepwalking

Sleepwalking is a series of complex behaviors that occur with sudden arousals from SWS and results in walking behavior during a state of altered consciousness. Episodes can range from sitting up in bed to walking and, rarely, running as if to escape an imminent danger. The patient may be difficult to awaken but, when aroused, is usually confused and may exhibit agitated, belligerent, or violent behaviors. Other inappropriate actions include urinating in a wastebasket, moving furniture around, walking outside, or climbing out a window. There is usually amnesia for the episode in the following morning, but adults can sometimes remember fragments of the event.

Sleepwalking has a strong familial pattern. Population-based studies suggest that genetic factors play a role in 65% of cases of sleepwalking. The prevalence of sleepwalking is as high as 17% in childhood, peaking by age 8–12 years. Most of these children had confusional arousals at a younger age. Childhood sleepwalking usually disappears spontaneously around puberty but may persist into adolescence. Up to 4% of adults sleepwalk, including de novo adult-onset sleepwalking. Complications include injury to self, the bed partner, or others in the same household, as well as disruption of the bed partner's sleep.

### Sleep Terror

Sleep terror is the most dramatic disorder of arousal. It is a frightening nocturnal event involving a cry or a piercing scream followed by fearful behavior and sympathetic hyperactivity. Event onset is abrupt, with patients exhibiting tachycardia, tachypnea, flushing, diaphoresis, and mydriasis. These striking events are certainly disruptive to witnesses, but typically, patients are seemingly unaffected. They are, however, confused and disoriented, and attempts to intercede can lead to violence, resulting in injury to the patient or the bed partner. Patients usually have no memory for the event, but adults may recall images or even more complex memories.

The prevalence rate of sleep terrors ranges from 1% to 6.5% in children and 2.3–2.6% in adults. Sleep terrors usually emerge in children aged 4–12 years and tend to resolve spontaneously during adolescence.

There are two major subtypes of parasomnias associated with REM sleep: REM sleep behavior disorder (RBD) and nightmare disorder.

### REM Sleep Behavior Disorder

RBD is characterized by increased muscle tone or excessive muscle twitch during REM sleep, as well as abnormal behaviors emerging during REM sleep that cause injury or sleep disruption. Behaviors often include talking, yelling, gesturing, punching, kicking, leaping, running, and arm flailing. These behaviors are thought of as an attempted enactment of distinctly altered, unpleasant, and violent dreams in which the patient is being confronted, attacked, or chased by unfamiliar people or

animals. A typical episode of these dream enactment behaviors lasts seconds to a few minutes. At the end of an episode, the patient awakens quickly, becomes rapidly alert, and reports a coherent dream with its actions corresponding to the observed sleep behaviors. Medical attention is usually sought after sleep-related injury has occurred to either the patient or the bed partner.

Because RBD occurs during REM sleep, it usually appears at least 90 min after sleep onset and tends to occur more frequently in the latter half of the night. In patients with coexisting narcolepsy, RBD can emerge shortly after sleep onset during a SOREMP. Periodic limb movements of sleep (PLMS) are also common with RBD and may disturb the sleep of the bed partner. The most common and important association, however, is between RBD and the development of neurodegenerative disorders. Up to 60% of patients with RBD will go on to develop Parkinson's disease, Lewy body dementia, or multiple system atrophy. Thus, RBD may be a marker for subsequent neurodegenerative disorders and lend an opportunity for earlier intervention.

The estimated prevalence of RBD in the general population is 0.38% and 0.5% in the elderly population. While any age group can be affected, RBD most frequently emerges after the age of 50 years and in a male-predominant population. An increasingly recognized precipitating factor for the development of RBD is medication use, particularly venlafaxine, selective serotonin reuptake inhibitors, mirtazapine, and other antidepressants with the exception of bupropion.

The pathophysiology of RBD may be related to the abnormal brain stem control of medullary inhibitory regions. It has been postulated that in a normal individual, atonia (muscle paralysis) in REM sleep is achieved by active inhibition of motor activity by the pons. Signals from the pedunculopontine centers stimulate the medullary centers, which in turn inhibit the spinal motor neurons, consequently result in whole body atonia. In RBD, there is a lack of pontine-mediated medullary inhibition of spinal motor neurons, resulting in loss of REM atonia and dream enactment behaviors.

RBD is diagnosed by a combination of historical and PSG features. Patients or witnesses should describe dream-enacting sleep behaviors, which are nonstereotypic and disruptive or injurious. The PSG recording must demonstrate REM sleep without atonia: an increase of phasic electromyographic (EMG) tone in the chin or limb leads during REM sleep (Fig. 83.4b). Furthermore, there must be no clinical suspicion of a seizure disorder, supported by an absence of electrographic epileptiform activity during PSG monitoring.

The onset of RBD can be gradual or rapid, and the course is progressive. Complications include disruption of the bed partner's sleep and sleep-related injuries to self or bed partner, which at times can be life threatening. Spontaneous remissions are very rare. However, RBD may subside after the emergence of an underlying neurodegenerative disorder, often more than a decade after the onset of RBD symptoms.

## Nightmares

Nightmares are coherent dream sequences that seem real and become increasingly more disturbing as they unfold. Nightmare disorder is based on recurrent distressing

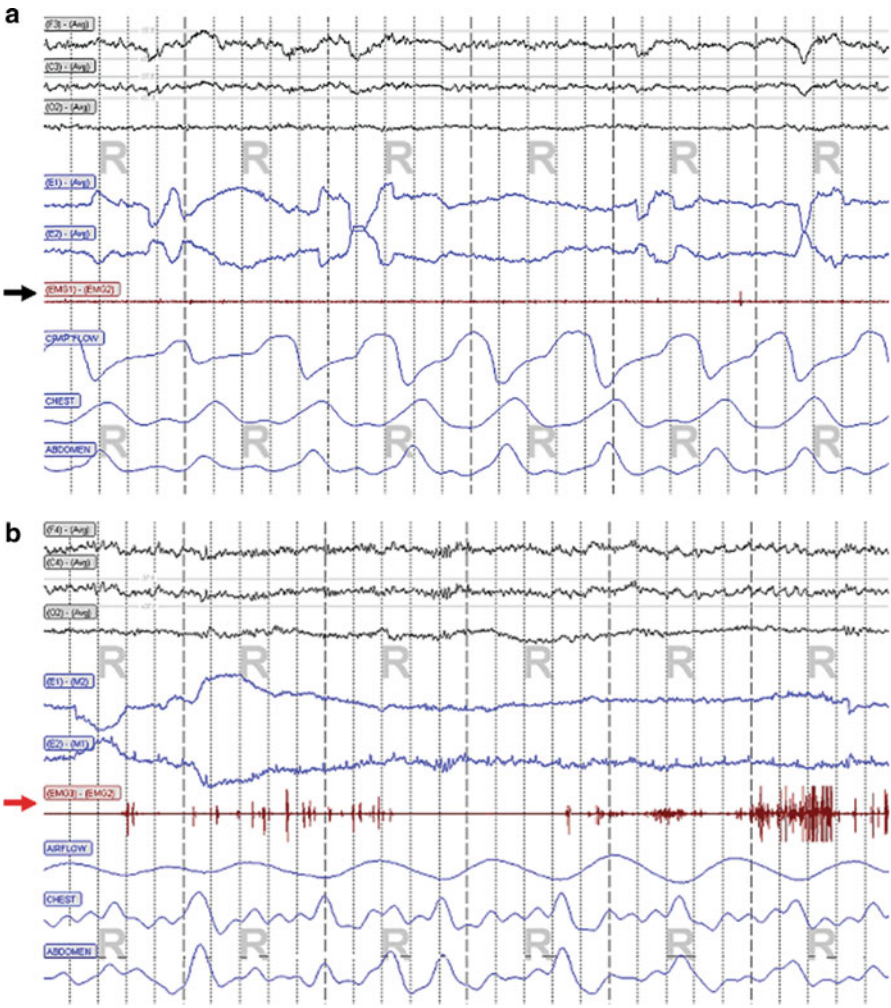


**Fig. 83.4** PSG of normal REM sleep versus REM sleep without atonia. (**a**) Normal REM sleep, note the lack of muscle twitches on the chin EMG lead (*black arrow*), indicating REM associated atonia. (**b**) REM sleep without atonia, note the significantly increased muscle twitches on the chin EMG lead (*red arrow*)

or frightening dreams involving clear visual imagery and auditory perception associated with disturbing emotions. Patients usually wake up with anxiety, fear, terror, anger, embarrassment, or other negative feelings. These events typically occur in REM sleep, and multiple episodes may occur within a single night or at any moment that REM propensity is high. Nightmare disorder can lead to sleep avoidance and deprivation and, thereby, to more intense nightmares, which can produce insomnia and daytime sleepiness.

**Table 83.3** Comparison of sleep terrors and nightmares

| | Sleep terrors | Nightmares |
|---|---|---|
| **Usual time of onset** | First third of the night | Last third of the night |
| **Stage of sleep** | SWS | REM sleep |
| **Vocalizations** | Common | Rare |
| **State on waking** | Confused and disoriented | Alert and oriented |
| **Autonomic discharge** | Severe and intense | Mild |
| **Violence** | Common | Rare |
| **Displacement from bed** | Common | Rare |
| **Recall** | Fragmented | Intact |

Among other features, the vivid imagery and the ability to recall the nightmare's content are essential characteristics in distinguishing nightmares from sleep terrors (Table 83.3).

Frequent nightmares are associated with enduring personality characteristics and psychopathologies. Nightmares with a recurring theme may stem from personal trauma or underlying psychological issues as part of acute stress disorder or posttraumatic stress disorder (PTSD). In addition, nightmares may be precipitated by the clinical use of pharmacologic agents affecting the neurotransmitters norepinephrine, serotonin, and dopamine. A majority of these agents are antidepressants, antihypertensives, and dopamine-receptor agonists. Lastly, an abrupt withdrawal of REM-suppressant medications may lead to REM sleep rebound and consequent increase in nightmare episodes.

Nightmares usually emerge between ages 3 and 6 years but can begin at any age. It is estimated that 10–50% of children aged 3–5 years have nightmares severe enough to disturb their parents. Nightmare prevalence tends to peak around 6–10 years of age and decreases thereafter. However, about 50–85% of adults report having at least one occasional nightmare. Adult females more frequently report nightmares and more readily discuss the nightmares than do their male counterparts. In patients with PTSD, up to 80% will experience nightmares beginning within 3 months of the traumatic event. While 50% of PTSD cases resolve within 3 months, posttraumatic nightmares can persist throughout life. Cognitive behavioral treatments have been applied with increasing frequency and success when reassurance does not alleviate nightmares.

## Sleep-Related Movement Disorders

Sleep-related movement disorders are conditions primarily characterized by simple, usually stereotyped, movements that disturb sleep or result in complaints of daytime sleepiness or fatigue. These disorders constitute a variety of syndromes, the most common is restless legs syndrome (RLS). Other syndromes include periodic limb movement disorder (PLMD), sleep-related leg cramps, sleep-related bruxisms, and sleep-related rhythmic movement disorder.

## Restless Legs Syndrome

RLS is a sensorimotor disorder characterized by a strong, nearly irresistible urge to move the legs. Patients describe a building of uncomfortable sensation to a point where they must give in and move their legs. Typical symptoms involve the ankle and the knee, but in severe cases, the thighs or feet, and rarely the arms, can also become involved. The symptoms are typically bilateral. RLS tends to become more pronounced during times of prolong inactivity, and it has a circadian tendency for symptoms to be maximal in the evening, increasing in intensity toward the early sleep period. Consequently, RLS may cause insomnia and prolonged awakenings, leading to significantly reduced total sleep time.

Symptoms of RLS have been identified in 5–15% of healthy subjects, with the highest prevalence in Western European countries (approximately 10%) and the lowest prevalence in Asia (approximately 1%). RLS occurs 1.5–2 times more commonly in women than in men. Genetically, it is often inherited in an autosomal dominant fashion: more than 50% of patients with primary RLS report a familial pattern. The risk of RLS is about three to six times greater for first-degree relatives of patients with RLS than for those from the general population.

Iron, dopamine, and genetics appear to be primary factors in the pathology of RLS. Increasing iron stores in the body significantly reduces symptoms in patients with RLS who have low serum ferritin levels. Postmortem studies of brain tissue from patients with early onset RLS have found abnormalities in the substantia nigra that include abnormal distribution or reduction of ferritin, reduced iron transporters, and possible impairment in cellular regulation of iron. Iron dysregulation may cause putative RLS dopamine abnormalities. Pharmacologic studies have shown that dopamine-promoting agents reduce all RLS symptoms and dopamine-receptor antagonists exacerbate RLS symptoms. Genome-wide scans have reported a significant linkage on chromosomes 9, 12, 14, and 20. Most chromosomal abnormalities were from families with an autosomal dominant mode of inheritance.

The diagnosis of RLS is made by meeting established clinical criteria. While PLMS (Fig. 83.5) is observed in more than 80% of RLS patients during PSG study, it also occurs with high prevalence in patients with RBD, narcolepsy, and even in the normal elderly population. Thus, PLMS is neither a sensitive nor specific for the diagnosis of RLS and should only be included as part of RLS' supportive features.

## Diagnostic Criteria for RLS in Adults

1. An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensation in the legs.
2. The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity, such as lying down or sitting.

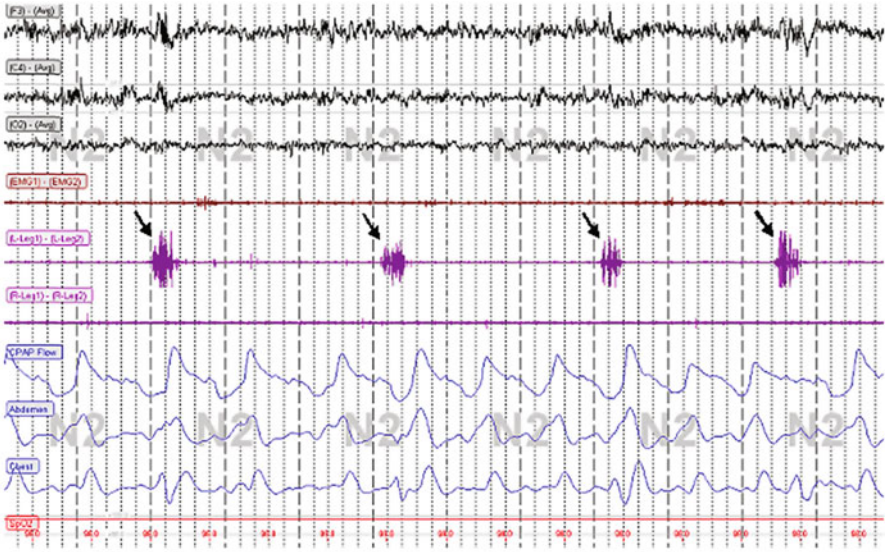


**Fig. 83.5** Periodic limb movements in sleep (PLMS) are shown on left anterior tibialis muscle (indicated by *arrows*)

3. The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
4. The urge to move or unpleasant sensations are worse or only occur in the evening or night.

## Periodic Limb Movement Disorder

In contrast to RLS, PLMD lacks the sensory complaints and is diagnosed based on PSG findings. The disorder is characterized by periodic episodes of repetitive and stereotyped limb movements that occur during sleep. The movements usually occur in the legs and consist of extension of the big toe in combination with partial flexion of the ankle, knee, and sometimes the hip. The movements are often associated with a partial arousal or awakening; however, patients are usually unaware of the limb movements or the frequent sleep disruption. Rather, they tend to experience symptoms of unrefreshing sleep or excessive daytime sleepiness.

PLMD is thought to be quite rare, and its exact prevalence is not known. However, it has been reported in both children and adults. PLMD may be an incidental finding, and the clinical significance of the movements needs to be decided on an individual basis. It is necessary to integrate a detailed clinical history and the PSG findings to assess the role of this phenomenon as a sleep disorder.

## PSG Diagnostic Criteria for PLMD

1. Repetitive, highly stereotyped limb movements (PLMS) that are:
   (a) 0.5–5 s in duration
   (b) Of amplitude greater than or equal to 25% of toe dorsiflexion during PSG calibration
   (c) In a sequence of four or more movements
   (d) Separated by an interval of more than 5 s and less than 90 s
2. The PLMS index exceeds 15 per hour in adults.

## Sleep-related Leg Cramps

Sleep-related leg cramps are painful sensations that cause sudden intense muscle contractions usually of the calves or small muscles of the feet. Episodes commonly occur during sleep without any specific preceding physiologic changes and may last for a few seconds. PSG reveals nonperiodic bursts of leg EMG activity. The cramps often cause arousals or awakenings from sleep. Relief may occur spontaneously or is often obtained by stretching the affected muscle. Many patients experience the cramps several times a week and describe a waxing and waning course of many years' duration.

Sleep-related leg cramps may be present in up to 16% of healthy individuals, with increased incidence among the elderly. Predisposing factors include diabetes mellitus, peripheral vascular disease, and metabolic disorders. The disorder can be associated with prior vigorous exercise, pregnancy, arthritis, and with fluid and electrolyte disturbances. The major complications include insomnia and occasional excessive daytime sleepiness due to interruptions in sleep.

## Sleep-related Bruxism

Sleep-related bruxism is a stereotyped oral activity characterized by grinding or clenching of the teeth during sleep. These events are usually associated with brief arousals from sleep but rarely with awakening. Severe cases, however, may result in sleep disruption to both the patient and the bed partner since the sounds made by friction of the teeth are usually quite loud and unpleasant. This condition induces dental damage with abnormal wear to the teeth and its surrounding structures. Over time, this leads to recession and inflammation of the gums and hypertrophy of the muscles of mastication and is often associated with teeth, jaw, or temporomandibular joint pain.

The prevalence of sleep-related bruxism is highest in childhood, approximately 14–17%, and then decreased over the lifespan. In middle-aged adults, it is approximately 8%, but in the elderly, it is as little as 3%. Predisposing factors may include dental malocclusion and anatomic defects, as well as specific personality types. For example, individuals who are highly motivated or characteristically maintain high

vigilance may have an increased prevalence of sleep-related bruxism. Precipitating factors include anxiety, situational stressors, and medications such as antidepressants, levodopa, and amphetamine. The use of alcohol, cigarettes, or caffeine before sleep may also contribute to increased tooth grinding.

The PSG feature of bruxism is an increased rhythmic masseter muscle activity during sleep accompanied by audio recording of the grinding sound. PSG monitoring, however, is rarely indicated. Rather, the diagnosis of sleep-related bruxism is based on careful history taking and the presence of tooth wear on dental evaluation. Tenderness or hypertrophy of the muscles of mastication may also be helpful in confirming the diagnosis.

### Sleep-related Rhythmic Movement Disorder

Sleep-related rhythmic movement disorder is a stereotyped, repetitive rhythmic motor behavior that occurs during drowsiness or light sleep and results in large movements of the head, body, or limbs. Typically seen in infants and children, this condition has three common subtypes:

1. Head banging: the child repeatedly lifts his or her head or entire upper torso and forcibly banging the head back down into the pillow or mattress.
2. Head rolling: the child moves his or her head in a side-to-side manner.
3. Body rocking: the child rocks his or her entire body forward and backward without head banging.

These episodes often occur near sleep onset, although they may also occur at any time during the night and even during quiet wakefulness. Duration of each episode is usually less than 15 min, and cessation of movements may occur following environmental disturbance or being spoken to. Children are typically amnestic of the events when asked in the morning.

Sleep-related rhythmic movements are common in normal infants and children. At 9 months of age, 59% of all infants have been reported to exhibit one or more subtypes of sleep-related rhythmic movements. At 18 months, the overall prevalence declines to 33%, and by 5 years to only 5%. This condition should be considered a disorder only if the behaviors markedly interfere with normal sleep cause significant impairment in daytime function or result in self-inflicted bodily injury that requires medical treatment.

## Outlook

### Future Directions

Sleep research is rapidly expanding due to the need to understand why we sleep and the physiological consequences of sleep. Sleep medicine is meeting the needs of countless patients who have problems with sleep, either too little, too much, or those who are troubled by abnormal events that occur during sleep. The expansion

of sleep medicine throughout the world continues as more people want a good night's sleep, and sleep disorders become recognized as having major health consequences. Newer neuroimaging techniques, genetic studies, and neurochemical analyses are being applied to understanding the brain's function during sleep and as these investigative techniques evolve they are likely to play a bigger role in the understand of sleep and sleep disorders.

## Further Reading

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