Neurology of Sleep

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KEYWORDS

• Sleep • Pediatric • Childhood • Sleep development • Sleep problems • Insomnia

KEY POINTS

- Sleep problems are common among typically developing children and more frequent among children with neurodevelopmental disabilities, like autism spectrum disorder.
- Sleep disorders contribute not only to problematic sleep but also to daytime challenges with cognition, behavior, and family quality of life.
- Screening for sleep problems, including snoring, should be performed routinely.
- Screening tools, such as the BEARS questionnaire, can identify sleep problems efficiently.
- Many sleep disorders can be evaluated by history and treated with behavior modification; a portion will need further assessment by polysomnography and management with pharmacotherapy and/or surgery.

INTRODUCTION

From the earliest years, differences in the timing, quality, and electrophysiologic architecture of sleep reflect and inform on brain state and overall neurodevelopmental trajectory. More clearly deciphering sleep's contribution in this space seems a natural fit for students of the developing brain. Sleep should be conceptualized as a complex state, behavior, and process without a monolithic function but rather an omni-phenomenon differentially focused on the needs of the organism as determined by developmental period. For example, in the earliest years, sleep's major role may be providing the necessary stabilization for building the synapses and refining the essential circuits crucial to the development of motoric fluency, language, and the behavior of socialization. As the individual develops, sleep's role in learning and memory and later in repair may become more important. Dysregulated sleep, in its many forms,

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has the potential to disrupt these essential processes and impact optimal functioning whenever in the life cycle it occurs. Primary disorders of sleep include the apneas, both obstructive and central, the insomnias, the parasomnias, sleep-related movement disorders, and circadian rhythm disorders. Their causes may be related to genetics, anatomic differences, cooccurring medical disorders, environmental factors, or some combination thereof. The practice of clinical sleep medicine requires a deep understanding of both the primary disorder and the subsequent secondary effects of interrupting the sleep process itself. The neurologic and neurodevelopmental consequences of chronic sleep disruption, whether from untreated obstructive sleep apnea (OSA) in a 6 year old with kissing tonsils or from chronic sleep insufficiency in a 17 year old with mismatched sleep need and sleep opportunity, are becoming more apparent as researchers from multiple disciplines more closely examine sleep's contribution to brain health.

DISCUSSION

Development of Sleep and Sleep Requirements

Sleep is a complex process governed by the interaction of circadian and homeostatic processes mitigated by genetic and environmental influences. Sleep cycles are established in utero with the suprachiasmatic nucleus (SCN) setting the circadian rhythm as early as 18 weeks after conception.[1] After 32 weeks' gestation, sleep is divided into active, quiet, and indeterminate sleep.[2] Neonatal sleep is polyphasic, with random intervals of sleep throughout a 24-hour period as the SCN matures and the infant is synchronized to the external environment. The most remarkable changes occur in the first 12 months, with major changes in sleep consolidation and architecture continuing through the preschool period. Unlike in adults outside of pathologic states, the newborn falls directly into active sleep, the predecessor of rapid eye movement (REM) sleep, which occupies fully 50% of the total sleep time in early life. REM versus non–rapid eye movement (NREM) sleep can be clearly differentiated by 2 months of age, when sleep spindles appear on the electroencephalogram (EEG), signaling the onset of N2.[3] Regular sleep-wake rhythms develop by 2 to 4 months of age and mark the transition from neonatal sleep to infant sleep. A diurnal pattern is established by 3 months with consolidation into a major nighttime sleep period and a series of shorter sleep bouts during the day. K-complexes form by 5 to 6 months age, allowing sleep to now be classified with increased certainty into stages N1, N2, N3, and REM.

Infants attain the ability to put themselves to sleep as early as 2 to 4 months of age and can sleep through the night by 6 to 9 months. Many children may require a daytime nap with an average frequency of 2 naps per day, lasting 2 to 4 hours.[4] Individual sleep need is difficult to determine, and the current parameters are consensus and vary by developmental stage, with no consensus reached for under the age of 4 months.[5] **Table 1** lists the sleep requirements for optimal health. Note that consensus recommendations for developmentally appropriate sleep durations are very broad and based on the requirements for typically developing children.

Problematic Sleep

Sleep disorders are reported in 10% to 25% of typically developing children and as many as 40% to 100% of children with neurodevelopmental disorders. Insomnia is the most common sleep complaint, reported in 10% to 30%[6–8] of children, and can stem from behavioral, medical, or psychiatric causes. Insomnia may include difficult initiating or maintaining sleep and must have attendant daytime consequences (International Classification of Sleep Disorders, 3rd edition).[9] In younger age groups, the

Table 1
Sleep requirements for optimal health

Age	Number of Hours per 24-h Period
4–12 mo	12–16
1–2 y	11–14
3–5 y	10–13
6–12 y	9–12
13–18 y	8–10

Data from Paruthi S, Brooks LJ, D'Ambrosio C, et al. Consensus statement of the American Academy of Sleep Medicine on the recommended amounts of sleep for healthy children: methodology and discussion. *J Cl Sleep Med*, 2016 12(11): 1549-1561. Published 2016 Nov 15. https://doi.org/10.5664/jcsm.6288.

clinical presentation may include bedtime refusal or resistance, delaying the actual time to fall asleep, or frequent night awakenings that require parental intervention. Most children outgrow behavioral insomnias, and treatment is based on working with families to set limits and manage expectations. In older age groups, the clinical presentation should be distinguished from delayed sleep phase syndrome, a mismatch between expected developmental changes in sleep propensity and cultural expectations (ie, school start times)[10] that often leads to sleep insufficiency. Importantly, the advent or exacerbation of insomnia in youth warrants special attention for the following reasons: adolescent insomnia is usually chronic, increases the risk for substance abuse and suicide irrespective of cooccurring diagnoses,[8,11,12] and according to a recent meta-analysis, predicts the development of psychopathology.[13] Parasomnias are also very common and may occur in 25% of children. Sleep walking and talking are generally not overly concerning, and most cases can be managed with behavioral support for the parents and attention to safety. Sleep terrors and confusional arousals are likewise not considered developmentally abnormal, although nontypical presentations, such as episodes that occur multiple times a night, should be differentiated from nocturnal epilepsies. Restless legs syndrome (RLS) or Willis-Ekbom disease is a sensorimotor abnormality with a prevalence in pediatric populations of between 2% and 4%,[14,15] and the relationship between genetics, iron stores, and dopamine dysfunction is still being worked out. Children and youth experiencing difficulty with sleep initiation may have RLS or the related periodic limb disorder of sleep (diagnosis is by polysomnography [PSG]), and along with a sensitive sleep history, serum ferritin should be obtained. Restless sleep disorder is a newly described pediatric sleep condition consisting of large body movements that are persistent throughout the night and impact daily behaviors.[16] It is often coexistent with other disorders of sleep, and prevalence is estimated at 7.7%.[16] OSA is estimated to affect 1% to 5%[17] of children, with higher rates among children with obesity, neurodevelopmental disorders, neuromuscular disorders, and certain genetic disorders that affect the anatomy of the head and neck.[18] Weight loss and surgical removal of the tonsils and adenoids are often used, but nasal steroids, continuous positive airway pressure (CPAP), and even watch-and-wait strategies have been used with treatment course dependent on age, cause, and severity. **Table 2** summarizes pediatric sleep disorders.

Children with autism spectrum disorder (ASD) tend to have very high rates of sleep dysfunction with estimates ranging from 53% to 83%.[19,20] Children with attention-deficit/hyperactivity disorder (ADHD) also report higher rates of sleep problems, with some estimates as high as 73%,[21] and because of the relationship between

Table 2
Summary of pediatric sleep disorders

Disorder	Age	Clinical and Diagnostic Features	Diagnostic Evaluation	Treatment
Insomnia Chronic • Behavioral insomnia of childhood • In older children Short term	Infants/toddlers/preschool School age through adolescence >6 mo of age	Difficulty initiating and/or maintaining sleep with daytime consequences, should be distinguished from DSWPD Precipitated by an acute identifiable stressor	History, rule out medical comorbidities, sleep diary, actigraphy, sleep questionnaires Add mental health screen to above History	Behavioral interventions, melatonin, pharmacotherapy
Parasomnias • NREM: confusional arousals, sleep walking, night terrors • REM: nightmares, REM sleep behavior disorder	Any age Confusional arousals: toddlers Sleep terrors: 4–12 y Sleep walking: peaks between 8 and 12 y RBD is rare in children; has been noted in narcolepsy, ASD, Tourette syndrome, and other NDD	1st third of night; increased sympathetic activity, confusion, difficult to awaken, no memory Last third of night; easily awakened, dream recall	History, caregiver video recording; PSG/full EEG montage for atypical presentations	Parent education, sleep extension, safety precautions, scheduled awakenings, benzodiazepine
Sleep-related movement disorder • Restless legs syndrome • Periodic limb movement disorder	Early childhood to adolescence; RLS diagnosed retrospectively to $\leq$6 mo of age	Urge to move legs, which is worse at rest and in the evenings, relieved by movement, and causes distress Sleep disturbance or daytime fatigue and PSG with $\geq$5 PLMS/hour of sleep	History, serum ferritin PSG, serum ferritin	Iron (oral or intravenous), warm compresses, pharmacotherapy
Obstructive sleep apnea	Any age, peaks between ages 2 and 8 y	Snoring, labored breathing, daytime behavior problems PSG with AHI >1	PSG	T&A, PAP therapy, positional therapy, intranasal steroids, weight reduction

Delayed sleep-wake phase disorder (DSWPD)	Adolescents to young adults	Desired sleep and wake times are significantly delayed compared with desired wake time for at least 3 mo	History, sleep diary, actigraphy	Behavioral intervention, light therapy, strategic melatonin dosing
Narcolepsy	Peaks in 2nd decade of life	Excessive daytime sleepiness, cataplexy, hypnogogic hallucinations, sleep paralysis MSLT with SOL <8 min, $\geq$2 SOREMPs	PSG + MSLT	Behavioral intervention, stimulants, wake-promoting agents, sodium oxybate

Abbreviations: PAP, positive airway pressure; PLMS, periodic limb movements of sleep; SOL, sleep onset latency; SOREMP, sleep onset REM periods.
Data from Medicine, A.A.o.S., International classification of sleep disorders, 3rd ed. 2014, American Academy of Sleep Medicine: Darien, IL.

chronic sleep disruption and daytime symptoms of hyperactivity and attention deficits, ruling out primary sleep disorders is paramount in this group.

Sleep Evaluation

All children and teenagers should be screened for sleep problems. An example of a short, easy-to-use starting place is The BEARS, a 5-question pediatric sleep screening tool, that helps the clinician cover all the potential problem areas and increases the likelihood that sleep issues will be detected.[22] A practice pathway for identification, evaluation, and management of insomnia in children and adolescents with ASD is delineated by Malow and colleagues.[23]

Overnight PSG is a multiparameter continuous recording encompassing the whole sleep period. It facilitates the objective identification, characterization, and determination of brain activity, breathing, and movement and "unusual" behaviors in relation to awake and sleep states. It is the gold standard for diagnosing OSA and other sleep-related breathing disorders and operationalizes the apnea-hypopnea index (AHI), the number of these events per hour of sleep. In children less than 17 years of age, an obstructive AHI of 1 or less is considered normal, between 1 to 5 is mild OSA, 5 to 10 is moderate OSA, and severe OSA is an AHI of greater than 10.[24] Although suspected OSA is the most common indication for a PSG, it is also indicated in PLMD and narcolepsy and can be beneficial in evaluating sleep-related movements, snoring, restless sleep, and differentiating parasomnias from certain epilepsies.

True disorders of circadian rhythm are rare in prepubescent, typically developing children but may be underdiagnosed in children with NDDs where the complex relationship between cognition, neurologic function, and regulation of circadian rhythmicity may be disturbed.[25] Delayed sleep-wake phase disorder is the most common circadian rhythm disorder in adolescents. Commonly, adolescents may experience a developmentally expected shift in bedtime with the desire to fall asleep falling later in the evening. Because of societal constraints whereby rise time is fixed, these children may develop chronic sleep insufficiency manifesting as daytime sleepiness along with changes in attention, mood, and behavior.[26] Workup for suspected circadian sleep-wake phase rhythm disorders and some types of insomnia can involve the use of actigraphy, a noninvasive, safe, reliable, and validated method for measuring sleep durations, patterns, and efficiency. The actigraphy device is worn on the nondominant wrist and measures sleep in the home environment over days to weeks.

Case Presentations

The authors illustrate the common pediatric sleep complaints through a series of vignettes.

Insomnia: Two cases of sleepy mothers and not-so-sleepy children.

Patient 1

A 15-month-old girl is evaluated for frequent nighttime awakenings. She is habitually rocked to sleep and put to bed at 8 PM For the past 4 months, she has had recurrent night awakenings, requiring her to be rocked back to sleep again. Her parents are frustrated and sleep deprived. She takes 1 to 2 naps per day, has age-appropriate development, and has no medical issues. Her examination reveals a happy child and is entirely normal. She is diagnosed with chronic insomnia, behavioral insomnia of childhood, sleep onset association subtype. After explanation of the problem, a thorough review of sleep expectations for toddlers, and a discussion of various management approaches, the mother opts for a behavioral approach called unmodified extinction,

and the following plan is developed: (1) consistent bedtime and morning out of bed time, ensuring developmentally appropriate adequate time for sleep; (2) specified bedtime routine followed by being put to bed awake but drowsy; (3) opportunity to "cry it out"; (4) close follow-up with weekly phone check-in; (5) both parents will be responsible for adherence. After a challenging first weekend, parents report success after 1 full week. Child continues to experience awakenings but is now able to put herself back to sleep without crying or parent intervention, and the family opts to continue the program.

Conditions that are habitually present at the time of sleep onset are termed sleep associations. Similar conditions are thus required for the child to return to sleep following normal, periodic night arousals, which then result in awakenings. These children may also present with difficulty napping, delayed sleep onset, and daytime behavior problems, all of which can lead to family stress. "Crying it out," also known as unmodified extinction, is an efficacious method of treatment, but may not be acceptable for all families. Graduated extinction, bedtime fading, and other positive routines offer an alternative.[27]

Patient 2

A 5-year-old boy with behavior problems and ASD has difficulty attaining and maintaining sleep and is perceived by his mother to sleep less than his neurotypical brothers. His mother is frustrated and sleepy and has difficulty performing her best at work because of the child's chaotic sleep schedule. His nurse practitioner discusses sleep expectations for a child of this age with ASD and makes a diagnosis of chronic insomnia. She also reviews coexisting conditions, such as constipation and gastroesophageal reflux disease, and discusses ways to optimize management to facilitate better sleep. A sleep program is designed with a 24-hour invariant schedule, including a bedtime routine, graduated responses to night awakenings, a reward system, and bedtime passes. A trial of melatonin at bedtime is initiated with follow-up in 1 month.

Sleep problems are ubiquitous in children with ASD, and improving sleep may ameliorate multiple aspects of physical and mental well-being for the patient and family. Practice guidelines by the American Academy of Neurology in 2020 provide recommendations for use of low-dose, pharmaceutical-grade melatonin if behavioral strategies fail and after coexisting medical and pharmacologic factors have been addressed.[28] **Table 3** summarizes medications that can be used to treat insomnia.

Sleep-Disordered Breathing: A Case of Restless Sleep

Patient 3

A 4-year-old girl with Down syndrome (DS) presents with snoring, witnessed apneas, and restless sleep. She often sleeps sitting up with her head bent forward. She has typical Down facies with a short neck, enlarged tongue, and generalized hypotonia. As part of her routine care of children with DS, the pediatrician orders a PSG, which shows severe OSA with 19.6 respiratory-related arousals per hour, 24.9 obstructive respiratory events per hour, an oxygen nadir of 75%, and maximum transcutaneous CO_2 of 53 mm Hg. She is referred to otolaryngology, and an adenotonsillectomy is performed. A repeat PSG shows some improvement but persistent sleep-disordered breathing. Referral is made to sleep medicine clinic for further evaluation and management.

OSA is a constellation of nocturnal and diurnal symptoms with ventilatory irregularities and obstructive events.[17] Peak incidence is between 2 and 8 years, with prevalence especially high in certain populations, ranging from 69% to 76% in children

Table 3
Pharmacologic treatment of insomnia

Medication	Therapeutic Category	Dose at Bedtime	Side Effects	Clinical Pearls
Melatonin	Dietary supplement	Hypnotic dose: 1 mg 30 min before bedtime Increase by 1 mg/wk to maximum 3 mg (<40 kg) or 5 mg (>40 kg) Circadian rhythm adjustment doses: 0.1–0.5 mg, 5–6 h before habitual bedtime	Morning sedation, headache, enuresis, dizziness, mood changes, gastrointestinal complaints, vivid dreaming	Reasonable choice in general and special populations of children with sleep onset insomnia Beneficial in those with circadian phase delay Uncertain reliability of over-the-counter preparations
Gabapentin	Anticonvulsants/mood stabilizers	5 mg/kg, increase weekly by 5 mg/kg to maximum 15 mg/kg	Emotional lability, daytime somnolence	Consider in those with comorbid RLS or PLMD
Clonidine	Alpha-agonist	0.05 mg to 0.3 mg	Morning drowsiness, mid-sleep awakening, hypotension, irritability, rebound hypertension, exacerbation of parasomnias due to increasing N3 sleep	Short half-life supports potential middle-of-the-night dosing Reasonable choice for ADHD-related insomnia
Trazodone	Atypical antidepressant	18 mo to <3 y: 25 mg, increase by 25 mg every 2 wk to maximum 100 mg/dose Ages 3 to adolescents: 50 mg, increase by 25 mg every 2 wk to maximum 150 mg/dose for ages 3–5 y, 200 mg/dose for ages >5 y to adolescents	Sedation, hypotension, arrythmias, serotonin syndrome; risk of priapism in boys (at doses of 100–150 mg)	REM suppressant, rebound may lead to nightmares; likely most useful with comorbid mood disorders ± anxiety
Clonazepam	Benzodiazepine GABA receptor agonist	0.25–0.75 mg	Cognitive impairment, rebound insomnia, anterograde amnesia,	Utility limited to those who may benefit from its anxiolytic and long duration

			disinhibition, dependence, abuse	of action properties; potential for dependence
Ramelteon	Melatonin receptor agonist	2–8 mg	Dizziness, fatigue, increase prolactin/decrease testosterone	Reasonable choice for mild sleep onset insomnia
Mirtazapine	Atypical antidepressant	7.5 mg	Daytime sedation, orthostatic hypotension, weight gain	
Eszopiclone	Non–benzodiazepine receptor agonist	1–3 mg	Headache, dysgeusia, dizziness	Studied in ADHD-related insomnia, limited utility to older adolescents
Zolpidem	Non–benzodiazepine receptor agonist	0.25 mg/kg, maximum 10 mg	Dizziness, headaches, hallucinations	Same as above

No medications are FDA approved in children for insomnia.

with DS.[29] Untreated OSA can have numerous repercussions on overall health with negative impact on neurocognitive and behavioral functioning, cardiovascular health, metabolic morbidity, and increased health care utilization.[30] Adenotonsillectomy remains the first-line treatment in children for moderate to severe OSA, although outcomes postsurgery may not be as favorable as expected, particularly in high-risk children.[31] CPAP therapy should be used in those with moderate to severe residual OSA.

Non–Rapid Eye Movement Parasomnias: Unusual Nighttime Behaviors

Patient 4

A typically developing 8-year-old girl presents with episodes of confusion and wandering an hour after going to bed. Parents are requesting a sleep study, as the child attempted to exit the house on 2 occasions. Her mother reports she herself had sleep walking as a young child but thinks that her daughter's episodes are different. The girl has no memory of the episodes and has been noted to snore. She is doing well academically and socially. Her pediatrician thinks these are parasomnias but orders a sleep study. During the PSG, the child experiences episodes of arousals and sitting up, and must be prevented from getting out of bed by the technologist. She is noted to have significant sleep-disordered breathing with 10.1 obstructive events per hour with an oxygen nadir of 89%. The obstructive events are associated with arousals. EEG findings are normal. A dual diagnosis of NREM parasomnias and OSA is made. The pediatrician advises safety precautions to prevent injury, which include taking her back to bed while not attempting to wake her, as this may prolong confusion and combativeness. Parents are encouraged to maintain a routine sleep/wake schedule that allows her to obtain an age-appropriate amount of sleep and avoid sleep debt. In addition, an ear, nose, and throat specialist referral is made. Following tonsillectomy and adenoidectomy (T&A), repeat PSG demonstrates resolution of sleep-disordered breathing. The episodes of confusional arousals and sleep walking diminish to only monthly and over the following years stop completely.

Parasomnias are undesirable behaviors and movements that occur during sleep and sleep-wake transitions and can be divided into REM, NREM, and other parasomnias.[9] REM-related parasomnias usually occur in the latter third of the night and include nightmares, REM sleep behavior disorder, and sleep paralysis. NREM parasomnias, which happen during the first third of the night, are also known as disorders of partial-arousal and include confusional arousals, sleep walking, and sleep terrors.

Confusional arousals are differentiated from sleep terrors in that they consist of disorientation and crying, whereas the latter is characterized by an abrupt change in physiologic state resulting in an explosion of activity.[32] Provocative factors include sleep deprivation, hypnotic medications, alcohol, and conditions that provoke arousals, in this case, respirator events. History and caregiver recording of events are helpful, and episodes must be distinguished from nocturnal frontal lobe epilepsy. Mainstays of treatment include reassurance, sleep extension, safety measures, and scheduled awakenings before the habitual time of the events. Medications suppressing slow-wave sleep, such as clonazepam, can be used in select cases.[33]

Insufficient Sleep and Delayed Sleep Phase Syndrome: Sleepy Teenagers

Patient 5

A developmentally and socially appropriate 16-year-old young man is seen after failing several classes because he is falling asleep in school. In the afternoons, he is awake and excels in soccer and baseball. He consistently is in bed by 10 PM and gets up each

day at 6 AM to be at school by 7:30 AM Although in bed, he is unable to fall asleep at 10 PM and is most likely to be texting on his phone for several hours until sleep onset at around at 1 AM He has difficulty waking in the morning and is sleepy for the first half of the day. When he does sleep, he reports no problems. His examination is normal for a Tanner 4 boy. A urine drug screen is negative, and a 2-week sleep diary confirms the sleep/wake schedule reported. A diagnosis of insufficient sleep syndrome is made. The pediatrician is aware of the school administration's plan to initiate later school start time for teenagers soon. After discussion, a plan of delaying school start time by 1 hour is agreed upon, allowing the patient to extend morning wake time by 90 minutes to 7:30 AM He is instructed to avoid use of electronic media before bedtime, move his bedtime back to 11 PM, and set awake up time of 7:30 AM, including on weekends. A trial of melatonin to advance sleep onset time is considered. As a motivator, he will not start drivers' education until improvement in his sleepiness is verified.

Between 3.3% and 8.4% of teens and young adults experience a delay in circadian phase with intrinsic preferences for later sleep onset.[34,35] When sleep preferences are incongruent with socially acceptable schedules, this can lead to chronic sleep insufficiency and impaired daytime function. Delayed sleep-wake phase syndrome can be treated with behavioral modifications and strategies to advance circadian phase, including strategically timed melatonin and phototherapy.[36]

Narcolepsy: Excessive Daytime Sleepiness

Patient 6

A 16-year-old young woman presents with declining academic performance and difficulty staying awake in school with random daytime sleep attacks of 4 years' duration. She reports buckling of her knees with emotional events and excessive weight gain. Her examination is remarkable for the following: (1) she is witnessed to fall asleep during the evaluation; (2) her body mass index is now 25 vs 18 two years ago; (3) drooping of the eyelids and intermittent twitching of the facial muscles are observed. Her sleep medicine provider requests a 2-week sleep diary and PSG followed by an Multiple sleep latency test (MSLT). Her PSG reveals a total sleep time of 8.2 hours with normal sleep stage distributions and an REM sleep latency of 10 minutes. Awakenings and transitions from all stages of sleep to awake are recorded. There are no significant respiratory findings. During the MSLT, her average sleep latency is 2.3 minutes, and REM sleep is achieved during the nap sessions. Between naps, a humorous story was read to her with video recording documenting episodes of cataplexy (buckling of the knees, falling forward, and dropping of objects held in her hands). A diagnosis of narcolepsy type 1 (with cataplexy) is made. Management options, including scheduled naps, medications, and driving limitations, were discussed.

Narcolepsy with cataplexy, also known as narcolepsy type 1, is a chronic, lifelong condition related to deficiency of the wake-promoting neuropeptide, hypocretin-1 (orexin).[37] It accounts for 50% of cases of narcolepsy and is distinguished from type 2 narcolepsy by the presence of cataplexy.[9] Manifestations of narcolepsy classically include the tetrad of excessive daytime sleepiness, sleep paralysis, cataplexy, and hypnogogic hallucinations, which stem from intrusion of fragments of REM sleep into wakefulness. It is a rare disorder, with a prevalence of 0.025% to 0.05%, presenting most commonly in the second decade of life. Treatment is with lifestyle and behavioral modifications (planned naps, regular exercise, sleep time optimization) and pharmacotherapy. Medications to treat sleepiness include stimulants and wake-promoting agents, such as modafinil and armodafinil.[38] Cataplexy can be addressed with sodium oxybate, atomoxetine, and other classes of medication.[38]

Restless Legs

Patient 7

A typically developing 6-year-old boy is seen by his pediatrician for complaints of hyperactivity and inability to sit still during school. On further history, it is noted that he moves a lot during sleep and has mild snoring. His examination is remarkable for mild enlargement of his tonsils, and that he is frequently out of his chair and his attention must be redirected. A sleep study reveals adequate total sleep and sleep stage distribution, 1.65 respiratory events (all obstructive) per hour, 14.2 periodic limb movements per hour (many of which are associated with arousals), an oxygen nadir of 95%, and a transcutaneous CO_2 maximum 40 mm Hg. After consultation with otolaryngology, T&A is scheduled in 4 months to occur during spring break. He is seen in the sleep clinic where he endorses uncomfortable feelings in his legs during the night that are described as though "bugs are crawling up his legs," requiring him to move his legs or get up out of bed and walk to relieve this feeling. A diagnosis of RLS with periodic limb movements of sleep is made. Notably, his serum ferritin is 20 μg/L. A course of iron supplementation is initiated during the 4 months before the planned T&A. On iron therapy, he begins to sleep better, and his teacher reports that he can sit in the classroom with a longer attention span.

The diagnosis of restless legs is based primarily on a careful history and exclusion of common complaints, such as numbness, positional discomfort, growing pains, and nocturnal leg cramps. Iron deficiency is implicated in the pathogenesis, as suggested by low cerebrospinal fluid ferritin levels in RLS patients compared with healthy controls,[39] and is likely related to the fact that iron is important in cerebral dopamine production.[40] For adolescents 12 years of age and older, 65 mg to 130 mg elemental iron once daily, and for children under 12 years of age, 3 mg/kg/d of elemental iron (maximum 130 mg elemental iron daily) administered once daily, is recommended.[41] Intravenous iron therapy may be considered for refractory cases. No Food and Drug Administration (FDA) -approved drug exists for pediatric RLS, but gabapentin, benzodiazepines, clonidine, and dopamine agonists may be considered.[42]

SUMMARY

The relationship between sleep and neurodevelopment is complex and bidirectional with neurodevelopmental differences likely contributing to dysregulated sleep and the subsequent disruptions in turn interfering with optimal development. As Pediatric Sleep Medicine grows as a field, we are beginning to better understand the importance of identifying salient disruptors of sleep, delineating their potential influence on cognitive development and behavioral health, and thereby moving closer to sleep-mediated interventions. Child neurologists are uniquely situated to meaningfully contribute to the elucidation of mechanisms that will both inform on the mysteries of how sleep shapes the brain and shed light on how best to intervene. General clinicians see mostly typically developing, healthy children with the common sleep complaints of behavioral insomnia of childhood, OSA, parasomnias, and insufficient sleep. The rare and challenging sleep problems can be referred to the sleep specialist.

CLINICS CARE POINTS

Insomnia:

- Chronic insomnia is characterized by problems initiating or maintaining sleep, early morning awakenings, bedtime resistance, and/or difficulty sleeping without parental intervention, as reported by the child or caregivers.

- Management of insomnia in adults and children begins with behavioral programs that have been shown to be effective.
- In some cases, such as children with cognitive impairment, when parents or children are experiencing significant stress, medications may be appropriate. These are frequently prescribed, but there are no approved medications for children with insomnia. When prescribed, medications should always be combined with a behavioral program.
- Insomnia in teens should prompt a careful sleep history and consideration of sleep insufficiency as well as screening for mental health issues.

Excessive sleepiness:

- Insufficient sleep syndrome is a common problem among today's youth and can result in poor academic performance and drowsy driving in adolescents and young adult.
- Narcolepsy is a rare but important cause of excessive daytime sleepiness, but its onset and diagnosis may be missed or delayed because lack of clinical experience with the diagnosis in children, including subtle manifestations of cataplexy.

Obstructive sleep apnea:

- Pediatric sleep-disordered breathing has a prevalence of 1% to 5% and may be more common in children with neurodevelopmental disabilities because of craniofacial dysmorphology, hypotonia, and central nervous system dysregulation of breathing.
- Risk factors for obstructive sleep apnea in neurotypical children are obesity and adenotonsillar hypertrophy.
- All pediatric patients should be screened for snoring.

Nocturnal behaviors:

- Parasomnias are generally benign, although frequent occurrences may cause parental distress and prompt concerns for safety.
- An important differential in atypical presentations is frontal lobe epilepsy.

Restless legs syndrome and PLMD:

- Periodic limb movement disorder (PLMD) is a polysomnography-based diagnosis, whereas restless legs syndrome is a clinical diagnosis. Prevalence in pediatric patients is 2% to 4% and can be associated with nighttime sleep problems and daytime cognitive and behavior dysfunction mainly because of sleep disruption.
- Iron therapy may be effective therapy, which can lead to improved nighttime and daytime symptoms.

FUTURE DIRECTIONS

Given the lack of evidence-based and FDA-approved treatments for many pediatric sleep disorders, research efforts should focus on well-designed pediatric clinical trials. Melatonin is the best-studied agent for pediatric insomnia; however, long-term side effects of chronic use still need investigation. Sleep disorders are well known to cause disruptions in numerous aspects of health and well-being. However, further evaluation is still needed to understand the full impact of early-life sleep disruption on neurodevelopment trajectory.

DISCLOSURE

The authors have nothing to disclose.

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