Current Classification of Sleep Disorders

3

Jagdeep Bijwadia

Abbreviations

AHI	Apnea-hypopnea index
ASWPD	Advanced sleep-wake phase disorder
BMI	Body mass index
CCHS	Congenital central alveolar hypoventilation syndrome
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
CRSWD	Circadian rhythm sleep-wake disorders
CSA	Central sleep apnea
DSWPD	Delayed sleep-wake phase disorder
FVC	Forced vital capacity
GERD	Gastroesophageal reflux disorder
ICSD	International Classification of Sleep Disorders
IH	Idiopathic hypersomnia
ISWD	Irregular sleep-wake rhythm disorder
MSLT	Multiple sleep latency test
NREM	Non-rapid eye movement
OHS	Obesity hypoventilation syndrome
OSA	Obstructive sleep apnea
$PaCO_2$	Partial arterial pressure of carbon dioxide
PCO_2	Arterial pressure of carbon dioxide
RBD	Rapid eye movement sleep behavior disorder
REM	Rapid eye movement
SE	Sleep enuresis
SIDS	Sudden infant death syndrome

J. Bijwadia (✉)
Sleepmedrx, Saint Paul, MN, USA
e-mail: jbijwadia@sleepmedrx.com

G. G. Demerjian et al. (eds.), *Dental Sleep Medicine*,
https://doi.org/10.1007/978-3-031-10646-0_3

SNRI	Norepinephrine reuptake inhibitor
SOREM	Sleep onset rapid eye movements
SRBD	Sleep-related breathing disorder
SRED	Sleep-related eating disorder
SRHD	Sleep-related hypoventilation disorder
SRMD	Sleep-related movement disorder
SSRI	Selective serotonin reuptake inhibitor

3.1 Introduction

The field of sleep medicine is rapidly advancing with greater clarity emerging for sleep disorders from diagnosis to treatment options. The International Classification of Sleep Disorders (ICSD) is a primary diagnostic, epidemiological, and coding resource for clinicians and researchers in the field of sleep and sleep medicine. The current version of ICSD-3 was published in 2015 [1].

Building on the foundation of the ICSD-2, the new ICSD-3 retains the major diagnostic sections with extensive literature reviews for each diagnosis and its associated features. Additional text headings and coding recommendations were also added. Of note, the ICSD-3 task force elected to consolidate all insomnia diagnoses (i.e., "primary" and "comorbid") under a single, chronic insomnia disorder. This decision was not intended to suggest that there may not be important differences among the various chronic insomnia subtypes, but rather the recognition that it is not possible to reliably distinguish or translate each subtype into more customized therapeutic approaches. Similar to ICSD-2, pediatric diagnoses are not distinguished from adult diagnoses, with the exception of pediatric OSA.

The goals of the ICSD classification include description of all currently recognized sleep disorders, to present the disorders with a rational and scientifically valid structure and to ensure as much compatibility with the ICD10 coding system as possible.

Although the criteria for each diagnosis are written to be as specific to the disorder as possible, there are still gaps in the science and knowledge about the classification of these disorders. As a result, it is important that clinicians allow some room for judgment in the application of these criteria. In general, unless otherwise specified, all criteria must be met to establish a diagnosis. It is very likely, for example, that there may be individuals with clinically significant sleep disorders who do not meet all the criteria for a given diagnosis. In such cases, it is important to have provisional diagnoses with careful follow-up and retesting when appropriate. Application of the criteria should be guided by the notes that follow many of the criteria sections.

3.2 Insomnia

Individuals with insomnia disorders have difficulty falling or staying asleep, despite adequate circumstances for obtaining sufficient sleep. Their sleep may not be consolidated, resulting in poor quality. They are dissatisfied and distressed about the poor quality of sleep and impairment in their personal lives. Individuals with chronic or short-term insomnia commonly feel fatigued and unmotivated during the day. They may have difficulty with memory function, struggle to concentrate, and be irritable. These difficulties can lead to poor job or academic performance. Somatic symptoms are not uncommon, such as headaches and gastrointestinal complaints.

Insomnia is one of the most prevalent health concerns in the population and in clinical practice. Clinicians may be reluctant to address insomnia because of its many potential causes, unfamiliarity with behavioral treatments, and concerns about pharmacologic treatments [2].

Approximately 30% of a variety of adult samples drawn from different countries report one or more of the symptoms of insomnia: difficulty initiating sleep, difficulty maintaining sleep, waking up too early, and in some cases nonrestorative or poor quality of sleep [3]. Onset can be acute or insidious. The course can be intermittent, persistent, or situational; and the nature of insomnia can change from difficulty falling asleep to difficulty staying asleep or vice versa. Some patients suffer with difficulty falling asleep and an inability to stay asleep. Symptoms may not be consistent and there could be significant night-to-night variability.

Risk factors include female sex, psychiatric disorders, substance disorders, and lower socioeconomic status. Older adults are more likely to be diagnosed, likely because increased age is associated with a decrease in sleep continuity and increase in medical comorbidities.

3.2.1 Chronic Insomnia Disorder

No distinct structural changes have been identified in the brains of chronic insomnia disorder patients, aside from those present for other known reasons (e.g., stroke, brain trauma, or multiple sclerosis lesions). Studies of autonomous and central nervous system parameters have identified hyperarousal as a final common pathway pathophysiology, implicating an imbalance of sleep-wake regulation consisting of either overactivity of the arousal systems, hypoactivity of the sleep-inducing systems, or both [4]. Studies suggest that the physiologic changes observed with insomnia disorders are related to increased sympathetic nervous system and hypothalamic-pituitary-adrenal axis activity during sleep and wakefulness. Reported changes include physiological arousal, which is associated with increases in heart rate, heart rate variability, metabolic rate, cortisol levels, adrenocorticotropic hormone, and corticotropin releasing factor. During non-rapid eye movement (NREM)

sleep, body temperature may be elevated, and increased high-frequency activity on electroencephalograms can be observed. These pathophysiologic changes may not be underlying factors for individuals suffering with a mental disorder. The prevalence of insomnia disorder is approximately 10–20%, with approximately 50% having a chronic course [2]. Complications of chronic insomnia include increased risk for depression, increased risk for hypertension, and decreased work or school performance. They may rely on prolonged use of sleep-aid medications.

Complaints about poor quality of sleep are insufficient to diagnose insomnia. Many people do not accurately assess the duration or quality of their sleep, with self-described "poor" sleepers often underestimating their amount of sleep and "good" sleepers overestimating their amount of sleep. The degree of sleep interruption used to diagnose chronic insomnia is subject to the individual's own interpretation, and the degree of interruption that is clinically meaningful differs across age groups. Taking longer than 20 min to initially fall asleep or to return to sleep after waking is usually interpreted as clinically meaningful in children and young adults, but this increases to 30 min in middle- and older-aged adults. Complaints of waking too early in the morning are also subjective and relative to the time the individuals routinely go to bed and their perceived sleep duration before the insomnia began.

The frequency and duration criteria must be met to diagnose a case as chronic insomnia disorder. More serious daytime consequences occur when sleep is difficult three or more times a week or at least 3 months. Cases not meeting these criteria should be assigned a diagnosis of short-term insomnia disorder, although it is recognized that these cases can have substantial clinical consequences and impacts on the patient's quality of life.

Chronic insomnia disorder can overlap with delayed and advanced sleep-wake phase disorders. Patients with delayed patterns of sleep may experience chronic anxiety related to their inability to fall asleep due to the circadian rhythm being out of sync with their sleep schedule, and this anxiety can reinforce the issue. Patients who wake up too early in the morning may have sleep disruption during the advanced stages of sleep. These patients should be evaluated for comorbid chronic insomnia disorder and circadian rhythm sleep-wake disorder.

Patients being evaluated for chronic insomnia disorder should also be investigated for other obvious causes of inadequate sleep. Environmental factors such as light, noise, and temperature can be disruptive to sleep. Feelings of being unsafe can also prevent sleep. When obvious factors that would disrupt the sleep of anyone are identified, a chronic insomnia disorder should not be diagnosed; and the patient may be classified as having an "other sleep disorder." Patients who report insufficient sleep and daytime fatigue should also be asked about the amount of time they devote to sleep or if their daytime schedules are too demanding, as this would not constitute a case of insomnia when the patient can sleep well when time is allowed. Note that chronic insomnia is not often associated with excessive daytime sleepiness and unintentional sleep episodes, which are common in people willingly restricting their own sleep.

Insomnia symptoms may occur due to comorbid conditions, such as restless leg syndrome and sleep apnea [5]. A chronic insomnia diagnosis would not be issued if

effective treatment of the comorbid condition resolved the insomnia. Polysomnography and multiple sleep latency testing are not routinely used as a diagnostic tool for insomnia disorders, but they can be useful in ruling out other sleep disorders. Certain personality traits predispose to chronic insomnia, including health anxiety, feeling repression or internalization, and overconcern with daytime functioning after a night of insomnia. Medical conditions that increase the risk of chronic insomnia include gastroesophageal reflux disorder (GERD), alcohol abuse, restless leg syndrome, generalized anxiety disorder, chronic pain, and breathing disorders.

The triggers and symptoms of chronic insomnia disorder may vary with age. This may be due in part to age-related changes in circadian rhythms and the increased amount of normal waking in older adults [6]. Adolescents and younger adults are more likely to have difficulties falling asleep or achieving enough restful sleep, while older adults are more likely to have difficulty staying asleep or waking up too early in the morning. There is some limited, emerging, evidence that suggests that insomnia is associated with an increased risk of dementia in older adults [7].

3.2.2 Short-Term Insomnia Disorder

An estimated 15–20% of adults suffer with short-term insomnia in any given year. Sleep is becoming an increasingly precious commodity as more and more people are reporting issues with sleep in our busy society [8]. Like chronic insomnia, short-term insomnia is more common in females and older individuals. Individuals who have trouble sleeping during times of high stress or who are light sleepers are more likely to develop insomnia. Major life events, such as job loss, job change, or death of a loved one can precipitate onset of insomnia. Short-term insomnia may remit when the triggering circumstances are removed or the individual adapts to the situation, but the disorder can last well beyond resolution of the events for some individuals. Left untreated, insomnia can worsen and progress to chronic insomnia.

Short-term insomnia disorders should be distinguished from jet lag, shift work effects, and circadian rhythm sleep-wake disorders; in the case of true short-term insomnia, removing these factors would not help disorder.

3.2.3 Insomnia in Children

Children may also experience insomnia disorder. An estimated 10–30% of children are unable to fall asleep or stay asleep due to dependence on the caregiver being present at bedtime or failure to set limits during the night, although the latter is open to interpretation in the context of family culture. Chronic illness or neurodevelopmental disorders are also associated with insomnia in children. After the third year of life, the prevalence of insomnia remains at about 15% [9].

Parents overly concerned with the child's sleep pattern may make it worse by putting them to bed too early. Insomnia due to difficulty separating from the

caregiver may relent as the child gets older, due to increased need for privacy and independence. Children may outgrow insomnia, but some individuals continue to suffer into adulthood. Impact on families can be substantial, with parents overtired and irritable or unable to perform duties at their job.

In children, insomnia related to limit-setting may be characterized by bedtime stalling or refusals to comply that are reinforced by the caregiver giving in and reinforcing the behavior. Some children may have anxiety or fears of being alone in the dark or nightmares. Behavior problems and limit-setting difficulties may also be observed during the day. Parents may offer excessive bottle feeding, rocking, or physical contact. As normal children are not expected to sleep through the night until 3–6 months of age, an insomnia diagnosis is not usually considered until at least 6 months of age, unless symptoms are severe.

3.2.4 Other Insomnia Disorder

Other insomnia disorder is used sparingly as a diagnosis, because it is nonspecific and based on failure to meet all criteria for chronic and short-term insomnia disorders. These individuals may complain about sleep difficulties; and in some situations, it may be provided as a diagnosis while more data is gathered to fully characterize if a chronic or short-term insomnia disorder is present.

3.2.5 Isolated Symptoms and Normal Variants

Some patients may have isolated symptoms of insomnia, such as difficulty falling asleep or long periods of wakefulness at night, but they do not complain about their symptoms. In children, this can occur when caregivers have unrealistic expectations of how long the child needs to sleep each night. In adults, it is most common in retired or unemployed individuals who stay in bed for excessive amounts of time but are not bothered by this. Others spend a relatively short time in bed compared to others, apparently requiring less sleep than their peers without feeling negative effects. It is unknown if only objective measures of sleep duration and quality are associated with adverse health outcomes or if perceived dissatisfaction with sleep also has negative effects.

3.3 Sleep-Related Breathing Disorders

3.3.1 Obstructive Sleep Apnea Syndromes

During periods of wakefulness, numerous muscles of the upper airway work together to dilate the lumen of the pharynx. Air passes freely when inhaling and exhaling. Obstructive sleep apnea (OSA) occurs when the airway becomes partially or completely blocked during sleep, resulting in hypopnea (periods of abnormally

slow or shallow breathing) and apnea (periods of no breathing). The airway obstruction occurs repeatedly during sleep and can have serious consequences for the patient, as the patient is unable to achieve adequate restful sleep, resulting in numerous sequelae and a negative impact on quality of life [10].

This disorder is common globally and occurs in both children and adults. It is remarkable that despite all of the clinical and scientific advancements regarding obstructive sleep apnea in the last two decades, a great majority (70–80%) of those affected remain undiagnosed [11]. Substantial methodological heterogeneity in population prevalence studies has caused a wide variation in the reported prevalence, which, in general, is high. At ≥5 events/h apnea-hypopnea index (AHI), the overall population prevalence ranged from 9% to 38% and was higher in men. It increased with increasing age and, in some elderly groups, was as high as 90% in men and 78% in women. At ≥15 events/h AHI, the prevalence in the general adult population ranged from 6% to 17%, being as high as 49% in the advanced ages. OSA prevalence was also greater in obese men and women [12]. Known factors that increase risk for both sexes are age and obesity. About 40% of obese with no complaints of sleep disorders have obstructive sleep apnea (OSA) that was present in 55% of all adolescents who underwent bariatric surgery, and up to 71% of morbid obese present with OSA [13]. As obesity levels rise across the globe and the world's population ages, more cases are likely to be diagnosed. Asian race is another well-known risk factor, and this is thought to be due to cranial-facial structural features [14]. However, adults who do not have any of these risk factors may also develop OSA; and contributing factors can vary, including neuromuscular issues with the respiratory control system, low threshold of arousal from sleep, decreased lung volume, and cigarette smoking. Given the increasing incidence of obesity, the estimated prevalence rates have increased substantially over the past two decades [15]. In children, OSA is associated with obesity, craniofacial syndromes, achondroplasia, trisomy 31, allergic rhinitis, and asthma; and various factors such as altered reflexes in the neuromuscular airways, general airway inflammation, and structural anatomical features are thought to play a role [16].

Patients with OSA report symptoms such as snoring, dry mouth, sore throat, gasping during sleep, and morning headaches. The most common symptom in patients presenting with obstructive sleep apnea is excessive daytime sleepiness. Patients also complain of difficulty with concentration and nonrestorative sleep. Children may have enlarged adenoids or tonsils, behavioral problems, poor academic performance, bedwetting, and developmental delays. Many patients report a family history of OSA and have other known risk factors, such as obesity or advanced age. Some studies have shown that type 2 diabetes is a risk factor, but it is unclear if this is due to defective glucose regulation, neuropathy, or obesity.

Diagnosis is made after a physician evaluates the patient for risk factors and symptoms. The gold standard test for OSA is polysomnography conducted overnight in a sleep laboratory. During this test, the patient is continuously monitored before and during sleep for cardiac, respiratory, and brain activity. Breathing patterns, limb movement, and blood oxygen levels are also assessed. The results are reported as an apnea-hypopnea index. Although the exact calculation differs by

laboratory, they all report a measure of the number of apneas and hypopneas per hour of sleep.

Results are analyzed by the stage of sleep to inform if the amount of sleep spent in each stage is normal or reflects a profile of OSA. The assessment also tests if sleep position impacts the amount of apnea experienced by the patient, and it can help rule out other sleep disorders.

As an alternative to polysomnography, some patients may be offered an in-home version of the test. Home testing can also be used to assist in OSA management by allowing frequent monitoring and assessment of treatment effectiveness [15].

The disturbances in gas exchange caused by OSA result in substantial health consequences. In children, the clinical relevance of OSA resides in its association with significant morbidities that affect the cardiovascular, neurocognitive, and metabolic systems [17].

Fragmented sleep and excessive daytime drowsiness can have a major impact on the patient's quality of life.

OSA contributes to reduced quality of life, impaired work performance, and increased motor vehicle crash risk. OSA is associated with an increased incidence of hypertension, type 2 diabetes mellitus, atrial fibrillation, heart failure, coronary heart disease, stroke, and death [18].

Lifestyle changes may be helpful in managing OSA. Avoiding alcohol, losing weight, exercising, avoiding cigarettes, and avoiding a back-sleeping position have all been shown to help some patients with OSA. These changes are usually advised for all OSA patients, regardless of the other treatments they are receiving.

3.3.2 Central Sleep Apnea Syndrome

Central sleep apnea (CSA) results in inadequate breathing during sleep. Unlike OSA, in which the patient makes visible efforts to breathe, CSA is characterized by a lack of drive to breathe during sleep, resulting in repetitive periods of insufficient ventilation and compromised gas exchange. The nighttime breathing disturbances can lead to significant comorbidity and increased risk of adverse cardiovascular outcomes [19].

Breathing is controlled through complex mechanisms. Issues with any of these can lead to central sleep apnea syndromes. Chemoreceptors in medullary neurons respond to changes in H^+ and CO_2 concentration and arterial pressure, which directly affects the apnea threshold that triggers awakening. Individuals who are highly sensitive to these stimuli are at increased risk of overresponding to chemical changes, resulting in unstable breathing patterns. Similarly, people with delays in responding to chemical stimuli may have increased hyperventilation with subsequent breathing instability. In addition to chemical controls, chest wall and respiratory muscle activities play an important role in controlling breathing rate and depth during sleep. Apneic threshold is the arterial pressure of carbon dioxide (PCO_2) below which the ponto-medullary respiratory rhythm generator is paused, silencing motor nerves that innervate inspiratory muscles. Consequently, ventilation ceases, and central

apneas ensue. Sleep unmasks a highly sensitive hypocapnic-induced apneic threshold, which in health at sea level approximates the waking eupneic partial arterial pressure of carbon dioxide ($PaCO_2$). When ventilation increases in response to a transient spontaneous arousal or sigh, the subsequent ventilatory overshoot often elicits sufficient hypocapnia causing central apneas [20].

CSAs are likely to manifest during sleep-state changes because these are periods when respiratory control mechanisms change. Deficits in regulating breathing may manifest during a particular sleep stage, depending on the precipitating factor of the individual. The transition from being awake to sleeping requires a loss of wakefulness stimuli, loss of behavioral influences, and downregulation of respiratory control mechanisms. At normal sleep onset, upper airway muscle tone is reduced, thereby increasing the resistance of upper airway dilator muscles that can reduce airflow for a period. Responses to chemical stimuli are reduced at sleep onset. Individuals vary in the magnitude of physiological responses, and dysrhythmic breathing can be observed even in healthy individuals without CSA. During healthy, stable sleep, an increased blood CO_2 level (hypercapnia) and decreased O_2 level (hypoxia) are recognized by the body as normal, and ventilatory responses to hypoxia and hypercapnia are reduced. When breathing is compromised, the individual will wake; but in CSA patients, low arousal threshold and the ventilatory response to arousal may be compromised.

All adult CSAs share common characteristics, such as the presence of at least one of the following symptoms: daytime sleepiness, difficulty staying asleep, awakening shortness of breath, and witnessed apneas. Unless due to high altitude or medication/substance use, snoring is also commonly observed. The cause of apnea varies with the type of CSA.

3.3.2.1 CSA with Cheyne-Stokes Breathing

A Cheyne-Stokes breathing pattern is cyclical, in which an individual has an increase in breath, followed by a gradual decrease that eventually stops completely and finally returns to normal. It is commonly observed in individuals suffering with diseases that affect the cardiorespiratory system (up to 50%), such as congestive heart failure, stroke, or end-stage kidney disease [21].

3.3.2.2 CSA Due to a Medical Disorder Without Cheyne-Stokes Breathing

These are cases of CSA without Cheyne-Stokes breathing patterns that are attributed to another medical or neurological condition. These patients often have brainstem lesions due to developmental, degenerative, demyelinating, neoplastic, traumatic, or vascular origin.

3.3.2.3 CSA Due to High-Altitude Periodic Breathing

A central apnea breathing pattern can be caused by exposure to very high altitude, where oxygen levels are low, and the body has not adapted to it yet. It can occur in susceptible individuals at altitude above 2000 m, but at very high altitude, say above

5000 m, it will occur in most subjects. Unless living at extreme altitudes, individuals can adapt over weeks or months to regain normal sleep breathing patterns [22].

3.3.2.4 CSA Due to a Medication or Substance

Some medications are known respiratory depressants, such as opioids. These may cause irregular breathing or complete temporary cessation for the duration of use. More evidence is currently needed on how to effectively manage opioid-induced sleep-related breathing disorder (SRBD) [23].

3.3.2.5 Primary CSA

With this type of CSA, physicians have not been able to determine the cause of CSA. While healthy individuals may have central apneas during the wake-sleep transition, they should not have more than 5/h during stable sleep.

3.3.2.6 Treatment-Emergent Central Sleep Apnea

Some individuals who have OSA develop comorbid CSA when undergoing continuous positive airway pressure (CPAP) therapy. In some cases, the CSA was preexisting but not recognized until the OSA was treated [24].

The above CSA forms can also be observed in children, although it is less common than in adults. There are childhood-specific forms of CSA.

3.3.2.7 Primary Central Sleep Apnea of Infancy

In children older than 37 weeks of conceptional age, cyanosis and breathing interruptions may be observed, even resulting in the need for stimulation or resuscitation. Prevalence is low (0.5% for the first 6 months of life) and decreases as the child ages, suggesting developmental causes in many cases. It is thought to be due to immaturity of the brainstem or secondary medical conditions that depress central respiratory control. Although a small percentage of children who die of sudden infant death syndrome (SIDS) were found to have had periods of apnea, CSA is not an established cause of SIDS.

3.3.2.8 Primary Central Sleep Apnea of Prematurity

Apnea is very common in infants born preterm. Although the pathogenesis is poorly understood, the immature pulmonary reflexes and breathing responses to hypoxia and hypercapnia likely contribute to the occurrence or severity of primary central apnea of prematurity [25].

The gold standard for CSA diagnosis is overnight polysomnography. This can also rule out other disorders that have similar symptoms, such as obstructive sleep apnea and periodic limb movements. Because of the complex physiologic processes involved in regulating cardiorespiratory responses during sleep, neurologists, cardiologists, and sleep specialists work together (and may order additional tests) to make the diagnosis and develop a treatment plan. If the cause of CSA cannot be identified through polysomnography, MRI may be used to rule out other obvious causes of central apnea, such as brain injury and neurological lesions.

CSA is a serious medical condition. The repeated awakening and resulting lack of restorative sleep lead to extreme daytime drowsiness and irritability. Work and regular activities, such as driving a car, can be difficult. In addition, when sudden decreases in respiration cause blood oxygen levels to fall dramatically, existing cardiovascular disease can be exacerbated; and the individual is at risk for developing arrhythmia.

In the case of comorbid conditions or medication use that cause or exacerbate CSA, effective treatment of the underlying condition or reduction of offending medication is necessary. Nighttime use of a CPAP device, or other forms of positive airway pressure therapy, is typically recommended for the duration of the CSA symptoms. Supplemental oxygen can also be provided during sleep. If positive airway pressure cannot be used or tolerated, medications that stimulate breathing, such as acetazolamide or theophylline, can be prescribed.

3.3.3 Sleep-Related Hypoventilation Disorders

Nocturnal hypoventilation can be attributed to either decreased ventilatory drive ("will breathe") or worsening mechanics ("cannot breathe"). Nocturnal hypoxemia follows due to the displacement of oxygen in the alveoli from rising carbon dioxide levels, as predicted by the alveolar air equation. Alternatively, arterial hypoxemia alone may be the product of worsening ventilation/perfusion mismatch with greater effective shunt [26].

During sleep in healthy individuals, respiratory volume is substantially reduced. When underlying conditions further increase hypoventilation, it is typically observed first in sleep. Thus, sleep-related hypoventilation disorders (SRHDs) may be an early stage of chronic hypoventilation disorders, with daytime hypoventilation appearing in some cases. If presented during wakefulness, the hypoventilation is exacerbated during sleep.

SRHDs can occur at any age. Many different medical conditions can contribute, and the symptoms vary. Poor quality of sleep and sequelae (e.g., daytime sleepiness, morning headache, stomach problems) are common. Many people do not report any symptoms initially, allowing the disorder to progress to a more serious condition. Diagnosis is made with blood gas testing, and polysomnography may also be used to rule out other causes.

Left untreated, SRHDs can contribute to cardiovascular disease or lead to respiratory failure. Treatment primarily relies on addressing any underlying medical conditions or substance use that contribute to hypoventilation. Positive airway pressure can be used to improve oxygen delivery to the lungs during sleep. Common medical conditions associated with sleep-related hypoventilation are described below.

3.3.4 Obesity Hypoventilation Syndrome

Obesity hypoventilation syndrome (OHS) is defined as daytime hypercapnia ($PaCO_2$ >45 mmHg) in an obese patient [body mass index (BMI) ≥30 kg/m^2] with sleep-disordered breathing after all known causes of hypoventilation have been excluded, such as severe obstructive pulmonary disorders [chronic obstructive pulmonary disease (COPD)] or restrictive chest wall deformities, severe hypothyroidism, neuromuscular disease, or central hypoventilation syndromes [27]. The diagnosis requires a demonstration of daytime hypoventilation. During sleep, the already exacerbated CO_2 levels worsen. While some individuals report no or few issues with sleep, many experience excessive daytime sleepiness. The disorder may go unrecognized until a sudden cardiac arrest or respiratory failure prompts evaluation.

Electrolyte panels showing elevated serum CO_2 and increased hematocrit are suggestive of OHS. Pulmonary function tests may find reduced forced vital capacity (FVC), and electrocardiography and echocardiography show several features consistent with strained cardiac function. Pulmonary artery hypertension, enlarged heart, and neurocognitive dysfunction can result when this condition is not treated.

OSA can be comorbid with OHS. Up to 90% of obese OHS patients also have OSA. Among obese patients with OSA, approximately 20–30% also have OHS [28]. Overall, obesity is thought to be the main physiologic factor predisposing patients to hypoventilation and hypercapnia. BMI is positively correlated with increased SRHD severity. Obesity is known to increase CO_2 production (e.g., working harder due to increased weight on the pharyngeal muscles and diaphragm) and to reduce its elimination (e.g., changes in chemosensitivity, resistance to leptin, and decreased lung volume).

3.3.5 Congenital Central Alveolar Hypoventilation Syndrome

Congenital central alveolar hypoventilation syndrome (CCHS), a rare syndrome, is caused by failure of the autonomic central control of breathing due to a mutation in the PHOX2B gene [29]. This gene plays a role in differentiation of embryonic cells that form parts of the autonomic nervous system. As a result, the regulation of breathing, heart rate, temperature, and blood pressure may be defective. Symptoms are usually present at birth and are most notable during sleep. The neonate may initially appear normal, before they develop cyanosis, difficulty feeding, and poor muscle tone. In some cases, no obvious symptoms appear until a cardiorespiratory failure requires intervention.

Most individuals with CCHS require ventilation support while sleeping, either with a positive pressure machine or tracheostomy. Approximately 15% of CCHS patients require daytime ventilation support. If hypoventilation is well controlled, most patients will develop normally. Even with adequate treatment, patients with CCHS require close monitoring, because minor illnesses, including respiratory infections or diarrhea, can precipitate respiratory failure.

3.3.6 Other Sleep-Related Hypoventilation Disorders

3.3.6.1 Late-Onset Central Hypoventilation with Hypothalamic Dysfunction

In this disorder of unknown etiology, central control of ventilation is inadequate. Patients appear healthy until 2 or 3 years of age and then develop severe, insatiable hunger that leads to obesity. This results in hypoventilation and can cause respiratory failure. The patient requires ventilatory support when sleeping, and the disorder does not resolve with weight loss. Patients often develop hypothalamic disruption that interrupts normal growth and development [30].

3.3.6.2 Idiopathic Central Alveolar Hypoventilation

CCHS is a very rare disorder diagnosed in the absence of primary neuromuscular, lung, or cardiac disease or an identifiable brainstem lesion. It is characterized by generally adequate ventilation while the patient is awake but alveolar hypoventilation with typically normal respiratory rates and shallow breathing (diminished tidal volume) during sleep [31].

3.3.6.3 Sleep-Related Hypoventilation Due to a Medication or Substance

Some long-acting narcotics, anesthetics, sedatives, and muscle relaxants are known to decrease ventilatory drive. Intermittent or sustained hypoventilation may be present during wakefulness and sleep.

3.3.6.4 Sleep-Related Hypoventilation Due to a Medical Disorder

Severe lung disease, chest wall disorders, hypertension, neurologic disease, and neuromuscular disorders can lead to hypoventilation. The clinic presentation varies with the underlying cause and its severity.

3.3.7 Sleep-Related Hypoxemia Disorder (SRHD)

Hypoxemia during sleep is suspected to be secondary to another medical or neurological disorder. This diagnosis is used when the hypoxemia cannot be explained by other breathing disorders (e.g., OSA, CSAs, or SRHDs). In some patients, hypoxemia is observed during wakefulness as well as sleep. Patients may be asymptomatic or have the typical complaints associated with poor sleep quality. Presentation varies with the comorbid condition, which can include pulmonary disease, pulmonary hypertension, neurologic disease, and neuromuscular disorders.

3.3.8 Isolated Symptoms and Normal Variants

3.3.8.1 Snoring

The ICSD-3 describes primary snoring as "audible vibrations of the upper airway during respiration in sleep" [32]. It occurs when the uvula and soft palate vibrate, although additional structures of the pharyngeal walls may be involved. Snoring itself can cause morphological changes in the palate that are thought to be neurologic trauma from vibration. The snoring is usually loudest during N3 sleep or REM sleep.

Snoring is a cardinal symptom of sleep apnea and common during hypoventilation, but it may occur on its own. Snoring that is not associated with other sleep disorders (i.e., diagnosis actively excluded) and fails to cause insomnia or daytime sleepiness is referred to as habitual snoring. However, it should be noted that individuals with isolated snoring have an increased risk of developing OSA with age or weight gain.

Occasional snoring is experienced by most healthy individuals. Approximately, 10–12% of children snore. In adults, it is more common in men (40%) than women (24%). Snoring becomes more common with age in both sexes, but it reportedly decreases in men over 70 years of age. It is unclear if the decrease is due to reduced hearing in this age group and their partners. Obesity, alcohol consumption, opioid use, and smoking are risk factors for isolated snoring. In children, increased adenoid and tonsil size is associated with snoring.

Treatment may be desirable, especially in cases where a spouse or living partner complains that their sleep is interrupted by the snoring. Oral devices can help in some cases. In children, adenotonsillectomy may cure the snoring.

3.3.8.2 Catathrenia

Catathrenia is groaning during sleep. Typically, a deep inhalation is followed by a prolonged exhalation that is accompanied by a monotonous vocal sound. The affected individual is usually unaware, unless family members observe and report the sound. No known symptoms occur, aside from social considerations.

3.4 Central Disorders of Hypersomnolence

Not all cases of excessive sleepiness (hypersomnolence) are caused by disturbed nighttime sleep or circadian rhythm misalignments. Hypersomnolence occurs in varying frequencies and severities, with some patients aware of the increasing sleepiness before falling asleep and others unaware. To be diagnosed with one of the chronic central disorders of hypersomnolence, sleepiness must generally last for at least 3 months, and alternative causes (e.g., SRBDs and insomnia) must be ruled out or adequately treated.

Severity of daytime hypersomnolence is quantified using the Epworth sleepiness scale (a subjective measure) and multiple sleep latency test (an objective measure, MSLT). The results of each do not always correlate with one another, and clinical

judgment must be made to assess the relative results of each. The MSLT is not used for children under 6 years old, because normative data are not available. The MSLT is done to assess ease of falling asleep at quiet times during the day (8 AM–6 PM). Individuals with central hypersomnolence disorders generally fall asleep in 8 min or less, with 90% of patients with narcolepsy meeting this definition. At least two sleep-onset rapid eye movement periods (SOREMPs) should be observed during the MSLT or polysomnography for narcolepsy definitions. The spectrum of central disorders of hypersomnolence is described further below.

3.4.1 Narcolepsy Type 1

Narcolepsy type 1 is a rare disorder characterized by excessive daytime sleepiness and cataplexy (sudden weakness or limpness of muscles). Type 1 narcolepsy is caused by extensive loss of hypothalamic neurons that produce the neuropeptides orexin-A and orexin-B (also referred to as hypocretin-1 and hypocretin-2), a neuropeptide that regulates appetite, alertness, and sleep [33]. Normal individuals increase hypocretin production during wakefulness; this leads to increased activity in neurons with hypocretin receptors resulting in wakefulness and suppression of REM sleep. The daytime sleepiness is a cardinal symptom of narcolepsy and can be extremely debilitating, limiting performance in school or work, and limiting the ability to safely perform normal life tasks (e.g., driving a car, walking, or swimming). Even when awake, lapses in alertness can occur, and patients may have odd behaviors, such as writing gibberish or switching conversational topics mid-sentence. Type 1 narcolepsy is characterized by low levels of hypocretin in the cerebrospinal fluid. Cataplexy is a symptom unique to type 1 narcolepsy and manifested by a sudden loss of muscle tone due to the intrusion of REM sleep atonia during the waking period.

Approximately 0.02–0.18% of the US population live with narcolepsy.

Diagnosis is usually based on clinical history and confirmatory findings on multiple sleep latency testing. Clinicians often do not observe the cataplexy during a clinic visit, so its presence is established through clinical interviews of the patients or people who live with them. Cataplexy is usually bilateral. In adults, the episodes are almost always associated with laughter or other strong positive emotions. In children (but not adults), cataplexy can present with facial hypotonia (e.g., droopy eyelids, open mouth, protruding tongue), gait unsteadiness, and involuntary chewing movements. Anticipation of a reward is a common trigger for children. Episodes can occur relatively infrequently (e.g., once per month) or numerous times a day. They start suddenly and build in intensity, but they usually resolve in under 2 min.

Additional nonspecific symptoms are common. Inability to maintain sleep is a frequent complaint. Hypnagogic hallucinations (vivid dreamlike experiences at the transition from sleep to wake) and sleep paralysis are reported in 33–80% of narcolepsy patients. Sleep paralysis can be particularly distressing, because fully conscious patients are unable to open their eyes or move for several minutes. Blurred

vision and double vision are also common. Unexplained obesity at time of onset is another common symptom.

Associated clinical features that are common include periodic limb movements, REM disorder, sleep talking, and SRBDs. Approximately 20% of narcoleptics also have anxiety or panic disorders. An increased prevalence of depressive symptoms, but not necessarily clinical depression, has been observed [34].

Onset typically occurs between the ages of 10 and 25 years. Sleepiness is often the first symptom to appear. Cataplexy follows within 1 year, but it can appear before or after sleepiness, sometimes occurring up to 40 years later. Other symptoms appear at varied times over the course of the disease.

Diagnosis requires multiple sleep latency testing (MSLT) and polysomnography. Polysomnography is typically normal; however, it is useful in ruling other causes for excessive sleepiness and establishing an adequate amount of sleep prior to the MSLT. The MSLT requires the patient to take five 20-min naps during daytime hours, each at least 2 h apart. The time required to fall asleep is measured. The combination of a short latency to sleep onset of less than 8 min with two or more sleep onset REM periods (SOREM) is considered supportive of a diagnosis of narcolepsy; left untreated, narcolepsy type 1 is debilitating. Symptoms may be controlled with medications such as various oral stimulants, selective serotonin reuptake inhibitors (SSRIs), or serotonin and norepinephrine reuptake inhibitors (SNRIs).

3.4.2 Narcolepsy Type 2

Narcolepsy type 2 results in similar symptoms as type 1, but cataplexy is absent and cerebrospinal hypocretin levels are typically well above 100 pg/mL [35]. Patients report that daytime naps are refreshing. Like type 1, diagnosis requires an MSLT of 8 min or less and at least two SOREMPs (on MSLT or polysomnogram). Onset typically occurs during adolescence. Contributing factors are not well understood, but case reports suggest that head trauma and viral illnesses may contribute. Patients with relatives who have been diagnosed with type 1 epilepsy are more likely to be diagnosed with type 2, suggesting a genetic factor may play a role. Approximately 10% of patients develop cataplexy later in life; and in these cases, the diagnosis is changed to type 1.

The impact of narcolepsy type 2 on patients' lives can be profound. They may struggle in school and to perform at their jobs. Driving can be dangerous or even avoided completely due to the fear of having an accident. Depression and weight gain are common. Diagnosis may be delayed in kids, because parents focus on behavioral problems that are symptoms of the disorder. Hallucinations, insomnia, inattentiveness, and lack of energy which may lead to incorrect diagnoses are psychiatric illnesses.

3.4.3 Idiopathic Hypersomnia

Idiopathic hypersomnia (IH) is a chronic neurologic disorder of daytime sleepiness, accompanied by long sleep times, unrefreshing sleep, difficulty in awakening, cognitive dysfunction, and autonomic symptoms. Idiopathic hypersomnia is diagnosed when an individual has daytime sleepiness for at least 3 months, an MSLT with sleep latency of 8 min or less with no more than one sleep-onset REM period, and/or at least 11 h of sleep in a 24-h period documented by polysomnography or averaged across a 7 day period with actigraphy without cataplexy. It is a diagnosis of exclusion of other sleep disorders, and the cause is not known. An estimated 50% of individuals have a severe form of sleep inertia, in which they have difficulty waking up (even with alarm clock use), are irritable and confused, and frequently fall back asleep [35]. Even with long naps of an hour or more, approximately half to two-thirds of these individuals do not feel refreshed. The symptoms are not due to poor sleep efficiency or low hours of sleep, as they score high on both measures.

Some symptoms suggest a role of autonomic nervous system dysfunction: headache, orthostatic disturbance, perception of temperature discomfort, and peripheral cardiovascular issues (e.g., cold hands and feet). Sleep disorders and hypnagogic hallucinations are also common.

Idiopathic hypersomnias are likely a heterogenous spectrum of disorders. Earlier editions of the ICSD explicitly defined a subset of IH defined by long sleep times (i.e., >10 h for the main sleep period). Although current criteria do not distinguish those with long sleep from those without, long sleep times can be used to confirm an IH diagnosis [36].

3.4.4 Kleine-Levin Syndrome

Kleine-Levin syndrome is a rare disorder, occurring in 1–2 people per million. Recurrent hypersomnia is characterized by episodes of excessive sleep lasting from a few days to several weeks. Patients may sleep for at least 18 h a day and rise only to eat and void. The episodes are typically separated by weeks or months, during which normal sleep patterns are resumed. Excessive sleep may accompany behavior abnormalities, such as overeating, sexual disinhibition, and other mental disturbances [37]. Upper respiratory infections may be a precipitating factor for these episodes. Between episodes, symptoms are absent. Anterograde amnesia is common.

Adolescent males are the most at risk, and males are twice as likely as females to have the condition. The underlying cause is unknown, but episodes tend to decrease as individuals age. The median time to resolution is 14 years, except if the disease has an onset during adulthood, in which case it may take longer to resolve. Unfortunately, there are no consistently effective medications to control this disorder, but stimulants and mood stabilizers help some patients.

3.4.5 Hypersomnia Due to a Medical Disorder

In some cases, hypersomnia with excessive sleep at night or during the day can be attributed to an existing medical condition. The amount of daytime sleepiness varies, and individuals differentially report on how refreshing they find sleep. These patients do not have cataplexy or low hypocretin levels as is observed in narcolepsy, and SRBDs have been ruled out (or are well treated).

A range of medical conditions can be associated with hypersomnia. These include brain tumors, encephalitis, head trauma, hypothyroidism, stroke, certain rare genetic disorders, neurodegenerative diseases (e.g., Parkinson's disease), and system inflammation (e.g., autoimmune disease, cancer, and chronic infection).

3.4.6 Hypersomnia Due to a Medication or Substance

Certain prescription medications are known to cause excessive sleep and feelings of sleepiness. Patients may experience hypersomnia if they are taking anticholinergics, anticonvulsants, antipsychotics, barbiturates, benzodiazepines, and some antihistamines. Substance abuse that can cause this includes alcohol, barbiturates, benzodiazepines, opioids, and marijuana. Withdrawal of stimulants, such as caffeine and amphetamines, can also produce excessive sleepiness.

3.4.7 Hypersomnia Associated with a Psychiatric Disorder

Hypersomnia is known to be associated with psychiatric disorders, including mood disorders and conversion or undifferentiated somatoform disorder. Less frequently, adjustment disorder, personality disorders, or schizoaffective disorder can cause excessive sleepiness. In patients with major depression or seasonal affective disorder, hypersomnolence is common and varies across age, gender, and studies, ranging from 8.9% in childhood (6–13 years old) to a high rate of 75.8% in young adulthood [38].

3.4.8 Insufficient Sleep Syndrome

Insufficient sleep syndrome occurs when individuals fail to obtain the amount of sleep their body requires to maintain normal levels of wakefulness and alertness (average of 7 h per night but can be substantially more in some people). They are chronically sleep-deprived, but there is no physical cause for the lack of sleep or quality of sleep. Often, the patient fails to recognize the disparity in their sleep needs, but they may try to "make up" sleep on weekends or holidays.

3.5 Circadian Rhythm Sleep-Wake Disorders

Circadian rhythms are genetically determined; approximately 24-h biological rhythms are present in all living organisms. In order to stay in rhythm, the cycle needs to be reset each day with optimal sleep. Disorders or behaviors that impact the timing or quality of sleep can disrupt the internal timing. In general, circadian rhythm sleep-wake disorders (CRSWD) are characterized by difficulty falling or staying asleep, resulting in excessive sleepiness. They may have negative health, social, professional, and academic consequences. In the past two decades, rapid progress has been made in understanding how genes influence regulation of the sleep state and its circadian rhythmicity [39].

Multiple tools are used to assess sleep-wake patterns and how well they match endogenous circadian rhythms. Actigraphy, sleep logs, circadian chronotype questionnaires (to determine if an individual is naturally a "morning" or "evening" person), and physiologic measures (e.g., melatonin concentrations) can help measure if an individuals' sleep-wake patterns align with their natural circadian rhythm.

3.5.1 Delayed Sleep-Wake Phase Disorder

Delayed sleep-wake phase disorder (DSWPD) involves sleep-wake timing that is habitually delayed by 2 or more hours compared to socially accepted timings. This can make it difficult to obtain enough sleep. These individuals can usually obtain sufficient quality and duration of sleep if allowed to wake naturally, but they may have difficulty waking up at a socially acceptable time (e.g., work and school start). Attempts to fall asleep at "normal" times may cause frustration and anxiety or even lead to development of insomnia disorder. Attempts to cope with the sleep delay, including prescribed medications and substance abuse, do not cure the disorder.

Prevalence of DSWPD is estimated to range from 0.13% to 10% of the population [40]. Symptoms that develop in adolescence may last into later decades, but some improvement may be observed with age. The case is not well understood, but avoidance of certain social situations and chronic underlying medical conditions may play a role. Timed exposure to bright light (phototherapy) is an evidence-based treatment for delayed sleep-wake phase disorder (DSWPD). Melatonin administration can advance circadian phase and sleep timing in patients with DSWPD, although relapse may be high after discontinuation [41].

3.5.2 Advanced Sleep-Wake Phase Disorder

Advanced sleep-wake phase disorder (ASWPD) occurs when sleep-wake timing is habitually early by 2 h or more. Like DSWPD disorder, this can result in mismatched sleep and social schedules [41]. Individuals with ASWPD may experience early morning insomnia, as they try to force sleep until socially normal waking times. If they are unable to sleep at the earlier times their body naturally desires,

sleep deprivation and its effects will occur. ASWPD is more common with increasing age, which is not surprising given that circadian chronotype questionnaires trend toward increased morningness with increasing age. An estimated 1% of adults 40–64 years old have ASWPD. The cause is unclear, but factors may include an overly sensitive response to light during sleep, voluntarily induced sleep schedules, and a true circadian rhythm difference.

3.5.3 Irregular Sleep-Wake Rhythm Disorder

Irregular sleep-wake rhythm disorder (ISWD) is characterized by lack of a clear major sleep period [42]. Sleep-wake periods are variable, and this can lead to insomnia and excessive sleepiness, depending on the specific sleep-wake pattern and time of the day. The sleep-wake cycles are fragmented, and the longest period of continuous sleep is usually less than 4 h. These individuals may require several naps throughout the day.

ISWD is found in children and adults, and it is associated with neurodevelopmental and neurodegenerative disorders (e.g., Alzheimer's, Parkinson's, and Huntington's diseases). It is rarely observed in children with normal development, but it can be environmentally or behaviorally induced. ISWD in both children and adults should be distinguished from poor sleep hygiene, irregular sleep cycles, and comorbid conditions.

3.5.4 Non-24-h Sleep-Wake Rhythm Disorder

Non-24-h sleep-wake rhythm disorder is a circadian rhythm sleep-wake disorder characterized by an inability to entrain to the 24-h environment [43]. These individuals can have shorter clocks, but they are often longer than 24 h. Because they desynchronize from a 24-h cycle, the symptoms and their severity will vary depending on when sleep is attempted and required wake times of their external environment.

While first recognized in blind individuals without light perception, the disorder can also be seen in individuals with intact vision [44].

3.5.5 Shift Work Disorder

Any type of shift work schedule that includes waking or staying awake at night has the potential to interrupt normal sleep patterns and duration. Shifts that deviate significantly from the traditional work schedule inevitably require employees to work at times when sleep typically occurs (i.e., during the night) and sleep during the daytime. Many shift workers have trouble adapting to this scheduling, leading to poor or insufficient daytime sleep and excessive nocturnal sleepiness during their

work shifts [45]. The decreased quality and quantity of sleep obtained with shift work disorder can be a safety concern, as alertness may be compromised at work or while driving in the car between work and home. Mental health can also be negatively impacted. The disorder usually resolves when shift work ends, but it can be lasting for some individuals.

3.5.6 Jet Lag Disorder

Jet lag disorder occurs when individuals' sleep-wake schedule is out of sync with their circadian clock, due to a change in time zone. In addition to the commonly recognized symptoms of sleep pattern disturbances and decreased alertness, jet lag disorder can lead to a feeling of general malaise and gastrointestinal discomfort in some individuals. The severity of symptoms depends on the number of time zones traveled, ability to sleep during travel, exposure to circadian cues in the new time zone, and individual tolerance to the effects of staying awake during biological night. Most people find traveling to the east (advancing circadian rhythms and sleep times) more difficult than traveling to the west [45].

3.5.7 Circadian Sleep-Wake Disorder Not Otherwise Specified

Patients who have altered circadian sleep-wake patterns that is not attributable to a CRSWD are grouped in this category. Changes in circadian sleep-wake patterns are usually due to underlying medical conditions.

3.6 Parasomnias

Parasomnias are sleep disorders characterized by undesirable physical movements, emotions, dreams, or sensations that occur during sleep or while transitioning to sleep or wake states. Parasomnias may result in injuries, disrupted sleep, and negative psychosocial effects for the individuals or their bed partner. The three states of consciousness are wake, non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep. There are three stages of NREM sleep during which the individual falls into a progressively deeper sleep. REM sleep is a brief stage during which dreams occur.

The transitions between wake, NREM, and REM sleep stages are controlled by aminergic (e.g., serotonin, dopamine, and norepinephrine) and cholinergic (e.g., acetylcholine) neurochemical bias, CNS activation, and external inputs. In a normal individual, the circadian rhythm controls these processes. Parasomnias occur due to disruptions of these smooth transitions between the sleep stages or between wakefulness and sleep.

3.6.1 NREM-Related Parasomnias

3.6.1.1 Disorders of Arousal

Several parasomnias result in a confused, incomplete arousal state during NREM: confusion arousals, sleepwalking, and sleep terrors. All these NREM-related parasomnias share genetic inheritance patterns, partial arousal from deep sleep, and similar precipitating factors (sleep deprivation, stress, external stimuli).

There are common diagnostic criteria for NREM-related disorders of arousal. Individuals have recurring incomplete awakenings during sleep. When others try to interact with them during an episode, they either do not respond or respond inappropriately. They do not have vivid dreams during these episodes, and they do not remember them happening (or remember very little). The symptoms are unable to be explained by other medical conditions or substance use. Episodes are generally brief, but they can last up to 30 or 40 min, especially in children.

Confusional Arousals

Individuals with this disorder have episodes of confused thoughts or actions while sleeping. They may sit up, but they do not get out of bed or feel scared. Physical symptoms, such as increased heart or respiratory rate and sweating, are absent. Eyes may be open, but the individuals are not aware of their surroundings or actions.

Sleepwalking

These individuals get out of bed and walk around, and they may engage in more complex activities. They are unaware that this is happening, despite the appearance to observers that they are awake. Speech is slowed and confused. This can be dangerous if they fall or bump into objects. A recent meta-analysis showed that the estimated lifetime prevalence of sleepwalking is 6.9% [46].

Sleep Terrors

Individuals with sleep terrors awake with intense fear, accompanied by increased heart and respiratory rate and sweating. They can stay in bed or sleepwalk. Attempts to console will be unsuccessful and take several minutes to resolve, especially in young children. Attempts to intervene during an episode can result in violent reactions.

Disorders of arousal are common in children and young adults. Approximately 17% of children 3–13 years of age have confusion arousal, and the lifetime prevalence is estimated to be nearly 20%. Up to 40% of children aged 6–16 years sleepwalk, but only 4% of adults do. One-quarter of children have intermittent sleep terrors, but these are rare in adults (2% or less).

3.6.1.2 Sleep-Related Eating Disorder

Sleep-related eating disorder (SRED) results in involuntary food and beverage intake during sleep arousals. Individuals vary in their level or recall of the episode, even within the same individual. This can be dangerous, because individuals who are not fully aware can try to use sharp kitchen utensils or they may

consume unsafe solids or liquids (e.g., cleaning solutions or inedible objects). Uncontrollable weight gain can be a major problem for some individuals with this condition.

3.6.2 REM-Related Parasomnias

3.6.2.1 REM Sleep Behavior Disorder

Rapid eye movement sleep behavior disorder (RBD) is diagnosed by a clinical history of dream enactment accompanied by loss of atonia in REM sleep demonstrated on polysomnography (rapid eye movement sleep without atonia) [47]. Periodic limb movements are common and may prevent bed partners from sleeping. However, the individual with RBD rarely feels excessively tired during the day.

RBD is rare (<1% prevalence) [48] and occurs predominantly in men over the age of 50 years. When the disorder occurs in adults younger than 50 years, the episodes tend to be less aggressive and less violent, possibly related to the greater presence of females in this demographic. Clinical assessment shows excessive muscle tone on electromyogram, and episodes occur during REM sleep on polysomnography. After an episode, the individuals become alert quickly and will usually recall a dream matching their observed sleep behaviors. Episodes occur approximately 90 min of sleep onset, corresponding with the time of REM sleep. Several other disorders can cause complex, sometimes violent, sleep-related behaviors. When diagnosing RBD, sleepwalking, sleep terrors, OSA, SRDs, and nocturnal seizures must be ruled out.

RBD onset can be gradual or rapid, and it may progress over time. When RBD onset occurs in men over 50 years of age and no other known cause (e.g., medication use) is causing the symptoms, there is a high risk (>80%) of future development of a neurodegenerative disorder, such as Parkinson's disease, multiple system atrophy, or dementia [49]. When RBD onset occurs during childhood, it is usually associated with type 1 narcolepsy, CNS structural abnormalities, or the use of psychotropic medications [50, 51].

3.6.2.2 Recurrent Isolated Sleep Paralysis

Recurrent isolated sleep paralysis describes when an individual cannot perform voluntary movements when falling asleep or waking. Consciousness is fully preserved during these episodes, which can last several minutes. Hallucinations may occur, adding to the sense of anxiety that can occur. Episodes can sometimes be interrupted by auditory or physical stimulation. Disrupted sleep and mental stress are thought to be precipitating factors. There are no known consequences, aside from anxiety over the episode.

3.6.2.3 Nightmare Disorder

Individuals with nightmare disorder suffer repeated, highly upsetting, vivid dreams. Emotions are strongly negative and can span anxiety, fear, anger, and embarrassment. These dreams usually occur during REM sleep and may awaken the individual, who may be able to recount the dream in detail.

Nightmares can start after a traumatic event, and the individual may be tormented by reexperiencing the event repeatedly. Up to 80% of individuals with post-traumatic stress disorder have recurrent nightmares within 3 months of the traumatic event. Nightmares are very common in children, with up to 75% experiencing them occasionally. It can be difficult to separate these from confusional arousals or sleep terrors. Fortunately, frequent nightmares are not common, with prevalence estimates ranging from 1% to 5%. In the general adult population, 2–8% of people have frequent nightmares.

3.6.3 Other Parasomnias

3.6.3.1 Exploding Head Syndrome

Exploding head syndrome describes a sudden, loud noise or perceived violent (painless) explosion inside the head. These sensations are not real and occur when the patients are falling asleep or waking in the middle of the night. These sensations may be frightening, because they induce worries of a serious clinical issue, such as stroke. However, no physical issues are found in these patients.

3.6.3.2 Sleep-Related Hallucinations

Some individuals experience hallucinations when waking or falling asleep. It can be difficult for patients to know if the hallucinations were real or not, as they can be complex and vivid. The hallucinations may last for a few minutes, despite the patient being clearly awake. Hallucinations can occur concurrently with sleep paralysis. Sleep-related hallucinations are more common in younger individuals and in people who have used alcohol or drugs, have anxiety, or perceive insufficient sleep.

3.6.3.3 Sleep Enuresis

Sleep enuresis (SE) describes a condition in individuals who are at least 5 years of age who have repeated involuntary urination at least twice a week while sleeping. Primary SE is defined in patients who have these symptoms for six or more consecutive months and who had never been dry at night. Secondary SE is defined when a child or adult who was previously dry at night for six consecutive months begins voiding during sleep. SE is thought to result from difficulty waking up in response to an urge to urinate.

SE occurs in 15–20% of children aged 5 years and 2.1% of older adults. The etiology of SE is complicated, and it is usually not possible to identify the factor triggering SE on any given night and sleep stage. Difficulty staying asleep is thought to play a role in most cases of primary SE, while bladder overactivity or control is thought to be important for many cases of secondary SE. Sleep disorders that result in fragmented sleep are associated with SE, so treating these disorders may cure or reduce the SE symptoms.

3.6.3.4 Parasomnia Due to a Medical Disorder

Parasomnia can sometimes be clearly attributed to an underlying medical condition. This term is reserved for cases where another parasomnia cannot be specifically diagnosed.

3.6.3.5 Parasomnia Due to a Medication or Substance

Parasomnia can sometimes be clearly attributed to a medication use, especially when there is a close temporal relationship between drug exposure and the onset of symptoms. A strong likelihood of a causal relationship can be assumed when withdrawal of the offending drug resolves the parasomnia symptoms. This term is reserved for cases where another parasomnia cannot be specifically diagnosed.

SSRIs, antidepressants, MAOIs, and cholinergic treatments have been associated with parasomnia. Abuse of caffeine and alcohol, or withdrawal from some illicit drugs (e.g., cocaine, amphetamine, barbiturates), can result in parasomnia.

3.6.3.6 Parasomnia, Unspecified

This term is used when symptoms of a parasomnia are present, but a specific parasomnia cannot be diagnosed, or enough information has not been collected to allow meeting specific diagnostic criteria.

3.6.3.7 Isolated Symptoms and Normal Variants

Sleep Talking

Sleep talking describes talk during REM or NREM sleep. The talking can vary in comprehensibility. It may be associated with parasomnias or be idiopathic. The lifetime prevalence is high with 66% of people experiencing it at some point in their lives. The onset and course are unknown.

3.7 Sleep-Related Movement Disorders

Sleep-related movement disorders (SRMDs) involve involuntary or uncontrollable physical movements that disturb sleep or falling asleep. While complex physical movements (e.g., carrying out a task) may also be observed with parasomnias, those associated with SRMDs are simple and repetitive.

3.7.1 Restless Leg Syndrome

Restless leg syndrome is a disorder in which the patient complains of an uncomfortable urge to move or stretch the legs and arms. Patients often report uncomfortable sensations deep inside the limbs, using words to describe them such as twitch, painful, and numb. These sensations are worse when resting, improve with movement, and occur mostly at night.

Individuals with restless leg syndrome suffer from disrupted sleep and may have excessive daytime fatigue. The most common reason these patients seek help is for disturbed sleep, although they are often less fatigued than would be expected by the amount of sleep disruption they experience. This suggests that hyperarousal plays a role in the disorder.

Restless leg syndrome is found across all age groups, although it is most common in the third and fourth decades. An estimated 5–15% of individuals of Caucasian descent are affected with low incidence among Asians and Hispanics. Women over the age of 35 are twice as likely to have RLS compared to men [52]. Known precipitating factors include chronic renal failure, immobility, iron deficiency, and pregnancy. Antihistamines and antidepressants have also been shown to trigger or aggravate this condition.

3.7.2 Periodic Limb Movement Disorder

Periodic limb movement disorder involves episodes of repetitive limb movements that occur during sleep and cannot be attributed to another cause. These movements interrupt sleep and cause daytime fatigue. Periodic limb movements affect the legs more often than the arms. Periodic limb movements in sleep may also be observed as an isolated polysomnographic finding that may not be associated with any clinical symptoms.

3.7.3 Sleep-Related Leg Cramps

Sleep-related leg cramps are sudden, strong involuntary muscle contractions that occur during sleep. They can last several seconds and result in pain. Sleep can be disrupted, and the individuals may need to spend several minutes massaging or stretching the area for them to resolve.

3.7.4 Sleep-Related Bruxism

Bruxism is defined as repetitive teeth grinding and jaw clenching. Abnormal wear of the tooth surfaces and pain in the teeth or jaws are symptoms. The tooth grinding can be so severe that teeth fracture or the inside of the mouth is cut. Temporal headaches may also occur. The noise can be loud and annoying, which interrupts the sleep of the individuals or their bed partner.

Bruxism during sleep is most common in childhood, with approximately 14–20% of children affected. The prevalence decreases with age, with only 8% of middle-aged adults and 3% of older adults affected [53]. Individuals who are highly motivated and highly watchful may be predisposed.

3.7.5 Sleep-Related Rhythmic Movement Disorder

Sleep-related rhythmic movement disorder involves rhythmic motor behaviors that are repetitive. They usually occur during sleep or falling asleep. The entire body may rock, or only part of the body moves back and forth (e.g., head banging or lifting of the upper torso). Episodes usually last less than 15 min. It is more common in children than adults, with 59% of infants exhibiting body rocking, heading banging, or head rolling. The incidence declines with development and is only 5% by 5 years of age. The movements may be used as methods of self-soothing and they may promote motor development [54].

3.7.6 Benign Sleep Myoclonus of Infancy

Benign sleep myoclonus of infancy involves repetitive jerky myoclonic movements during sleep. It may be mistaken for epilepsy; however, unlike epilepsy, the movements occur exclusively during sleep. It resolves without intervention in nearly all infants by 12 months of age.

3.7.7 Propriospinal Myoclonus at Sleep Onset

Propriospinal myoclonus at sleep onset involves myoclonic jerks during transitions between sleeping and wakefulness when the body is relaxed. The jerks occur suddenly and start from the spinally innervated muscles (e.g., abdominal muscles) and then spread to the limbs and neck. The jerks disappear when externally stimulated or awakened, but the timing of their occurrence can result in difficulty falling or staying asleep.

3.7.8 Sleep-Related Movement Disorder Due to a Medical Disorder

Many neurological conditions are associated with movements during sleep, and sometimes the abnormal nighttime movements are noted before the other neurological symptoms. This is a diagnosis used when unusual movements during sleep cannot be attributed to a specific movement disorder.

3.7.9 Sleep-Related Movement Disorder Due to a Medication or Substance

This is a diagnosis used when unusual movements during sleep cannot be attributed to a specific movement disorder, but they are associated with the use of a medication or substance.

3.7.10 Sleep-Related Movement Disorder, Unspecified

This diagnosis is used when patients have unusual movements during sleep that do not meet the diagnostic criteria for another SRMD.

3.7.11 Isolated Symptoms and Normal Variants

3.7.11.1 Excessive Fragmentary Myoclonus

Excessive fragmentary myoclonus involves small movements of the muscles at the fingers, toes, or corners of the mouth. It may be observed only incidentally during polysomnography, and there is no known clinical consequence.

3.7.11.2 Hypnagogic Foot Tremor and Alternating Leg Muscle Activation

When transitioning to sleep, some individuals rhythmically move their feet or toes during drowsiness or light sleep. It can occur in one or both feet, and it may alternate sides. There are no known clinical consequences.

3.7.11.3 Sleep Starts (Hypnic Jerks)

Hypnic jerks are the sudden, brief contractions of the body that occur at sleep onset. Isolated or multiple muscles can contract; and other sensory perceptions can be present (e.g., loud noise or flashing light). These occur in up to 70% of individuals who are not generally problematic unless they occur with such intensity or frequency that insomnia results.

References

1. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest. 2014;146(5):1387–94. https://doi.org/10.1378/chest.14-0970. PMID: 25367475.
2. Roth T. Insomnia: definition, prevalence, etiology, and consequences. J Clin Sleep Med. 2007;3(5 Suppl):S7–10. PMID: 17824495; PMCID: PMC1978319.
3. Pavlova MK, Latreille V. Sleep disorders. Am J Med. 2019;132(3):292–9. https://doi.org/10.1016/j.amjmed.2018.09.021. Epub 2018 Oct 4. PMID: 30292731.
4. Buysse DJ. Insomnia. JAMA. 2013;309(7):706–16. https://doi.org/10.1001/jama.2013.193. PMID: 23423416; PMCID: PMC3632369.
5. Riemann D, Nissen C, Palagini L, Otte A, Perlis ML, Spiegelhalder K. The neurobiology, investigation, and treatment of chronic insomnia. Lancet Neurol. 2015;14(5):547–58. https://doi.org/10.1016/S1474-4422(15)00021-6. Epub 2015 Apr 12. PMID: 25895933.
6. Sutton EL. Insomnia. Med Clin North Am. 2014;98(3):565–81. https://doi.org/10.1016/j.mcna.2014.01.008. PMID: 24758961.
7. Sexton CE, Sykara K, Karageorgiou E, Zitser J, Rosa T, Yaffe K, Leng Y. Connections between insomnia and cognitive aging. Neurosci Bull. 2020;36(1):77–84. https://doi.org/10.1007/s12264-019-00401-9. Epub 2019 Jun 20. PMID: 31222500; PMCID: PMC6940406.
8. Momin RR, Ketvertis K. Short term insomnia. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020. PMID: 32119403.

9. Nunes ML, Bruni O. Insomnia in childhood and adolescence: clinical aspects, diagnosis, and therapeutic approach. J Pediatr (Rio J). 2015;91(6 Suppl 1):S26–35. https://doi.org/10.1016/j.jped.2015.08.006. Epub 2015 Sep 21. PMID: 26392218.
10. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. Lancet. 2014;383(9918):736–47.
11. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):136–43. PMID: 18250205.
12. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, Hamilton GS, Dharmage SC. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev. 2017;34:70–81. https://doi.org/10.1016/j.smrv.2016.07.002. Epub 2016 Jul 18. PMID: 27568340.
13. de Sousa AG, Cercato C, Mancini MC, Halpern A. Obesity and obstructive sleep apnea-hypopnea syndrome. Obes Rev. 2008;9(4):340–54. https://doi.org/10.1111/j.1467-789X.2008.00478.x. Epub 2008 Mar 18. PMID: 18363635.
14. Lam B, Ip MSM, Tench E, et al. Craniofacial profile in Asian and white subjects with obstructive sleep apnoea. Thorax. 2005;60:504–10.
15. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013;177(9):1006–14. PMID: 23589584.
16. Garg RK, Afifi AM, Garland CB, Sanchez R, Mount DL. Pediatric obstructive sleep apnea: consensus, controversy, and craniofacial considerations. Plast Reconstr Surg. 2017;140(5):987–97. https://doi.org/10.1097/PRS.0000000000003752. PMID: 29068938.
17. Gozal D, Kheirandish-Gozal L, Kaditis AG. Home sleep testing for the diagnosis of pediatric obstructive sleep apnea: the times they are a changing...! Curr Opin Pulm Med. 2015;21(6):563–8. https://doi.org/10.1097/MCP.0000000000000205. PMID: 26390329.
18. Tan HL, Gozal D, Kheirandish-Gozal L. Obstructive sleep apnea in children: a critical update. Nat Sci Sleep. 2013;5:109–23. PMID: 24109201.
19. Marin-Oto M, Vicente EE, Marin JM. Long term management of obstructive sleep apnea and its comorbidities. Multidiscip Respir Med. 2019;14:21. https://doi.org/10.1186/s40248-019-0186-3. PMID: 31312448; PMCID: PMC6609382.
20. Eckert DJ, Jordan AS, Merchia P, Malhotra A. Central sleep apnea: pathophysiology and treatment. Chest. 2007;131(2):595–607. https://doi.org/10.1378/chest.06.2287. PMID: 17296668.
21. Javaheri S, Barbe F, Campos-Rodriguez F, Dempsey JA, Khayat R, Javaheri S, Malhotra A, Martinez-Garcia MA, Mehra R, Pack AI, Polotsky VY, Redline S, Somers VK. Sleep apnea: types, mechanisms, and clinical cardiovascular consequences. J Am Coll Cardiol. 2017;69(7):841–58. https://doi.org/10.1016/j.jacc.2016.11.069. PMID: 28209226; PMCID: PMC5393905.
22. Rudrappa M, Modi P, Bollu PC. Cheyne stokes respirations. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020. PMID: 28846350.
23. Burgess KR, Ainslie PN. Central sleep apnea at high altitude. Adv Exp Med Biol. 2016;903:275–83. https://doi.org/10.1007/978-1-4899-7678-9_19. PMID: 27343103.
24. Van Ryswyk E, Antic NA. Opioids and sleep-disordered breathing. Chest. 2016;150(4):934–44. https://doi.org/10.1016/j.chest.2016.05.022. Epub 2016 Jun 1. PMID: 27262224.
25. Hoffman M, Schulman DA. The appearance of central sleep apnea after treatment of obstructive sleep apnea. Chest. 2012;142(2):517–22. https://doi.org/10.1378/chest.11-2562. PMID: 22871763.
26. Zhao J, Gonzalez F, Mu D. Apnea of prematurity: from cause to treatment. Eur J Pediatr. 2011;170(9):1097–105. https://doi.org/10.1007/s00431-011-1409-6. Epub 2011 Feb 8. PMID: 21301866; PMCID: PMC3158333.
27. Casey KR, Cantillo KO, Brown LK. Sleep-related hypoventilation/hypoxemic syndromes. Chest. 2007;131(6):1936–48. https://doi.org/10.1378/chest.06-2334. PMID: 17565028.
28. Iftikhar IH, Roland J. Obesity hypoventilation syndrome. Clin Chest Med. 2018;39(2):427–36. https://doi.org/10.1016/j.ccm.2018.01.006. PMID: 29779600.

29. Athayde RAB, Oliveira Filho JRB, Lorenzi Filho G, Genta PR. Obesity hypoventilation syndrome: a current review. J Bras Pneumol. 2018;44(6):510–8. https://doi.org/10.1590/S1806-37562017000000332. PMID: 30726328; PMCID: PMC6459748.
30. Maloney MA, Kun SS, Keens TG, Perez IA. Congenital central hypoventilation syndrome: diagnosis and management. Expert Rev Respir Med. 2018;12(4):283–92. https://doi.org/10.1080/17476348.2018.1445970. Epub 2018 Feb 28. PMID: 29486608.
31. Patwari PP, Wolfe LF. Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation: review and update. Curr Opin Pediatr. 2014;26(4):487–92. https://doi.org/10.1097/MOP.0000000000000118. PMID: 24914877.
32. Idiopathic congenital central hypoventilation syndrome: diagnosis and management. American Thoracic Society. Am J Respir Crit Care Med. 1999;160(1):368–73. https://doi.org/10.1164/ajrccm.160.1.16010. PMID: 10390427.
33. De Meyer MMD, Jacquet W, Vanderveken OM, Marks LAM. Systematic review of the different aspects of primary snoring. Sleep Med Rev. 2019;45:88–94. https://doi.org/10.1016/j.smrv.2019.03.001. Epub 2019 Mar 13. PMID: 30978609.
34. Scammell TE. Narcolepsy. N Engl J Med. 2015;373(27):2654–62. https://doi.org/10.1056/NEJMra1500587. PMID: 26716917.
35. Bassetti CLA, Adamantidis A, Burdakov D, Han F, Gay S, Kallweit U, Khatami R, Koning F, Kornum BR, Lammers GJ, Liblau RS, Luppi PH, Mayer G, Pollmächer T, Sakurai T, Sallusto F, Scammell TE, Tafti M, Dauvilliers Y. Narcolepsy—clinical spectrum, aetiopathophysiology, diagnosis and treatment. Nat Rev Neurol. 2019;15(9):519–39. https://doi.org/10.1038/s41582-019-0226-9. Epub 2019 Jul 19. PMID: 31324898.
36. Kornum BR, Knudsen S, Ollila HM, Pizza F, Jennum PJ, Dauvilliers Y, Overeem S. Narcolepsy. Nat Rev Dis Primers. 2017;3:16100. https://doi.org/10.1038/nrdp.2016.100. PMID: 28179647.
37. Trotti LM. Idiopathic hypersomnia. Sleep Med Clin. 2017;12(3):331–44. https://doi.org/10.1016/j.jsmc.2017.03.009. Epub 2017 Jun 16. PMID: 28778232; PMCID: PMC5558858.
38. Dauvilliers Y, Buguet A. Hypersomnia. Dialogues Clin Neurosci. 2005;7(4):347–56. PMID: 16416710; PMCID: PMC3181743.
39. Barateau L, Lopez R, Franchi JA, Dauvilliers Y. Hypersomnolence, hypersomnia, and mood disorders. Curr Psychiatry Rep. 2017;19(2):13. https://doi.org/10.1007/s11920-017-0763-0. PMID: 28243864.
40. Chong SYC, Xin L, Ptáček LJ, Fu YH. Disorders of sleep and circadian rhythms. Handb Clin Neurol. 2018;148:531–8. https://doi.org/10.1016/B978-0-444-64076-5.00034-X. PMID: 29478598.
41. Magee M, Marbas EM, Wright KP Jr, Rajaratnam SM, Broussard JL. Diagnosis, cause, and treatment approaches for delayed sleep-wake phase disorder. Sleep Med Clin. 2016;11(3):389–401. https://doi.org/10.1016/j.jsmc.2016.05.004. Epub 2016 Jul 16. PMID: 27542884.
42. Culnan E, McCullough LM, Wyatt JK. Circadian rhythm sleep-wake phase disorders. Neurol Clin. 2019;37(3):527–43. https://doi.org/10.1016/j.ncl.2019.04.003. Epub 2019 May 29. PMID: 31256787.
43. Oyegbile T, Videnovic A. Irregular sleep-wake rhythm disorder. Neurol Clin. 2019;37(3):553–61. https://doi.org/10.1016/j.ncl.2019.04.002. Epub 2019 May 29. PMID: 31256789.
44. Abbott SM. Non-24-hour sleep-wake rhythm disorder. Neurol Clin. 2019;37(3):545–52. https://doi.org/10.1016/j.ncl.2019.03.002. Epub 2019 Apr 30. PMID: 31256788.
45. Cheng P, Drake C. Shift work disorder. Neurol Clin. 2019;37(3):563–77. https://doi.org/10.1016/j.ncl.2019.03.003. Epub 2019 May 7. PMID: 31256790.
46. Herxheimer A. Jet lag. BMJ Clin Evid. 2014;2014:2303. PMID: 24780537; PMCID: PMC4006102.
47. Stallman HM. Assessment and treatment of sleepwalking in clinical practice. Aust Fam Physician. 2017;46(8):590–3. PMID: 28787563.
48. St Louis EK, Boeve BF. REM sleep behavior disorder: diagnosis, clinical implications, and future directions. Mayo Clin Proc. 2017;92(11):1723–36. https://doi.org/10.1016/j.mayocp.2017.09.007. Epub 2017 Nov 1. PMID: 29101940; PMCID: PMC6095693.

49. Boeve BF. REM sleep behavior disorder: updated review of the core features, the REM sleep behavior disorder-neurodegenerative disease association, evolving concepts, controversies, and future directions. Ann N Y Acad Sci. 2010;1184:15–54. https://doi.org/10.1111/j.1749-6632.2009.05115.x. PMID: 20146689; PMCID: PMC2902006.
50. Chiaro G, Calandra-Buonaura G, Cecere A, Mignani F, Sambati L, Loddo G, Cortelli P, Provini F. REM sleep behavior disorder, autonomic dysfunction and synuclein-related neurodegeneration: where do we stand? Clin Auton Res. 2018;28(6):519–33. https://doi.org/10.1007/s10286-017-0460-4. Epub 2017 Sep 4. PMID: 28871332.
51. Kotagal S. Rapid eye movement sleep behavior disorder during childhood. Sleep Med Clin. 2015;10(2):163–7. https://doi.org/10.1016/j.jsmc.2015.02.004. Epub 2015 Mar 12. PMID: 26055864.
52. Gonzalez-Latapi P, Malkani R. Update on restless legs syndrome: from mechanisms to treatment. Curr Neurol Neurosci Rep. 2019;19(8):54. https://doi.org/10.1007/s11910-019-0965-4. PMID: 31250128.
53. Mayer P, Heinzer R, Lavigne G. Sleep bruxism in respiratory medicine practice. Chest. 2016;149(1):262–71. https://doi.org/10.1378/chest.15-0822. Epub 2016 Jan 6. PMID: 26225899.
54. Gwyther ARM, Walters AS, Hill CM. Rhythmic movement disorder in childhood: an integrative review. Sleep Med Rev. 2017;35:62–75. https://doi.org/10.1016/j.smrv.2016.08.003. Epub 2016 Aug 26. PMID: 27884450.