

EDITORIAL

Sleep Disorders in Childhood and Adolescence

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INTRODUCTION

By early school age, the average child has spent nearly half of his/her life asleep. In fact, it can be argued that sleep is the primary activity of the brain during early development. By two years of age, the average child has spent almost 10,000 hours (nearly 14 months) asleep (1). In these two years, the brain has reached 90% of adult size (2), and the child has attained remarkable complexity in areas such as physical abilities, cognitive skills and socio-emotional development (3,4). Based on this evidence, a strong argument can be made that sleep must serve some essential aspect of brain function. Despite the ubiquity of this state in young children, the basic function of sleep and its relationship to development remain a mystery.

Sleep-related problems occur frequently in children and adolescents. Numerous well-controlled studies have documented prevalence rates for significant sleep problems ranging from 20% to 30% in community samples as well as in pediatric clinic populations (5-11). In many cases, disturbed sleep is simply an isolated mild behavioral problem. In other cases, however, sleep-related symptoms may represent a serious disorder, such as narcolepsy (12), or may be one component in a larger set of behavioral or emotional symptoms (13). Also, the relationship between sleep and behavioral/emotional problems appears to be complex; behavioral and emotional problems can contribute to sleep disturbances and conversely, sleep difficulties can adversely affect mood and behavior. Given these complexities, careful assessment and appropriate treatment decisions are warranted when a youngster has any of the above described problems.

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ASSESSMENT OF SLEEP COMPLAINTS IN CHILDREN AND ADOLESCENTS

The initial assessment of a child or adolescent with sleep complaints involves a thorough interview of the patient and parents. It is important to obtain developmentally appropriate and culturally sensitive information focused on both sleep and waking behaviors. This should include sleep/wake habits, bedtime routines, details regarding nighttime behaviors (including parental responses to arousals), wake-up times, morning routines, and symptoms of daytime sleepiness or irritability. Duration, frequency and pattern of symptoms, including timing, changes with weekends and vacations, and changes with stresses or special events should be assessed. Obtaining information on past medical history, medications (especially stimulants, asthma medications, anti-seizure drugs and sedatives), as well as family history of sleep problems and current family sleep practices, is also important. Structured sleep diaries and sleep habits questionnaires serve as useful adjuvants. Parents and/or child should record the details of bedtime, estimated time to fall asleep and wake-up times. When events such as night terrors interrupt sleep, both actual clock time of the event and time since sleep onset are important to determine. Specific questions about snoring, stopped breathing, and sleep-related behaviors such as walking, talking, enuresis, head banging, and body rocking need to be inquired.

There appear to be developmental factors related to both the biological maturation of the sleep-wake state and the physiological development, that interact at certain age periods to increase the risk for specific sleep disorders. During infancy, rapid eye movement (REM) sleep predominates, and since REM sleep is associated with arousals, infants are likely to manifest disorders associated with sleep maintenance. In the preschool and school-age years, non-REM sleep (particularly stages III and IV) predominates, leading to

sleep problems occurring at times of transition from deep sleep to REM sleep. During adolescence, increased physiological need for sleep conflicts with more academic, social and work demands, thus disrupting the regularity of sleep-wake schedules as well as reducing the amount of daily sleep (14).

COMMON SLEEP DISORDERS IN YOUNGSTERS

Two universal systems are available for the categorization of sleep disorders, namely, the International Classification of Sleep Disorders: Diagnostic and Coding Manual (ICSD) (15) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (16). The DSM-IV is more appropriate for classifying sleep disorders in adults than in youngsters. Although the ICSD system has been found to be more useful in the categorization of sleep disorders across the life span, the description of pediatric disorders is not comprehensive in this manual.

In the following sections, a brief review of the commonly observed sleep disorders in the pediatric population and treatment guidelines for these disorders will be provided. For a more comprehensive review, the reader is referred to additional publications (17,18). As delineated in the ICSD, there are three major categories of child and adolescent sleep disorders, namely, dyssomnias, parasomnias, and sleep disorders associated with medical or psychiatric disorders.

Dyssomnias

Dyssomnias are sleep disorders characterized by insufficient, excessive, or inefficient sleep. Frequently occurring dyssomnias in the child and adolescent population are outlined in Table 1. Intrinsic dyssomnias originate from causes within the body, extrinsic dyssomnias require external factors to initiate and maintain the disorder, and circadian rhythm dyssomnias are characterized by inappropriate timing of sleep within the 24-hour clock.

Intrinsic Dyssomnias: Two intrinsic dyssomnias that commonly affect children and adolescents are obstructive sleep apnea syndrome (OSAS) and narcolepsy. During sleep, and particularly in REM sleep, there is a considerable drop in muscle tone. This decreased tone affects the musculature maintaining the airway and the muscles assisting in respiration. In susceptible individuals, these physiological changes can lead to OSAS. In adults, the clinical picture of OSAS is typically an obese, hypersomnolent, lethargic individual. In children, the clinical appearance is quite different.

The most common cause of OSAS in children is hypertrophy of adenoids and tonsils. Congenital malformations of the mouth, palate and oropharynx also predispose to OSAS. Many of these children have little difficulty breathing when awake despite significant problems during sleep. In its severe form, the apneic episodes during sleep can result in nocturnal hypoxemia and bradycardia, and can lead to pulmonary hypertension with cor pulmonale. More commonly in children, however, they result in frequent brief arousals from sleep. The diagnosis of OSAS often can be made clinically, and many pediatric otolaryngologists are experienced in assessing children with signs of snoring and disturbed sleep for evidence of adenoidal hypertrophy. Treatment in children with OSAS commonly involves removal of enlarged, obstructing tonsils and adenoids. In other cases, nasal C-PAP (continuous positive airway pressure) or oral devices to maintain airway patency may be indicated. Other surgical treatments for severe, refractory cases without adenoidal obstruction include uvulopalatopharyngoplasty, mandibular and maxillary advancement, and tracheostomy.

Narcolepsy is a chronic disorder characterized by excessive daytime sleepiness and other abnormally timed elements of REM sleep physiology, such as muscle paralysis (cataplexy and sleep paralysis) and dream imagery (hypnogogic and hypnopopic hallucinations). Narcolepsy affects about 0.02% to 0.06% of the general population in the

Table 1. Commonly Observed Dyssomnias in Children and Adolescents

Intrinsic Sleep Disorders	Extrinsic Sleep Disorders	Circadian Rhythm Sleep Disorders
Obstructive sleep apnea syndrome Narcolepsy Idiopathic hypersomnia	Protodyssomnia of infancy Insomnia of childhood	Delayed sleep phase syndrome

United States and Europe, and it may be more prevalent in certain ethnic groups, such as the Japanese (0.16% to 0.18%) (19). Adolescence has been reported to be the peak age of onset for narcolepsy (12). A genetic component of this disorder has been established in both humans and canines. In humans, a strong link with the human leukocyte antigen (HLA) class II was established in the 1980s (20).

Across various ethnic groups, more than 85% of narcoleptic individuals with definite cataplexy share a specific HLA allele HLA DQB1*0602 (most commonly in combination with HLA DR2) compared with 12% to 38% of the general population (19). Because of the close association with the HLA system, it has been suggested that narcolepsy may be an autoimmune disease (21). A recent report, however, suggests the contribution of non-HLA genes (for example, chromosome 4p13-q21) even in cases with HLA association (22). Also, there is a suggestion that the cells that make the neuropeptides, hypocretins (orexins), might be involved in arousal state control and that genetic mutations of these cells might lead to narcolepsy and other disorders of arousal (23). A deletion mutation of the hypocretin (orexin) receptor 2 gene (*Hcrtr2/OX2R*), resulting in a truncated, non-functional receptor, has been identified in large breeding dogs suffering from narcolepsy (24).

The diagnosis of narcolepsy requires evaluation in a sleep laboratory. Individuals with narcolepsy show early REM periods near sleep onset, fragmented nighttime sleep, excessive daytime sleepiness in objective nap studies, and sleep-onset REM periods in naps. Treatment remains symptomatic and requires a combination of behavioral interventions and pharmacotherapy (12). Following a regular sleep/wake schedule to obtain optimal sleep is essential and this often involves scheduling daytime naps at regular intervals. Short-acting stimulant medication and modafinil are generally used for the treatment of daytime sleepiness (25). Cataplexy can be controlled by medications with noradrenergic reuptake-blocking properties (e.g., tricyclic antidepressants). Other REM sleep suppressants which do not directly block noradrenergic reuptake (including fluoxetine and clomipramine) also may be useful. Although the use of gamma-hydroxybutyrate (GHB) is controversial because of the potential for physical dependence, GHB has been found to be helpful in promoting sleep efficiency, delta sleep and daytime wakefulness in adult patients with narcolepsy (26).

In some youngsters, there is a significantly increased need for sleep despite evidence of

adequate amounts of nighttime sleep and without obvious REM sleep abnormalities. This condition is known as idiopathic hypersomnia. Often, there is a family history of excessive sleep need. Idiopathic hypersomnia is frequently treated with stimulant medication when daytime functioning is impaired.

Extrinsic Dyssomnias: In the pediatric age group, extrinsic dyssomnias commonly involve problems with initiation and maintenance of sleep. These disorders are most prevalent in the preschool years. Studies suggest that approximately 30% of toddlers have nighttime awakenings that disturb their parents. Because diagnostic criteria for primary insomnia are met rarely at this developmental period, such sleep complaints, characterized by repetitive waking and inability to fall asleep, may be more appropriately classified as "protodyssomnias" (17). It is not known whether these protodyssomnias lead to genuine dyssomnias. There is, however, evidence that these sleep disturbances persist through the latency period in a substantial proportion of youngsters (7,11,27).

Characteristics associated with extrinsic dyssomnias include temperament, perinatal complications, neonatal irritability, physical discomfort, breast-feeding, anxieties and worries, parent-infant interactions at bedtime, maternal psychopathology, and other family stresses, such as marital conflict, family accident or illness and unaccustomed daytime separation from the mother (8,9,11,28-32). Treatment of disturbed nocturnal sleep is primarily through behavioral interventions and elimination of precipitating/causal factors. Hypnotics or sedating antihistamines may be used in the short-term for acute sleep disruption.

Circadian Rhythm Disorders: Among circadian rhythm sleep disorders, the most common problem relevant to youngsters is delayed sleep phase syndrome (DSPS). This disorder is generally prevalent during adolescence. An adolescent experiencing DSPS typically displays an inability to fall asleep at the customary bedtime and an inability to rise at a reasonable hour in the morning. This process generally begins on weekends, holidays or summer vacations when youngsters dramatically change the sleep/wake schedule with late bedtime and wake-up times. Problems become apparent when the school schedule begins with the need for early awakening. Often, these adolescents cope through catch-up sleep on weekends by sleeping late into the afternoon. Short sleep periods followed by irregular long sleep periods, over time, disrupt the biological clock.

Although DSPS is considered to be relatively common in the adolescent population, its prevalence is not known. As a precautionary note, the distinction between normal developmental changes in circadian timing during adolescence and the diagnosis of DSPS is difficult, particularly in the context of early school start times (33,34). Whatever the reason(s) for changes in sleep-wake regulation during adolescence, there is evidence that disruption of the sleep/wake schedules has an adverse effect on functioning in emotional, behavioral and cognitive domains (35).

The treatment for DSPS consists of two phases. Initially, the sleep system should be aligned gradually to the desirable schedule (chronotherapy) following which the alignment is maintained (18). The process of alignment comprises gradual, small, consistent advances in bedtime and wake-up time (about 15 minutes a day). It is often best to begin from the time the adolescent usually goes to sleep without difficulty. During this process, it is important to avoid any naps and to be consistent across weekends and holidays. Upon awakening, the youngster should get some activity and if possible, exposure to bright light such as walking outside. In severe cases, some adolescents on very late schedules respond more favorably to successive delays in bedtime (2-3 hours/day). Particularly during the first two-to-three weeks following chronotherapy, rigid guidelines should be set about wake-up time throughout the week. Later, if the adolescent wants to stay up late on an occasional weekend night, he/she may be able to do so, but should not be permitted to sleep more than one-to-two hours beyond the usual wake-up time for school.

Parasomnias

Parasomnia is a term given to a group of unusual behaviors emerging from sleep. The behaviors are manifestations of CNS arousal, specifically of motor and autonomic activation. According to the ICSD nosology, parasomnias are classified as disorders of arousal, sleep-wake transition disorders, REM parasomnias and miscellaneous parasomnias (see Table 2).

Disorders of Arousal: Confusional arousals, sleep terrors and sleep walking are variations of partial arousals from deep non-REM sleep. Arousal disorders occur commonly from ages 3 to 8 years, a developmental period corresponding with the greatest amount and intensity of stage 4 sleep. These problems usually occur in the first 1 to 3 hours after sleep onset, at a time of transition from stage IV sleep to REM sleep. The character of these arousals can vary from mild events (a few awkward movements or mumbling) to intense events (a full blown night terror with agitated running and screaming). The episodes usually last from 30 seconds to 10 minutes and terminate with an abrupt return to deep sleep with the child having no memory of the event in the morning.

Conditions which lead to increased delta sleep, such as sleep loss and excessive fatigue, are associated with arousal disorders. Family stresses also have been reported to precipitate some of these episodes. Unless arousals are intractable in terms of frequency and persistence, no special intervention is warranted. Treatment usually consists of education and reassurance. Insuring optimal nighttime sleep is important. A brief afternoon nap may help to reduce the amount and intensity of stage IV sleep at night. In intractable cases, drugs which reduce delta sleep (e.g., benzodiazepines, tricyclic antidepressants) are often successful. Often, when the medication is stopped, there is rebound of delta sleep with a reappearance of the disorder.

Sleep-Wake Transition Disorders: These disorders occur in transition from wakefulness to sleep or vice versa. Sleep starts, sleeptalking, nocturnal leg cramps, head banging and body rocking come in this category. In young children, these conditions are relatively common and most often are variants of normal behavior. Reassurance and education provide sufficient support for the family. When intense rocking or head banging persists, insuring the child's safety from self-injury and behavioral modification programs are required.

REM Parasomnias: Nightmares are the most frequently occurring problems in children. Nightmares usually have an onset

Table 2. Parasomnias in Children and Adolescents

Arousal Disorders	Sleep-Wake Transition Disorders	REM* Parasomnias	Other Parasomnias
Confusional arousals	Sleep starts	Nightmares	Nocturnal enuresis
Sleep terrors	Sleeptalking	REM behavior disorder	Bruxism
Sleep walking	Nocturnal leg cramps		
	Rhythmic movement disorders (head banging, body rocking)		

*REM: rapid eye movement

between the ages of 3 and 6 years and affect about 10% to 50% of children in this age group. Frequent and recurrent nightmares, however, are uncommon. Frightening television programs, movies, and threatening events during the day are often important factors contributing to these events. Certain medications (e.g., β -adrenergic blockers), and the withdrawal from drugs that suppress REM sleep also can induce or increase the incidence of nightmares.

The differentiating characteristics between night terrors and nightmares are provided in Table 3. In contrast to night terrors, because nightmares generally occur during REM sleep, they are more likely in the second half of the night. The child does not wake up during a nightmare, but becomes awake following the nightmare. The child is alert and often describes in detail the disturbing scenes during the nightmare. The child typically has difficulty returning to sleep and seeks parental reassurance. Providing comfort at the time of occurrence and addressing the sources of a child's fears and anxieties are generally sufficient for addressing the nightmares. For children with regularly recurring nightmares associated with functional impairment, psychotherapy for the child and/or family may be indicated.

favorable response to clonazepam has been reported (36).

Miscellaneous Parasomnias: Nocturnal enuresis is an extremely common sleep-related problem. A number of etiological factors have been delineated including small functional bladder capacity, reduced strength of the urethral sphincter, and variance in the neurologic connections sensing and responding to bladder contractions and sphincter tone. In some children, enuresis occurs in the first third of the night, and very deep sleep is hypothesized to be associated with the disorder in such youngsters. Behavioral (nocturnal alarm, reinforcement techniques) as well as pharmacological (imipramine, vasopressin) treatments have been shown to be helpful in the treatment of nocturnal enuresis (37).

Bruxism is characterized by stereotypic movements of the mouth leading to the grinding or clenching of teeth during sleep. The etiology of the disorder is not well established. Possible etiological factors include deviations from ideal maxillary-mandibular occlusion, emotional stress and neurological conditions (38). Interocclusal appliances, nocturnal alarms, and behavioral regimens are the recommended interventions for bruxism.

Table 3. Characteristics of Night Terrors and Nightmares

Night Terrors	Nightmares
Occur out of stage 4 sleep	Occur out of REM sleep
Usually occur in first 1/3 of the night	Usually occur in second 1/2 of the night
Child appears confused, half asleep, or very agitated	Child is fully awake and often describes a detailed dream
Child cannot recognize parents, difficult to reassure	Child usually wants parental reassurance
Event terminates abruptly with return to deep sleep	Child has difficulty going back to sleep, may want to stay with parents
Accompanied by autonomic arousal	Child may appear frightened, but calms in response to reassurance

REM behavior disorder is rare in childhood. It begins more typically in adult life and may be associated with Parkinson's disease or dementia. In the rare cases reported during early developmental periods, they are associated with neurological lesion(s). Excessive augmentation of submental electromyographic activation and exaggeration of limb movements during REM sleep are observed on polysomnography. In adult patients with REM behavior disorder, a

Sleep Disorders Associated with Medical or Psychiatric Conditions

A wide variety of medical, behavioral and psychiatric disorders can disturb sleep in children. The sleep-related problems that occur in association with medical conditions during childhood and adolescence are primarily neurological. Some commonly occurring sleep disorders in association with neurological, other medical and psychiatric disorders are outlined in Table 4.

Table 4. Sleep Disorders Associated with Medical or Psychiatric Disorders

Neurological Disorders	Other Medical Disorders	Psychiatric Disorders
Sleep-related headaches	Sleep-related asthma	Mood disorders
Sleep-related epilepsy		Anxiety disorders
Developmental disorders		Attention-deficit hyperactivity disorder
Degenerative disorders		Substance use disorders
		Psychoses
		Tourette's syndrome

Neurological Disorders: These can range from headaches and seizures to mental retardation syndromes to degenerative disorders (39). Treatment of these conditions are generally symptomatic. Sleep-related headaches usually awaken the subject, resulting in sleep fragmentation. Up to 50% to 80% of epileptic patients have seizures during sleep or on arousal from sleep. The electroencephalographic (EEG) synchronization occurring during non-REM sleep may be conducive to the spread of abnormal discharges. Epileptic episodes rarely induce sleep disorders, but they may cause awakenings from sleep and thus reduced sleep efficiency. The physical anomalies associated with Down syndrome and Prader-Willi syndrome can lead to OSAS. The sleep disturbances associated with degenerative brain diseases generally reflect fragmentation with frequent awakenings. The resulting sleep deprivation may lead to excessive daytime sleepiness.

Klein-Levin syndrome is characterized by excessive somnolence, hypersexuality and compulsive overeating. Mental disturbances including irritability, confusion and occasional auditory or visual hallucinations also have been reported. The syndrome occurs more frequently in males (3:1). Typically, symptoms begin during adolescence either gradually or abruptly, and in about half the cases, the onset follows a flu-like illness or injury with loss of consciousness. Oftentimes, there is an episodic nature to the symptoms with cycles lasting from 1-30 days. The syndrome usually disappears spontaneously during late adolescence or early adulthood. It is important to rule out other organic causes of similar symptoms. A family history of bipolar illness or other signs suggesting bipolar disorder also should be considered in the differential. Despite lack of clear consensus on treatment, stimulant medication and lithium carbonate have been reported to be useful in individual cases.

Other Medical Conditions: Similar to the occurrence of seizure episodes during sleep, nocturnal exacerbation of bronchial asthma is common in children. Sleep, by itself, does not appear to trigger attacks. Neuroendocrine regulators of respiration and pulmonary function are sensitive to diurnal variation, and may predispose to these episodes. Nocturnal asthmatic attacks can be quite frightening to children, leading to anxiety associated with falling asleep. Frequent awakenings during asthmatic episodes also can cause sleep fragmentation.

Psychiatric Disorders: Among psychiatric conditions, mood disorders (including depression and bipolar disorder), anxiety

disorders (including separation anxiety disorder, panic disorder and post-traumatic stress disorder), attention-deficit hyperactivity disorder, substance use disorders, psychoses and Tourette's syndrome are frequently associated with sleep disturbances in youngsters (13,40). Prospective studies have shown that persistent sleep difficulties increase the risk for psychopathology (41,42). Conversely, the presence of psychiatric disorders can result in sleep disturbances.

Often, the sleep complaints include difficulty falling asleep, middle of the night awakenings, restless sleep and early morning awakening. In addition, there are many youngsters who report hypersomnia, especially in association with major depressive disorder. Some patients with Tourette's syndrome manifest increased incidence of partial arousals out of deep sleep.

In studies of adult psychiatric patients, the sleep complaints are frequently accompanied by objective changes in sleep, particularly in relation to major depressive disorder (43). The specific EEG sleep abnormalities described in adult depressed patients include difficulty initiating and maintaining sleep, earlier onset of REM sleep, altered REM sleep patterns, and diminished slow-wave sleep. In contrast, despite the evidence of frequent sleep complaints in children and adolescents suffering from depression (44), objective evidence of sleep disturbances are less consistent (45). One possibility is that high sleep efficiency and large amounts of delta sleep seen in youngsters mask the sleep disturbances associated with depression. It is also speculated that development in interaction with depressive illness may produce the observed sleep changes (43,46).

To our knowledge, there are no systematic studies on the treatment of sleep disorders associated with psychiatric conditions in youngsters. Common sense approaches include appropriate diagnosis and treatment of the identified behavioral/emotional condition, reduction of stress and behavioral interventions to target the specific sleep complaint(s). Sedating psychotropic agents are often chosen by clinicians when confronted with sleep disturbances in psychiatric patients. Occasionally, short-term use of hypnotics may be indicated.

FUTURE DIRECTIONS

Although much appears to be known about sleep disorders in the pediatric population, our knowledge in this area is in its infancy. Additional research is still needed to investigate

differences in clinical presentation of specific sleep disturbances among different age groups (i.e., children, adolescents and adults), the development and testing of more specific treatments for the different populations, and to study the effect of sleep disturbances on functioning and on the developmental trajectory. Ethnic/cultural (biological and non-biological) influences on sleep regulation and on the prevalence and clinical presentation of sleep disorders also should be investigated. Given the prevalence of sleep problems in the child and adolescent populations and their likely impact on emotional, behavioral and cognitive functioning, it is imperative to gain a better understanding of these disorders. The early identification and appropriate treatment of sleep disorders during childhood and adolescence potentially might have a beneficial effect on the general health and well-being of the individual during adult life, as well.

In considering future investigations on pediatric sleep disorders, attention should be paid to the limitations of existing data. The literature comprises more of case reports of specific sleep disorders than experimental studies. Empirical data have been derived largely from small sample sizes, oftentimes

obtaining information from a single source (parent or child) and involving short-term follow-up evaluations. Although studying youngsters in the sleep laboratory for extended periods of time is not feasible, available naturalistic technologies (including limb actigraphy, body movement detectors and infrared videosomnography) have not been utilized sufficiently.

Larger sample sizes with more experimental manipulations are required for a better understanding of the mechanisms underlying sleep disorders in children and adolescents. Assessment procedures need to be standardized as well as culturally-sensitive for comparison across studies and across samples. To ensure cross-validation and reliability, multiple sources of information and simultaneous recording methods should be employed. For intervention protocols, raters should be blind to the treatment condition and positive results should be confirmed with replication and cross-over designs. Longitudinal studies will be helpful in gaining knowledge on the factors influencing sleep problems and on the effect of sleep disturbances on development and on other neuroregulatory systems.

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