Behavioral Morbidity in Pediatric Sleep-Disordered Breathing

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Abstract

Pediatric sleep-disordered breathing (SDB) is associated with a wide range of emotional and behavioral symptoms. Despite high prevalence rates, symptoms of SDB and potential SDB contributions to behavioral difficulties are often over-looked. During the past several years, case series, cross-sectional studies, and meta-analyses have suggested higher frequencies of SDB in children who are also diagnosed with disruptive behavior disorders such as attention deficit hyperactivity disorder. Conversely, children with objectively defined SDB exhibit higher frequencies of these disorders or related symptoms. The precise neuroanatomic mechanisms of these associations are not clear; however, we here provide a neuroanatomic model that attempts to synthesize the links between sleep problems, associated neurophysiological disruption, and observed behavioral difficulties. We propose that repeated sleep fragmentation due to

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frequent respiratory-related arousals, as well as hypoxemia are likely to impede normal development of the frontal-subcortical circuits implicated in disruptive behavioral disorders. In addition, considerations for assessment and treatment are provided through a case example. Recommendations for future directions highlight the need to clarify optimal polysomnographic definitions for pediatric SDB and to develop more sensitive methods that better predict neurobehavioral consequences.

Introduction

Children with sleep-disordered breathing (SDB) experience a significant range of cognitive, emotional, and behavioral morbidities that cause significant distress for children and their families. Although a number of studies have documented these concerns, physicians frequently overlook the possible contribution of SDB and more often attribute parent-reported concerns to attention deficit hyperactivity disorder (ADHD) or other problems. Studies that have specifically addressed physician identification rates of SDB have shown that sleep symptoms are rarely identified by pediatricians, despite the high rate of sleep complaints by parents [1–3]. For example, Chervin [1] and colleagues surveyed 830 parents using the Pediatric Sleep Questionnaire (PSQ)—a rating scale that evaluates SDB symptoms in children—and performed a detailed current and retrospective chart review examining the rate of physician-identified sleep symptoms. The results showed that 50% of the study parents identified symptoms of SDB in their child, whereas medical records at the time of the survey, and records from the prior 2 years, revealed a diagnosis of SDB in only 11%. Further, in a three-state community survey of pediatric practice patterns [4], over 75% of the sampled pediatricians did not routinely assess sleep problems in their patients. These findings are concerning because children whose sleep disorders are not diagnosed are then left untreated and at potentially increased risk for future medical, cognitive, emotional, and behavioral morbidities.

In this chapter, we review the behavioral impact of sleep-disordered breathing (SDB) in children. We begin by providing brief overviews of SDB symptoms, as well as the Diagnostic and Statistical Manual of Mental Disorders: Fourth Edition-Treatment Revision [5] (DSM-IV-TR) classification of disruptive behavior disorders. We then review the literature related to neuroanatomical correlates and specific SDB symptoms associated with each of the disruptive behavior disorders. The next section provides a review of findings on the behavioral impact of SDB in children, including daytime sleepiness, inattention, hyperactivity, and aggression. We then provide a hypothetical model of mechanisms proposed to link SDB and behavior in children. We conclude with a case example that highlights the assessment and treatment issues in childhood SDB and behavior.

Sleep-Disordered Breathing

Sleep-disordered breathing (SDB) refers to a wide range of problems involving breathing difficulties during sleep ranging from subtle to more severe pathology. Habitual snoring, on the mild end of the spectrum [6, 7], is a common characteristic of increased upper airway resistance during sleep, with estimates of frequency varying depending on the age of the child (see Chap. 12). Obstructive sleep apnea (OSA) is on the severe end of the spectrum and is characterized by repeated episodes of partial or complete upper airway obstruction that interferes with normal ventilation and sleep. These episodes are also associated with hypoxemia, which, in adults and animal models, impacts developing neural structures. Although adenotonsillar hypertrophy

is one of the most frequent causes of OSA in children, other factors may also contribute including obesity, genetics, and syndromes that affect upper airway development [6, 8].

Disruptive Behavior Disorders and Sleep

Classification of behavioral disorders in childhood (developmental psychopathology) is relatively new, having become a separate area of study in the 1970s [9]. It was not until the DSM-IV [10] that empirically validated categories of childhood disorders were described and subsequently elaborated in the text revision. The DSM-IV-TR categories of childhood behavioral disorders include attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD) [5]. In this section, we provide an overview of the DSM-based disruptive behavior disorders including key symptoms, research findings related to the neuroanatomical features of these disorders, as well as findings related to sleep disruption.

Attention Deficit Hyperactivity Disorder

Attention deficit hyperactivity disorder (ADHD) is a developmental disorder characterized by inattention, impulsivity, and hyperactivity and is one of the most frequent reasons for clinical referrals in children. ADHD can cause significant problems at home and at school in younger persons and as symptoms persist across the lifespan, can cause significant functional impairment in adulthood [11]. The DSM-IV-TR category for ADHD includes three subtypes that are differentiated according to the prominence of symptom clusters: ADHD-primarily inattentive type, ADHD-primarily hyperactive type, and ADHD-combined type [5]. The core inattention symptoms include difficulty sustaining attention, being easily distracted, being disorganized, not listening, failing to finish tasks, losing things, and being forgetful. Hyperactive–impulsive symptoms include fidgeting, not staying seated, interrupting, and inappropriately "blurting" out [5]. Although the etiology of this disorder is not completely understood, research evidence points to several factors that may be involved including genetics, neurobiology, and social [11–14].

Neuroanatomically, ADHD has been hypothesized to involve frontal-subcortical circuitry, and neuropsychological and imaging studies have supported this conclusion [11, 12, 15]. For example, investigations have shown that children with ADHD perform poorly on measures of executive functioning and working memory thought to be subserved primarily by the frontal lobes [12, 13, 16, 17]. Imaging studies have reported abnormalities in frontal and subcortical regions as well [13]. Cognitive studies also support involvement of subcortical structures that have projections to the PFC [18]. Finally, because of the finding that stimulant medications are effective in treatment of ADHD, dysregulation of catecholamines—dopamine pathways, in particular—also has been implicated [19, 20].

Attention Deficit Hyperactivity Disorder and Sleep

Earlier versions of the DSM classification system included disturbed sleep as one of the diagnostic criteria for the diagnosis of ADHD. Despite its omission in later revisions, disturbed sleep is often reported by parents of children diagnosed with ADHD, and some ADHD rating scales include sleep problem items, such as the Conners' Rating Scales [21]. A good number of studies now have investigated associations between SDB or SDB symptoms and ADHD. Some of the earliest were case series that reported high frequencies of ADHD in children referred to sleep disorders centers for evaluation of SDB [22, 23]. Subsequent studies in both clinical and community-based settings have reported associations between snoring, other symptoms of SDB, and validated questionnaire items on inattention and hyperactivity [2]. Two longitudinal studies also have shown both prospectively [24] and retrospectively [25] that snoring and related symptoms predict later development of new problems with inattention, hyperactivity, or school performance.

Studies of behavior before and after adenotonsillectomy (AT) also support the hypothesis that untreated SDB increases risk for DSM-IV consistent ADHD. For example, Dillon and colleagues [26] examined the rate of diagnosis of DSM-IV disruptive behavior disorders in children referred for AT, in comparison to a surgical control group. At baseline, disruptive behavior disorders were diagnosed in 36.7% of the AT group, whereas only 11.1% of control group were diagnosed. One year later, group differences in disruptive behavior were no longer significant, and disruptive behavior disorders were diagnosed in only 23.1% of the AT group and 9% of controls. Although this study provides support that SDB increases risk of ADHD, randomized trials have been proposed as providing support for the observed association [6]. The first multicenter randomized controlled trial to test the hypothesis that childhood SDB contributes to problems with attention, among other neurobehavioral outcomes, is ongoing at the time of this writing. This study is designed to assess the efficacy of adenotonsillectomy (AT) for treatment of polysomnography (PSG)-defined pediatric OSA due to adenotonsillar hypertrophy. This study will also assist in clarifying the contributions of SDB including OSA in childhood behavior disorders.

It remains unclear whether clinical severity of ADHD symptoms can be used to diagnostically differentiate between "true" ADHD and SDB-related behavioral problems. To date, most studies suggest that the inattention and hyperactivity in children with SDB is not distinctly different or less severe than the symptoms required to diagnose ADHD. However, not all investigators have reached this conclusion. In a study examining SDB in children referred for ADHD treatment, Sangal and colleagues [27] proposed that ADHD symptoms in clinical populations and SDB-related ADHD symptoms are quite different. They point to prior studies that have reported associations between ADHD and SDB but failed to find associations between ADHD symptoms and objective measures of SDB, arguing that the reported symptoms of ADHD were more likely mediated by factors such as maternal education or socioeconomic status of the study populations. However, population-based studies that have controlled for factors including maternal education and socioeconomic status indicate high rates of parental reports of sleep disturbances, increased nighttime activity, reduced rapid eye movement (REM) sleep, and significant daytime somnolence in unmedicated children with ADHD when compared to controls [28]. Data have also suggested a possible increased prevalence of periodic limb movements in sleep in children with ADHD as well [29].

Any attempt to synthesize, at present, differing views on SDB and ADHD may be premature, as a clear dose–response-like relationship has not been demonstrated between disruptive behavioral symptoms and objective measures of SDB. It has even been suggested that children affected by subtle SDB—under detection threshold in some studies [27]—may be those who are as likely, if not more likely than others, with SDB to suffer from ADHD [24]. As pointed out by Chervin [6], a 25-year history of literature on this issue shows that clinically significant symptoms of ADHD are found in children who do not exhibit apneas or hypopneas but who do demonstrate subtler aspects of SDB including excessively negative esophageal pressures or upper airway resistance syndrome, and nocturnal tachypnea [6, 30, 31]. In addition, studies examining the rate of ADHD in children referred for AT have often failed to find significant associations between objective measures of SDB and disruptive behavior disorders, supporting the assertion that there may not be a clear dose–response relationship between SDB symptoms and ADHD or other disruptive behavior disorder symptoms [26].

Part of the problem is that the potential pathophysiology that mediates links between sleep disturbance and ADHD has not been clearly established; however, empirical evidence suggests overlap between the circuits that regulate sleep, attention, and arousal and disruption in one of these systems is likely to influence the others [32]. Further, the neuroanatomic structures associated with these systems, particularly the prefrontal cortex (PFC), also are affected. Consequently, children diagnosed with ADHD appear to be at greater risk of sleep difficulties.

Oppositional Defiant Disorder

Oppositional defiant disorder (ODD) is defined as a pattern of negativistic, hostile, defiant behavior for at least 6 months [5]. The essential features of this disorder include losing one's temper, arguing, refusing to follow rules or obey requests, deliberately annoying people, blaming others for one's mistakes, being angry often, and being easily annoyed. Some developmental researchers propose that disruptive behavior disorders reflect relatively stable personality traits, with ADHD and ODD representing precursor conditions to conduct disorder and antisocial personality disorder, particularly when aggression is a predominant feature [33].

Studies examining the linkages between neuroanatomic regions and features of ODD have highlighted deficits in frontal lobe functioning, although this body of work continues to evolve. Neuropsychological studies have shown that the children and adolescents with ODD perform worse on tasks of executive functioning, which are mediated by the PFC [33]. Positron emission tomography (PET) studies have also implicated disruption in the PFC. For example, Pliszka [34] and Raine [35] have shown that diagnosis of ODD is associated with hypometabolism of glucose in the prefrontal cortex. Further, a recent imaging study examining the presence of white matter hyperintensities (WMH) in psychiatric disorders in children showed a significantly higher rate of WMH in the PFC of children with disruptive behavior disorders including ODD [36]. Neurotransmitters and salivary cortisol levels have been examined as potential contributors to the appearance of aggressive behaviors as well. Van Goozen [37], for example, reported that low levels of salivary cortisol in a clinical sample of men were associated with ODD in both the early onset and persistence of aggression. Other researchers have proposed an under-arousal of the autonomic nervous system in those with disruptive behavior disorder, including lowered heart rate. Pliszka [34] and Mezzacappa [38] reported that lower heart rate in adolescents was associated with antisocial behavior and predictive of later criminality. Van Goozen also found lower heart rates in those diagnosed with ODD, in comparison to controls, during a frustration-inducing task [37].

Oppositional Defiant Disorder and Sleep

Investigations examining the association between ODD and sleep disturbance tend to center on studies investigating disruptive behavior disorders in general, or in studies investigating ADHD, as the comorbidity rates between ADHD and ODD are high [5]. Although some studies have found associations between ODD symptoms and sleep symptoms, others have reported mixed findings. For example, Dickerson Mayes and colleagues [39] examined the frequency and severity of parent-reported sleep problems in 681 children with disruptive behavior symptoms in comparison to 137 control children. These researchers found although symptoms of ADHD, including inattention and hyperactivity, were associated with higher rates of reported sleep problems, symptoms or diagnosis of ODD was not. In contrast, Coulombe and associates also examined parent ratings of behavior and sleep symptoms in two population-based studies involving younger children [40] and adolescents [41]. These studies are notable because variables that also impact sleep were controlled (e.g., stressful life events, poor family functioning, marital disharmony, maternal negative affect). The results showed that although the magnitude of association between behavior symptoms and sleep declined somewhat, the associations between them remained significant, suggesting that sleep disruption was a significant and independent contributor of behavioral symptoms. Likewise, in a population-based study of toddlers, SDB, and temperament, Reid and colleagues [42] examined the nature of the relationship between sleep, family environment, socioeconomic status (SES), and ratings of child behavior. These researchers also found that child sleep problems accounted for a significant proportion of the variance in externalizing problems, after controlling other risk factors.

Conduct Disorder

A diagnosis of conduct disorder (CD) is made in the presence of three or more symptoms of repeated and persistent behavior over a 12-month period that violates age-appropriate societal norms [5]. Categories of misconduct include

aggression, destruction of property, deceitfulness and theft, and serious violation of rules or code of conduct [5]. Prevalence rates of CD vary due to methodological differences in diagnostic criteria used in studies, populations included, and sources of information (parent, teacher, or child ratings). Neurobiological theories of this disorder come from investigations that have focused on aggression, one of the key features of this disorder. These theories generally propose that high levels of testosterone act as a possible mediator or potentiator of the aggressive or destructive behavior [43]. With respect to aggression and impulsive aggression, researchers have postulated that some individuals exhibit a lower threshold for activation of aggressive responses without consideration of consequences. Neuroanatomically, impulsive aggression is thought to be the result of inadequate behavioral inhibition typically provided by the orbital frontal cortex and anterior cingulate cortex [44], whereas aggressive reactions are hypothesized to arise from limbic regions, including the amygdala and insula.

Conduct Disorder and Sleep

As with ODD and sleep, no studies have examined sleep and conduct disorder specifically, although some investigations have examined sleep and childhood aggression—a key feature of CD. Lindberg and colleagues [45] performed objective sleep studies in a group of psychiatrically hospitalized, violent adult offenders. They reported that the most prominent finding was increased slow-wave sleep in this group as compared to normative data. Although these patients were screened for illicit drug and alcohol use at the time of the study, it is unclear whether they were still taking psychotropic agents that could have affected sleep. In children, Chervin and colleagues examined conduct problems including aggression in a survey of 872 parents [46]. Bullying and other aggressive behaviors were more frequently reported in a group of children with higher scores on a parent report measure of SDB. Similarly, parent behavioral ratings for children with SDB suggest that symptoms of aggression and conduct problems are relatively common [26].

In summary, the majority of population-based studies of toddlers, children, and adolescents report increased rates of disrupted sleep in children who also either exhibit symptoms of disruptive behavior disorders or who carry the diagnoses of ADHD, ODD, and CD. Despite the lack of clear evidence documenting a common pathophysiology in these disorders and SDB, there is substantial evidence of the overlap between these disorders and sleep symptoms.

Behavioral Morbidity in Children with SDB

In the previous sections, we discussed the association of sleep symptoms in disruptive behavior disorder in children. In this section, we provide a review of the findings related to behavioral morbidities associated with SDB including ADHD and aggression—a key feature in disruptive behavior disorders including ODD and CD. We focus on specific symptoms of sleepiness, inattention, hyperactivity, and aggression.

Sleepiness

One of the most neglected symptoms of SDB is excessive daytime sleepiness. Unlike adults with SDB who may yawn and complain of sleepiness, fatigue, tiredness, or lack of energy, younger children with SDB may not exhibit these classic symptoms. Rather, they may more often experience an actual increase in activity levels during the day. A proposed mechanism of this paradoxical relationship is that increased behavior may stave off sleepiness [24, 47]. Although younger children are reported to exhibit increased activity in response to sleepiness, adolescents do tend to have problems staying awake in school or during the ride to school [48]. Nonetheless, studies also have documented that children with more significant disturbances in sleep take less time to fall asleep. Chervin et al. [24, 25] reported a significant association between mean time to fall asleep on the sleep latency test (MSLT) and SDB severity during a baseline evaluation in a group of 106 children

referred for AT, but not at 1-year follow-up when objective measures of SDB had significantly improved. In addition, Gozal [25] also found shorter mean sleep latencies in children with SDB. Although MSLT provides objective evidence of excessive daytime sleepiness in children with SDB, parent ratings of sleepiness also can provide evidence of excessive daytime sleepiness. Although some have argued that parents may not be reliable observers with respect to sleepiness [49], Chervin and colleagues [24] found that parents could identify daytime sleepiness in their children when queried specifically about it. The researchers examined parents' ratings of children's sleepiness using the parent-completed Pediatric Sleep Questionnaire (PSQ)-Sleepiness subscale for children scheduled for AT and control children. The PSQ-Sleepiness subscale discriminated between the children with symptoms of SDB and control children, and ratings for sleepiness showed the expected, negative correlation with mean sleep latencies on multiple sleep latency tests.

Inattention and Hyperactivity

Case series and cross-sectional studies examining the association of SDB and behavior have shown significant behavioral morbidity. In SDB investigations in which parent-reported sleep problems are considered, significant associations with inattention and hyperactivity are common, particularly in comparison to non-SDB peers [15, 50, 51]. In a recent review examining cognitive and behavioral change after AT in children with SDB, Hodges and colleagues [52] reported that in 16 studies using parent-reported measures of SDB, parents reported higher rates of inattention and hyperactivity in comparison to control children. Further, aggression and inattention are the most frequent symptom clusters reported in studies that used objective measures of SDB (see Beebe [52] for review) [22, 23, 26, 29, 53, 54]. Importantly, studies examining improvement following surgical treatment of OSA also document reductions in inattention and hyperactivity symptoms whether OSA was provided by parent report or objective measures [24, 51, 52]. Thus, in studies that include parent's ratings and objective measures, there is solid evidence to indicate that SDB is associated with inattention and hyperactivity.

Aggression

As discussed in earlier sections, aggression is a key feature in CD, specifically, and is also observed in some children with ADHD and ODD [5]. Several studies have shown an association between SDB and aggressive behavior in children [15, 26, 46, 50–52, 55]. For example, Mulvaney and colleagues [55] found that among children with higher respiratory disturbance index scores on PSG, parents reported more frequent symptoms of aggression on a parent rating scale of disruptive behavior disorder symptoms. Further, reviews of SDB and behavioral morbidity have also reported that disruptive behavior, hyperactivity, and aggression in particular are common behavioral symptoms reported by parents [51, 52].

Cause and Effect

This chapter has focused on a relationship of SDB to behavioral symptoms in children. Although substantial evidence supports these associations, no proof of a causal link has been established. Most studies to date include case series, cross-sectional investigations, and correlational studies that do not provide evidence of cause and effect. However, the first randomized trial examining the efficacy of AT in the treatment of OSA is underway. This study will assist in clarifying the extent and nature and the relationship between behavioral morbidity and SDB in children. Nonetheless, given the number of discrepancies in the literature regarding SDB and behavioral morbidity, these findings do indicate that the relationship between these symptoms, SDB and behavioral symptoms, is complex.

Potential Mechanisms

The underlying mechanisms associated with SDB and behavior are likely multifactorial involving multiple brain regions, neurotransmitter substances,

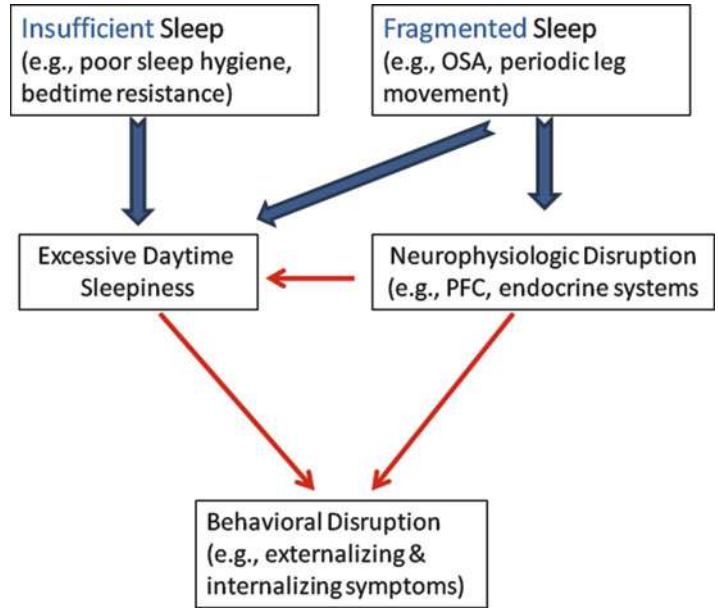


Fig. 32.1 A hypothetical model that synthesizes the findings related to disrupted sleep and behavior in children

and other factors. However, in this section, we provide a model that synthesizes the findings related to disrupted sleep and behavior in children.

Insufficient Sleep, Daytime Sleepiness, and Performance Decrements

Figure 32.1 provides a hypothetical model that incorporates research findings and possible linkages between poor sleep hygiene, SDB, and behavioral symptoms. Insufficient sleep in children is most often the result of poor sleep hygiene [47], which may be the result of bedtime refusal or poor sleep habits. Although several factors may contribute to poor sleep hygiene in children—some include child temperament, parenting styles, and possible environmental contributions (e.g., bed sharing)—the result is poor sleep quality or insufficient sleep [47]. Some investigations have shown that younger children are less likely to experience insomnia [56], but other studies have shown that younger children may experience difficulties with sleep onset and frequent requests for parental reassurance. In addition to sleep-onset difficulties, insufficient sleep may also be the result of frequent nighttime wakening. Although brief nighttime wakening is common in infants and toddlers, a typical developmental trend is for these episodes to decline with age. However, in a high percentage of cases, nighttime wakening may persist. For example, Zuckerman et al. [57] reported that in a sample of 308 parents who reported that their infant experienced problems with sleep at 8 months of age, 41% continued to exhibit sleep problems by the age of 3 years. These children were rated as experiencing more problem behaviors as well.

Insufficient sleep has been found to be associated with daytime sleepiness in children. For example, Fallone and colleagues [4] reported that excessive daytime sleepiness (EDS) was associated with sleep fragmentation. These authors also reported that objective EDS as measured by MSLT also was associated with parent reports of hyperactivity, behavioral disturbance at school, as well as mood problems.

Fragmented Sleep, OSA, and Neurophysiological Disruption

As shown in Fig. 32.1, we hypothesize that fragmented sleep as a result of frequent respiratory-related arousals leads to neurophysiological disruption. Evidence supporting this comes from

studies examining changes in sleep parameters after treatment. For example, in a study investigating a new computerized signal processing analysis of respiratory cycle-related electroencephalogram (EEG), Chervin et al. [58] showed improvements after AT in children with SDB. Importantly, the delta respiratory cycle-related EEG changes after AT were also associated with changes in children's attentional capacity, indicating more subtle aspects of SDB may be implicated in daytime behavior and amenable to treatment.

The chronic and cumulative effect of hypoxemia over time is likely to cause disruption to the normal development of the prefrontal cortex and related structures [15, 51, 59]. The prefrontal cortex has been reported to be particularly susceptible to disruption associated with hypoxemia in adults and animal models, although a clearly established link has not been documented in children [60]. Further, mouse models have also demonstrated that OSA is associated with oxidative stress and upregulation of proinflammatory cytokines that contribute to cell death at the cortical level and within the hippocampus. These effects further cause a reduction in hippocampal long-term potentiation (LTP) as well as functional deficits in spatial learning [15]. Although these structural findings have not been found in children, a recent study by Giordani and colleagues [61] examining neuropsychological functioning in children with SDB showed that children with OSA showed deficits in visual spatial functioning in comparison to control children. Research also has shown that disruptions in proinflammatory markers in adults with OSA are linked with behavioral manifestations of OSA including daytime sleepiness [62]. In addition, studies have also shown that modest sleep loss is associated with significant sleepiness, impairment of psychomotor performance, and increased secretion of proinflammatory cytokines in adults [63]. In children, research has also begun to establish the association of elevations in proinflammatory markers in children with OSA as well as symptoms of daytime sleepiness and difficulties in school [64]. Although some may argue that proinflammatory markers may be a consequence of obesity (known to be associated with OSA), Gozal [65] recently reported on a group of children who were not obese, but who exhibited elevated proinflammatory markers in the presence of OSA. Thus, evidence is accumulating that SDB in children is associated with neurophysiologic and neuroanatomic compromise that contributes to neurobehavioral morbidity in children.

In summary, Fig. 32.1 highlights the research findings that both insufficient sleep and SDB lead to similar symptoms of behavioral morbidity in children. Further, although fragmented sleep caused by OSA may be reversible with interventions such as AT, it is not clear that the pathophysiological changes associated with OSA-related changes are correctible.

Clinical Approaches

Assessment

Given the frequency of sleep problems in children, up to 37% in some studies, screening for problems with sleep in general is important and particularly when a child presents for evaluation of behavioral concerns [28, 47, 66]. However, assessments of sleep or behavior are inherently complex because, as highlighted in this chapter, sleep and behavior concerns overlap and interact and the context of child development is an evolving landscape. Although the American Academy of Pediatrics [67] recommends that children suspected of having SDB be referred for objective sleep assessment, there are no published guidelines to assess children with both disruptive behavior disorders and SDB. In this section, we outline considerations for the assessment and treatment of children and adolescents with sleep or behavior problems, with an emphasis on the need for a methodical, individualized, and ongoing approach.

Case Example

Joey, a 7-year-old boy, presented for evaluation of hyperactivity and school problems. Joey's mother reported that he has been "a handful" at

home and school since about preschool age. Persistent teacher concerns include trouble following directions or completing tasks, shouting out answers, and not staying seated. Now in second grade, Joey's teacher stated these behaviors are affecting Joey's ability to learn and establish friendships. At home, Joey's mother reported that he is always on the go and is easily distracted from chores and homework. He can be moody and emotional, especially later in the day and toward the end of the school week. Sometimes, Joey's parents "ground him" for what seems to them oppositional behaviors; however, Joey's parents have also wondered whether he is getting enough sleep. It is hard to get him to bed at night, and it is hard to get him up in the morning. In addition, he routinely falls asleep on the short car ride home after school. On a recent vacation, Joey's daytime behavior improved somewhat with more sleep; however, he was also noted to snore and be quite restless during sleep. Joey's past medical history was unremarkable, and development has been on target. Family history was notable for OSA for Joey's paternal grandfather and father was reported to snore loudly. A maternal uncle was reported to have a history of an ADHD diagnosis and legal problems later in life.

Assessment of SDB and Behavioral Disorders

When a child presents with a chief complaint in behavioral or sleep domains, it is important to inquire about both areas due to the documented relationships between them [47, 68–70]. However, while it can be challenging to tease out the influence of one area on the other initially, this becomes clearer over the course of treatment. As highlighted by this case, Joey's behavioral problems may be influenced by underlying genetic risk factors, SDB, disruptive behavior disorder, or parenting style. Nonetheless, Joey's possible poor sleep quality and insufficient sleep at night likely worsen the severity of the presenting behavioral concerns as well as quality of life for Joey and his family [71]. A comprehensive evaluation begins with a thorough history that includes questions about both physical functioning and sleep symptoms. In addition, questions pertaining to onset, course, duration, and impact of sleep problems are also essential. Questions should also focus on bedtime routines, sleep hygiene, child temperament, as well as family history of SDB. Changes in symptoms should also be ascertained such as when sleep is improved or worsened. In Joey's case, in addition to behavioral disruption and SDB symptoms, bedtime resistance was also endorsed on a parent-completed measure of SDB. In fact, screening tools can help focus on the relevant areas, and several tools are available for clinical practice. One such measure is the Pediatric Sleep Questionnaire [72]. This measure includes subscales that assess ADHD symptoms as well as sleep-related breathing disorder (SRBD) symptoms and individual items that assess sleep behaviors such as bedtime resistance. Answers in the positive direction provide an indication that sufficient morbidity exists to evaluate further. Research on the reliability and validity of the PSQ has shown good positive predictive value with regard to behavioral symptoms, as well as predictive validity in comparison to PSG for SDB symptoms [72]. Other measures are also available, but may not incorporate both sleep and behavioral aspects of a child's presentation. Therefore, clinicians should also question families of children with sleep concerns, such as Joey's, about symptoms related to daytime functioning including hyperactivity, inattention, aggression, irritability, mood lability, and daytime sleepiness. In addition, questions pertaining to school performance and learning can also be helpful.

Laboratory testing might be indicated to evaluate for underlying medical concerns (e.g., assessing iron status for restless sleep or thyroid function for daytime fatigue). Further, a neuropsychological evaluation can also provide more specific information related to cognitive symptoms of ADHD, as well as academic achievement level.

Treatment

The initial management plan should include education for parent and child about the significant relationships between behavioral and sleep disturbances. This education could help their understanding of what they are experiencing behaviorally at home and school. In addition, a discussion about the stepwise nature of the treatment process should help them focus on realistic

timetables and targets for improvement. For instance, during Joey's initial evaluation, polysomnography was recommended. The study showed an apnea–hypopnea index (AHI) of 6.2 apneas or hypopneas per hour of sleep, and a consultation with otolaryngology was recommended, and Joey underwent AT surgery. Two months after surgery, Joey and his parents noticed several significant changes. He was reported to be sleeping more soundly and waking refreshed. Further, Joey was reported to have been more likely to stay in his seat at school and was not as moody at home. However, the teacher still had concerns about Joey's distractibility in class, and parents continued to observe that he needed constant reminders to get things done at home. Thus, the steps involved in Joey's treatment specifically, and treatment in general, may require time; however, in the process, residual concerns in behavioral or sleep domains can become clearer.

Because surgical intervention may not be feasible, other treatment possibilities might include behavioral strategies. For example, behavioral management strategies that improve the predictability of routines and the likelihood of cooperative follow-through by the child at home and at school could be recommended. Strategies such as desensitization and incentive programs can be very helpful for children who are recommended to use continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) for management of their SDB. Behavioral management strategies can also be important especially when limit-setting problems are affecting needed sleep duration. How much and which behavioral or sleep treatments to recommend while proceeding through this process will likely be decided differently depending on the nature and extent of the symptoms. For example, a child with a primary concern of ADHD without other mental health, educational, or sleep concern may be recommended one treatment; however, a different plan would be recommended for a child with a primary concern of inattention but with poor sleep hygiene, shortened sleep duration, and heroic snoring. In Joey's case, work on his bedtime problem (sleep hygiene, sleep log to assess sleep–wake pattern and follow-up to assess progress) could help to improve his sleep duration. That might help to reduce the effect of his probable sleep-related breathing disorder on daytime functioning while awaiting evaluation with polysomnography and eventual treatment of SDB. However, it would be important to track the outcome of proposed interventions on an individual basis. One study demonstrated reduced time in bed was related to poorer academic performance [73]. On the other hand, a study of use of melatonin to reduce insomnia did not improve problematic behaviors or cognitive performance in children with ADHD [74]. Whether or not to evaluate the efficacy of psychostimulant medication for probable ADHD in the context of a significant concern for an underlying sleep problem is a question clinicians often face. One might argue that use of the psychostimulant might help Joey avoid school failure in the short run; however, there is no formal study of the effects of interval treatment of ADHD symptoms in patients with comorbid sleep concerns. In addition, there is evidence that the addition of medication might have negative effects on sleep. Studies assessing the effect of psychostimulant medications on sleep have demonstrated parent perception of problems like later sleep onset and more nocturnal awakenings [75].

Follow-up to assure that Joey's behavioral pattern is re-evaluated after SBD treatment is crucial. Studies suggest that treatment of SDB with adenotonsillectomy may reduce mild ADHD symptoms related to SDB [76]. However, moderate to severe ADHD symptoms are not completely alleviated by management of SDB [24]. In Joey's case, follow-up evaluation of his home and school behavioral pattern included the use of age- and gender-normed behavioral rating scales. This evaluation demonstrated the persistence of significant ADHD inattentive-type symptoms. He was then referred for medical and behavioral management of the residual symptoms and experienced good success.

Summary

As outlined in previous sections, although much is known about the consequences of SDB in children, much remains to be learned to advance the

field in terms of research and clinical practice. Although standardized procedures for objective assessment have improved, consensus regarding best practice patterns related to PSG methods or standards is elusive [77]. For example, studies have documented poor association between standard PSG measures and neurocognitive functioning [24, 61, 70]. This suggests that better polysomnographic methods or novel biomarkers will need to be developed for more reliable and valid assessment of the associations between SDB and neurocognitive function. Further, research that has begun to focus on possible biomarkers associated with SDB is now underway with promising results. The effort to identify the possible influence of proinflammatory markers in children with SDB is promising, but more work is needed. In addition, the lack of identification of possible SDB in children continues to be a problem in general clinical care settings [2]. It would be advantageous therefore to develop reliable screening instruments that can be used in pediatric clinics. With regard to clinical guidelines, efforts should be undertaken to standardize objective assessment and treatment recommendations for SDB in children, and alternative approaches to treatment should also be considered.

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