Insomnia, parasomnias, and narcolepsy in children: clinical features, diagnosis, and management

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Sleep problems are frequently encountered as presenting complaints in child neurology clinical practice. They can affect the functioning and quality of life of children, particularly those with primary neurological and neurodevelopmental disorders, since coexisting sleep problems can add substantially to neurocognitive and behavioural comorbidities. Additionally, symptoms of some sleep disorders such as parasomnias and narcolepsy can be confused with those of other neurological disorders (eg, epilepsy), posing diagnostic challenges for paediatric neurologists. The understanding of the neurophysiology of sleep disorders such as insomnia, parasomnias, and narcolepsy is still evolving. There is a complex relation between the sleeping brain and its waking function. The interplay among genetic factors, alterations in neurotransmitters, electrophysiological changes, and environmental factors potentially contribute to the genesis of these sleep disorders.

Introduction

Sleep disorders are frequently encountered in paediatric neurological practice and can occur alone or concomitantly with a broad range of neurological diseases. Overall, 25% of children have had at least one sleep problem by adolescence, and this proportion can be as high as 75% in children with autism spectrum disorder, attention deficit hyperactivity disorder (ADHD), epilepsy, or headache.[1–5] Sleep disorders disrupt normal sleep architecture and affect sleep quality or quantity, or both. Sleep medicine is gaining interest among neurology health-care providers as evidence shows that sleep disruptions can impair cognition, emotional regulation, and neurobehavioural functioning;[6–9] increase seizure[10,11] and headache frequencies;[12–14] and prolong recovery from acquired brain injuries such as traumatic brain injury[15] and stroke.[16] Furthermore, neurologists might be expected to diagnose and manage primary sleep disorders, such as narcolepsy and parasomnias. Paediatric neurologists aiming to improve the quality of life of patients and their families should recognise that improving a child's sleep problems can alleviate family stress and caregiver burden.[17–19] Thus, knowledge about sleep disorders is crucial for neurology health-care providers to ensure accurate diagnoses and optimise disease management.

More than 100 sleep disorders are listed in the International Classification of Sleep Disorders,[20] but in this Review we focus only on three disorders—insomnia, parasomnia, and narcolepsy—that exemplify the range of pathology in sleep medicine: insufficient sleep, disturbed sleep, and hypersomnia, respectively. These conditions deserve specific attention because they are likely to be encountered by paediatric neurology care providers and, in the cases of narcolepsy and parasomnias, may be misdiagnosed as other neurological conditions. Insomnia is the most common sleep disorder, and the resulting sleep deprivation is associated with daytime neurobehavioural and cognitive dysfunction. Such an association between insomnia and neurobehavioural morbidity is relevant to all paediatric neurology patients, but has been most extensively researched in children with ADHD or autism spectrum disorder. Parasomnias and narcolepsy are commonly misdiagnosed, which can result in delays to suitable management and inappropriate exposure to medications. For example, parasomnias can be difficult to distinguish from hyperkinetic seizure activity; in one study,[21] 29% of cases eventually diagnosed as nocturnal seizure based on nocturnal polysomnography were initially diagnosed as parasomnias. Likewise, symptoms of cataplexy associated with narcolepsy type 1 are often mistaken for epileptic and non-epileptic seizure activity, contributing to a median diagnostic delay of 10·5 years in patients with narcolepsy.[22–24]

In this Review, we aim to provide an overview of the clinical presentation, pathophysiology, diagnostic work-up, and treatment of paediatric insomnia, parasomnia, and narcolepsy. We also highlight the complex relation between sleep and neurobehavioural and cognitive functioning in children. Although other sleep disorders, such as sleep-disordered breathing, circadian disorders, periodic limb movements of sleep, and restless limb syndrome, are also important clinical entities, they are beyond the scope of this Review.

Insomnia

Insomnia is the most common sleep disorder presented to paediatric health-care providers,[25,26] and it is reported in otherwise healthy children as well as children with a range of neurological conditions, including headache,[27,28] epilepsy,[29] or neurodevelopmental disorders.[3,30] Insomnia in children is defined by the third edition of the International Classification of Sleep Disorders[20] as requiring at least one of the following symptoms to be reported by the patient or caregiver: difficulty initiating sleep, difficulty maintaining sleep, waking earlier than desired, bedtime resistance, or difficulty sleeping without an intervention from a parent or caregiver. Additionally, the definition requires a daytime consequence of these sleep difficulties, such as fatigue or sleepiness, limitations to academic and occupational functioning, impaired

cognitive capabilities, mood disturbances, or behavioural problems (eg, inattention and hyperactivity) for either the patient or the caregiver. For the insomnia to be defined as chronic, sleep disturbances need to occur for at least 3 days per week for a period of at least 3 months. Underlying the diagnosis of insomnia is the assumption that the child has sufficient time and an appropriate environment in which to sleep. This is particularly relevant as the use of electronic media devices (eg, television, computers, and e-readers) is nearly ubiquitous among children in high-income countries. The screens of these devices typically emit bright light that can affect the body's ability to regulate melatonin—a neurohormone that regulates the circadian sleep–wake cycle—which can delay sleep onset, particularly if exposure is close to bedtime. Of note, children with ADHD and autism spectrum disorder tend to spend more time using electronic media devices than do children with typical development,[31,32] and this use has been associated with less time sleeping at night in children with these neurodevelopmental conditions.[33]

The relation between insomnia and daytime cognition, mood, and behaviour

Associations between insomnia and emotional dysregulation, depression, suicidality, and externalising behavioural problems (eg, hyperactivity) have been well described in paediatric populations.[33–35] Sleep dysfunction in children with autism spectrum disorder is associated with poor verbal and socialisation skills, and poor adaptive functioning (eg, increased repetitive and stereotypic behaviours).[36] Likewise, increased frequency and severity of externalising behaviours, oppositional behaviour, and depressive symptoms are associated with sleep problems in children with ADHD.[37] Although studies of the emotional effects of acute sleep deprivation have been done in adults, ethical constraints preclude these types of studies in children. In adults, one night of sleep deprivation is sufficient to heighten the responses of brain areas that are sensitive to reward (ie, the ventromedial prefrontal cortex and ventral striatum) while dulling areas sensitive to losses (ie, the insula), thus impairing decision making.[38] Similarly, in young adults (aged 18–30 years) sleep deprivation has been shown to result in increased emotional reactivity that is associated with heightened activity of the amygdala and relatively decreased activity to the medial frontal and orbitofrontal cortices.[39] Such heightened amygdala responses were also detected in adults (mean age 40·7 years, SD 12·6) with chronic insomnia.[40] The effects of insomnia on cognition have been studied in children with and without neurodevelopmental disorders. Memory consolidation, the process by which a memory trace becomes more stable over time, is more dependent on sleep than a comparable period of wakefulness in both children and adults.[41–43] Deficits in sleep-dependent memory consolidation have been shown in children with ADHD and attributed to deficits in slow oscillation power (0·5–1·0 Hz) in prefrontal cortices during non-rapid eye movement (NREM) sleep.[44] Whether deficits in sleep-dependent memory consolidation would improve with better sleep among children with ADHD is unknown. In summary, chronic sleep disruption has negative effects on mood, memory, and behaviour in children, but the causal mechanisms are unclear.

Pathophysiology

Conceptually, insomnia is thought to be symptomatic of a hyperaroused state that results from heightened arousal systems or hypoactive sleep-inducing pathways, or both.[45,46] This hypothesis postulates the development of autonomic, somatic, and cortical arousal, usually in the context of precipitating factors (eg, stress) or predisposing conditions (eg, a prior history of insomnia) that increase sensory processing and result in insomnia.[46,47] Consistent with this hypothesis, Riedner and colleagues[48] showed that adults with insomnia have more high-frequency electroencephalogram (EEG) activity (>16 Hz) during sleep than healthy sleepers. Furthermore, participants in this study[48] had consistently elevated alpha activity during NREM sleep in sensory and sensorimotor cortical areas, perhaps reflecting heightened awareness to environmental stimuli. These studies have not yet been replicated in children; however, it has been shown that adolescents (mean age 16·7 years, SD 2·0) with insomnia have increased beta activity (15–35 Hz) during sleep onset and NREM sleep, suggesting that this hyperaroused state can be present early in life.[49]

In view of the high rates of insomnia (30–80%) in children with autism spectrum disorder or ADHD,[2,3] evidence of a hyperaroused state might be expected to be seen in children with these conditions. However, in two small studies (ie, <23 participants per group)[50,51] using qualitative EEG analysis of sleep, no differences in power spectra in NREM sleep were reported in participants with autism spectrum disorder or ADHD compared with healthy controls. Similarly, in a study of hypothalamic–pituitary axis functioning in children,[52] those with autism spectrum disorder did not have higher nocturnal cortisol concentrations than healthy controls. Research findings have also suggested that insomnia in children with autism spectrum disorder is related to dysregulation of endogenous melatonin. Several studies[53,54] have reported reduced concentrations of nocturnal melatonin or related metabolites in children with neurodevelopmental disorders, but results from more recent research have not confirmed these findings.[55]

Diagnosis

The diagnosis of insomnia is based on a detailed clinical history from both the child and the parent or caregiver; however, clinicians may not routinely ask about sleep problems.[26] Screening questionnaires such as the Children's Sleep Habits Questionnaire[56] (CSHQ; which includes domains of bedtime problems, excessive daytime