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State of the Art: Sleep Disordered Breathing in Children

# Neurocognitive and Behavioral Impact of Sleep Disordered Breathing in Children

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**Summary.** The consequences of poor quality and/or inadequate sleep in children and adolescents have become a major public health concern, and one in which pediatric health care professionals have become increasingly involved. In particular, insufficient and/or fragmented sleep resulting from primary sleep disorders such as obstructive sleep apnea (OSA), often compounded by the presence of comorbid sleep disorders as well as by voluntary sleep curtailment related to lifestyle and environmental factors, has been implicated in a host of negative consequences. These range from metabolic dysfunction and increased cardiovascular morbidity to impairments in mood and academic performance. The following review will focus on what is currently known about the effects of sleep disordered breathing (SDB) specifically on neurobehavioral and neurocognitive function in children. Because of the scarcity of literature on the cognitive and behavioral impact of sleep disorders in infants and very young children, this review will target largely the preschool/school-aged child and adolescent populations. In addition, the focus will be on a review of the most recent literature, as a supplement to several excellent previous reviews on the topic.[1–4] **Pediatr Pulmonol. 2009; 44:417–422.**


**Key words: obstructive sleep apnea; children; attention; learning; behavior.**

## MANIFESTATIONS OF DAYTIME SLEEPINESS IN CHILDREN

Excessive daytime sleepiness is commonly viewed as one of the primary mechanism through which sleep disorders exert their negative impact on mood, cognitive functioning, and behavior. In any discussion of the impact of sleepiness in the pediatric population, it should first be emphasized that impairments related to sleepiness are often acted out behaviorally (e.g., hyperactivity, impulsivity, increased aggression) by children rather than expressed verbally (e.g., complaining of being tired).[5] In addition, depending upon a number of child-related variables (e.g., age, developmental level, temperament), there is likely to be substantial variability in the types of behavioral manifestations of sleepiness observed; for example, young children are less likely than older children to act characteristically ''sleepy'' (e.g., yawning, rubbing eyes, and/or resting the head on a desk) following sleep restriction. Furthermore, sleepiness-related behaviors may also be interpreted according to the context in which they occur (e.g., a child who is ''hyperactive'' at bedtime may be presumed to be sleepy). Finally, what behaviors are defined as outside the range of ''normal'' (i.e., napping in a 2-year-old vs. a 12-year-old) often depends on developmental level and even cultural interpretation.

In terms of pathological causes, it is also helpful to conceptualize excessive or inappropriate daytime sleepiness in children as evolving from four basic etiologic mechanisms as follows (Fig. 1): sleep is either insufficient for individual physiologic sleep needs (e.g., ''lifestyle'' sleep restriction, sleep onset delay related to behavioral insomnia), or is adequate in amount but fragmented or

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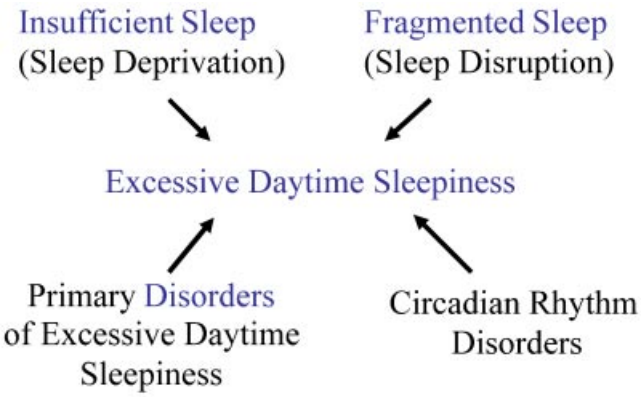


**Fig. 1. Conceptual framework of sleep dysfunction in children.**

disrupted by conditions that result in frequent or prolonged arousals (e.g., obstructive sleep apnea (OSA), periodic limb movement disorder). Third, sleep disorders in which there is a primary underlying defect in the regulation of wakefulness (e.g., narcolepsy) are less common, but important and under-recognized causes of excessive daytime sleepiness in children and adolescents. Fourth, circadian rhythm disorders, in which sleep is usually normal in structure and duration but occurs at an undesired time (e.g., delayed sleep phase disorder, in which the individual's intrinsic sleep onset and wake time are shifted to a later time than is desirable) may result in fatigue-related impairments. Finally, it should be recognized that more than one of these contributors to daytime sleepiness may be present in a given patient.

## COGNITIVE, MOOD, AND BEHAVIOR PROBLEMS IN CHILDHOOD SDB

Although virtually all sleep disorders resulting in insufficient and/or disrupted sleep may have similar impact on mood, attention, cognition, and behavior, the primary sleep disorder that has been most extensively studied in this regard is sleep disordered breathing (SDB). Pediatric SDB includes the broad spectrum of pathology ranging from primary snoring (snoring without observable ventilatory abnormalities) to obstructive hypoventilation/hypopneas to frank apneas with complete cessation of airflow, and includes such related entities as upper airway resistance syndrome. Etiologic factors are related to reduced upper airway patency and increased collapsibility related to obstruction, reduced tone, and upper airway anatomical features; specific risk factors include adenotonsillar hypertrophy, allergies/asthma, race (e.g., African American),[6] positive family history of SDB, and, increasingly, obesity in the pediatric population (Table 1). Although the association between OSA and ''backwardness and stupidity'' was initially noted in the late 1800's by Dr. William Hill, our understanding of the neurocognitive and neurobehavioral sequelae, as well as the specific factors contributing SDB-associated morbidity, has greatly increased in the last decade.

**TABLE 1—Risk Factors for Pediatric Sleep Disordered Breathing**

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| Upper airway obstruction |
| Upper airway narrowing |
| Reduced upper airway tone |
| Adenotonsillar hypertrophy |
| Craniofacial anamolies |
| Retrognathia, mid-face hypoplasia, choanal atresia, etc |
| Congenital syndromes (Pierre–Robin, Hunter's, Hurler's, Achondroplasia, etc.) |
| Trisomy 21 |
| Hypotonia/neuromusclar disorders |
| Cerebral palsy, muscular dystrophy, spina bifida |
| Chronic allergies, asthma |
| Gastroesoghageal reflux |
| Repaired cleft palate |
| Obesity |
| Adipose tissue neck, pharyngeal fat pads |
| Congenital syndromes—Prader–Willi, etc |
| ±pre-pubertal, ↑ 5× teens |
| Family history: ↑ 2–4× risk |
| Former pre-term: ↑ 3× risk |
| Prior adenotonsillectomy |

It should be noted, however, that although polysomnography (PSG) is considered to be the ''gold standard'' for diagnosis of SDB in children, many outcome studies have utilized subjective parent-reported symptoms of SDB (e.g., snoring, apneic pauses) to predict neurobehavioral and neurocognitive sequelae. In addition, there are no universally accepted specific pediatric polysomnographic parameters, which distinguish primary snoring from OSA, etc. Thus, there is variability in the literature regarding definitions of ''pathology'' versus ''non-pathology''.[1] There is also a considerable amount of variability in the outcome measures used (i.e., parent report of behavior, teacher observations of attention, academic achievement, performance on neurocognitive tests), which also creates some challenges in comparing results across studies. Finally, a variety of samples have been used in these outcome studies, ranging from general community populations, to children referred for symptoms of SDB, to children with identified behavioral/academic problems.

Despite these methodological limitations, most pediatric studies have supported a fairly consistent profile of deficits in children with SDB. These include an increase in subjective sleepiness and mood disturbance, behavior problems, and deficits in attention, memory, and executive functions.[7–10] Although to a lesser extent than typically found in adult studies, both subjective observations and objective documentation (i.e., multiple sleep latency test) of increased sleepiness have been demonstrated; children who are obese with SDB may be at relatively higher risk for these problems.[11] Mood disturbances, such as irritability and, in particular, mood instability and emotional dysregulation, have also been frequently reported in

these children. In terms of cognitive function, several studies have found deficits in general intelligence compared to controls;[12,13] however, it should be noted that the comparison groups in these studies had higher than average IQs, and that other studies have failed to find as association between IQ and SDB severity.[14] Studies which have compared specific neuropsychological functions in children with OSA have found the most significant impairments occur for tasks involving reaction time and vigilance, and sustained and selective attention.[2,3,15,16] Studies which have examined other cognitive deficits such as language delays, and impairments in visual perception, motor functions, and memory, have not found consistent significant impairments in these domains.[17] Not surprisingly, a number of studies have also found an association between low levels of academic achievement and SDB,[9,18] which likely represents the combined influence of a number of these learning and attention-based impairments.

A higher prevalence of parent-reported externalizing behavior problems, including impulsivity, hyperactivity, aggression, oppositional behavior, and conduct problems has been frequently reported in studies of children with either polysomnographically diagnosed OSA or symptoms suggestive of SDB.[19–23] The strength of these relationships has been reported to range from adjusted odds ratios of 2.4 (hyperactivity) to 9.7 (peer problems). Effect sizes across studies are typically in the range of 0.5–0.6, indicating a moderately high degree of correspondence, and the relationship persists even when controlling for confounding factors, such as obesity.[24] Other studies have also found higher levels of inattention and internalizing behaviors (somatic complaints, social withdrawal) as well, although effect sizes are generally less robust (i.e., 0.4).[1] Finally, quality of life (QOL) has been demonstrated in a number of studies to be negatively impacted in children with OSA,[25] including effects on caregivers and other family members, which are similar to the decrements in QOL in children with chronic medical conditions.[26]

## SDB SYMPTOMS IN CHILDREN WITH LEARNING AND BEHAVIOR PROBLEMS

Alternatively, the prevalence of SDB symptoms in children with identified attentional, behavioral, and academic problems has also been examined in several studies. One sample of first graders performing academically in the lowest 10th %ile found a prevalence of 18% of significant SDB symptoms.[18] A number of other studies have found a similar increased prevalence of snoring in young children with behavioral and school concerns, suggesting that there may be an approximately twofold increased risk of habitual snoring and SDB symptoms in children with high scores on hyperactivity scales.[21] A particular area of clinical research interest has been the association between SDB and attention deficit hyperactivity disorder (ADHD).[27] Obviously, from a clinical perspective, there is a substantial overlap between the impairments associated with SDB and the diagnostic criteria for ADHD. For example, one study suggested that as much as 25% of children with clinically significant symptoms of ADHD (i.e., hyperactivity/impulsivity) also had symptoms of SDB (i.e., snoring).[7] Another study by the same group found that not only did 28% of children scheduled for adenotonsillectomy meet the current Diagnostic and Statistical Manual (DSM-IV-R) criteria for ADHD (vs. 7% of otherwise healthy surgical controls), but 1-year post-adenotonsillectomy, 50% of those children no longer met ADHD criteria.[28] In another recent study, ADHD scores normalized in 78% of 40 children who had undergone adenotonsillectomy 6 months prior.[29] Habitual snoring is reported to be three times more common in children with ADHD than in other child psychiatric or general pediatric populations. A corollary of the relationship with ADHD is the impact of SDB specifically on ''executive functions,'' which include cognitive flexibility, task initiation, self-monitoring, planning, organization, and self-regulation of affect and arousal. For example, the results of one study suggested that SDB may be associated with impaired executive function in preschoolers, with its strongest impact on the inhibition dimension, further emphasizing the importance of early intervention for sleep-disordered breathing in this young group.[30]

## RISK FACTORS FOR NEUROBEHAVIORAL SEQUELAE IN CHILDHOOD SDB

Not all studies have found a relationship between SDB in children and deficits in specific neurobehavioral/neurocognitive domains. Most studies, for example, have failed to find a direct correlation between polysomnographically derived parameters of disease severity, (such as the number of apneic/hypopneic episodes per hour apnea hypopnea index, AHI) and oxygen saturation, and cognitive and behavioral problems. Therefore, there does not appear to be a direct dose–response relationship between disease severity and these outcomes. Furthermore, several recent studies have found neurobehavioral deficits associated with primary snoring in children that are similar to those found in children with OSA, further suggesting that disease severity-related variables alone may not account for the impairments observed.[10,31]

This has led to speculation that other factors, including individual genetic susceptibility, environmental influences such as passive smoking exposure, and co-morbid conditions, such as obesity, shortened sleep duration, and the presence of other sleep disorders, may also influence neurocognitive outcomes. For example, polymorphisms

involving more than one locus in the Apolipoprotein E gene (APOE e4) and its regulatory region have been found in association with OSA in children.[32] Furthermore, children with both habitual snoring and OSA are more likely than non-snoring children to have the APOE e4 allele (11% vs. 1.5%), which has been shown in adults to be associated with an increased risk of OSA.[33] Furthermore, this relationship appears to be more robust in children with OSA and neurocognitive dysfunction (22% vs. 4%; OR 6.8).[34]

Short sleep duration has been found to be a confounding factor in the relationship between SDB and adverse neurocognitive outcomes;[35] for example, children referred for SDB were found to be more likely to have impaired cognitive function if they also had a short/variable time in bed (TIB).[36] Insufficient sleep has also been identified as a potential risk factor for childhood obesity, further complicating the inter-relationships among these contributing factors.[37] In fact, the combination of obesity and OSA has been shown to be associated with more severe impairments.[38] In addition, the relative contribution of disease duration and of potential developmental ''windows of vulnerability'' regarding the impact of OSA have yet to be elucidated. Finally, the contribution of comorbid sleep disorders (i.e., restless legs syndrome/periodic limb movement disorder, insomnia, behaviorally induced insufficient sleep) to adverse neurobehavioral outcomes has been shown to be substantial.[35,39]

## IMPACT OF SDB TREATMENT

Finally, studies which have looked at changes in behavior and neuropsychological functioning, in children following treatment (usually adenotonsillectomy) for OSA/SDB have also largely documented significant improvement in daytime sleepiness, mood, behavior, and QOL post-treatment[25,28,40–51] compared to control samples. A recent review[52] evaluating outcomes in children after adenotonsillectomy included 25 studies which utilized single or combinations of measures ranging from parent-reported behavioral changes to academic class rankings to QOL improvements. Both short- and long-term positive changes were reported in these studies; for example, in one study, improvements in QOL persisted for up to 3 years post-intervention.[46] Improvements in behavioral ratings were demonstrated using both broad-based instruments such as the Child Behavior Checklist (CBCL)[49] and more targeted measures of attention, hyperactivity, and impulsivity.[23] Although many of these studies relied on relatively more subjective (parent-report) measures of improvement, which may be influenced by expectations regarding treatment outcome, other studies have documented objective improvements on direct testing in neuropsychological measurements of attention, vigilance and reaction time, and cognitive functions.[45,48,50] However, similar to the lack of correlation between disease severity and neurobehavioral outcomes, the correlation between improvements in post-treatment respiratory parameters, as documented by PSG, and improvements in cognition, behavior, and QOL is overall poor.[15,43,44,47] In particular, ''normalization'' of PSG measures did not predict functionally significant improvements, and improvement in parameters such as QOL were seen despite lack of resolution of OSA.[51] This has led to the search for potentially more sensitive markers of disruption of sleep architecture, such as pulse transit time[53] and cyclic alternating EEG patterns.[54] Alternatively, the lack of improvement in neurocognitive measures despite improvement in respiratory parameters in some children may imply that associated deficits may not be fully reversible with treatment, particularly in high-risk populations.[50]

## PATHOPHYSIOLOGY OF SDB AND COGNITIVE DYSFUNCTION

Although yet to be fully elucidated, one of the primary mechanisms by which SDB is believed to exert negative influences on cognitive function appears to involve repeated episodic arousals from sleep leading to sleep fragmentation and resulting sleepiness. In addition, a number of more recent studies have posited at least an equally important role for intermittent hypoxia leading directly to systemic inflammatory vascular changes in the brain.

It has also been postulated that these two mechanisms may have unique effects on neurocognitive function; that is, that intermittent hypoxia may result in selective impairments in executive function, while sleep fragmentation may preferentially affect attention.[16] Although studies have not been conducted in humans, animal models suggest that oxidative stress and inflammatory processes lead to structural and neurochemical changes in the hippocampus and prefrontal cortex (PFC), areas of the brain which are specifically involved in attention and executive functions. Importantly, animal models also suggest similar inflammatory mechanisms are operative in the central nervous system in association with restricted sleep;[1] in the case of insufficient sleep, disruption of the normal restorative features of sleep (i.e., slow wave or delta sleep) may also play a role in increasing neurocognitive dysfunction. In humans, sleep apnea in adults has been found to preferentially affect the hippocampus and cerebellum, and even mild levels of chronic or intermittent hypoxia from a variety of causes have clearly been shown to be associated in children with cognitive and behavioral disruption.[55] Furthermore, levels of inflammatory markers such as C-reactive protein (CRP) and cytokine IL-6[56] have been shown not only to be elevated in children with SDB, but also to be associated with

cognitive dysfunction in these children,[57] and to decrease with adenotonsillectomy.[58] Alternatively, the finding that higher systemic IGF-1 levels are associated with a decreased risk of cognitive morbidity in children with snoring has led to the speculation that IGF-1 may be relatively neuroprotective in these children.[59] Abnormal vascular reactivity and endothelial dysfunction in the central nervous system may also play a role in neurocognitive dysfunction.[60] Finally, the relative contributions of additional factors such as hypercarbia, changes in REM latency/percentage, and alternations in other stages of sleep have yet to be fully explored.

## CONCLUSIONS

As the prevalence of pediatric sleep disorders, as well as the percent of children who have chronically insufficient sleep, continues to rise,[61] it is imperative that pediatric practitioners are aware of the potential connection between poor sleep, sleepiness, and impaired daytime function. In particular, vulnerable populations, such as children living in poverty, may experience ''double jeopardy'' as a result of sleep disorders.[62] Not only are these children at higher risk for developing SDB, as well as other sleep problems as a result of such conditions as chaotic home environments, they are potentially likely to suffer more serious consequences from those sleep problems than their less vulnerable peers. Caretakers as well as clinicians caring for children need to emphasize that maintaining adequate quality and quantity of sleep could play an important role in mitigating the effects of underlying learning, behavioral, or mood problems, and in preventing them from developing in the first place.

## REFERENCES


1. Beebe DW. Neurobehavioral morbidity associated with disordered breathing during sleep in children: a comprehensive review. Sleep 2006;29:1115–1134.
2. Halbower AC, Mahone EM. Neuropsychological morbidity linked to childhood sleep-disordered breathing. Sleep Med Rev 2006;10:97–107.
3. Gozal D, Kheirandish-Gozal L. Neurocognitive and behavioral morbidity in children with sleep disorders. Curr Opin Pulm Med 2007;13:505–509.
4. Capdevila OS, Kheirandish-Gozal L, Dayyat E, Gozal D. Pediatric obstructive sleep apnea: complications, management, and long-term outcomes. Pro Am Thorac Soc 2008;5:274–282.
5. Fallone G, Owens JA, Deane J. Sleepiness in children and adolescents: clinical implications. Sleep Med Rev 2002;6:287–306.
6. Rosen CL, Storfer-Isser A, Taylor HG, Kirchner HL, Emancipator JL, Redline S. Increased behavioral morbidity in school-aged children with sleep-disordered breathing. Pediatrics 2004;114: 1640–1648.
7. Chervin RD, Archibold KH. Hyperactivity and polysomnographic findings in children evaluated for sleep-disordered breathing. Sleep 2001;24:313–320.
8. Chervin RD, Dillon JE, Bassetti C, Ganoczy DA, Pituch KJ. Symptoms of sleep disorders, inattention, and hyperactivity in children. Sleep 1997;20:1185–1192.
9. Gozal D, Pope D. Snoring during early childhood and academic performance at ages 13–14 years. Pediatrics 2001;107:1394–1399.
10. O'Brien LM, Mervis CB, Holbrook CR, Bruner JL, Klaus CJ, Rutherford J, Raffield TJ, Gozal D. Neurobehavioral implications of habitual snoring in children. Pediatrics 2004;114:44–49.
11. Gozal D, Wang M, Pope DW Jr. Objective sleepiness measures in pediatric obstructive sleep apnea. Pediatrics 2001;108:693–697.
12. Carskadon MA, Vieira C, Acebo C. Association between puberty and delayed phase preference. Sleep 1993;16:258–262.
13. Randazzo AC, Muehlbach MJ, Schweitzer PK, Walsh JK. Cognitive function following acute sleep restriction in children ages 10–14. Sleep 1998;21:861–868.
14. Kaemingk KL, Pasvogel AE, Goodwin JL, Mulvaney SA, Martinez F, Enright PL, Rosen GM, Morgan WJ, Fregosi RF, Quan SF. Learning in children and sleep disordered breathing: findings of the Tucson Children's Assessment of Sleep Apnea (tuCASA) prospective cohort study. J Int Neuropsychol Soc 2003; 9:1016–1026.
15. Mitchell RB, Kelly J. Behavior, neurocognition and quality-of-life in children with sleep-disordered breathing. Int J Pediatr Otorhinolaryngol 2006;70:395–406.
16. Blunden S, Lushington K, Lorenzen B, Martin J, Kennedy D. Neuropsychological and psychosocial function in children with a history of snoring or behavioral sleep problems. J Pediatr 2005; 146:780–786.
17. Hamasaki Uema SF, Nagata Pignatari SS, Fujita RR, Moreira GA, Pradella-Hallinan M, Weckx L. Assessment of cognitive learning function in children with obstructive sleep breathing disorders. Rev Bras Otorrinolaringol (Engl Ed) 2007;73:315–320.
18. Gozal D. Sleep-disordered breathing and school performance in children. Pediatrics 1998;102:616–620.
19. O'Brien LM, Holbrook CR, Mervis CB, Klaus CJ, Bruner JL, Raffield TJ, Rutherford J, Mehl RC, Wang M, Tuell A, Hume BC, Gozal D. Sleep and neurobehavioral characteristics of 5- to 7-year-old children with parentally reported symptoms of attention-deficit/hyperactivity disorder. Pediatrics 2003;111:554–563.
20. Goodwin JL, Kaemingk KL, Fregosi RF, Rosen GM, Morgan WJ, Sherrill DL, Quan SF. Clinical outcomes associated with sleep-disordered breathing in Caucasian and Hispanic children–the Tucson Children's Assessment of Sleep Apnea study (TuCASA). Sleep 2003;26:587–591.
21. Chervin RD, Archbold KH, Dillon JE, Panahi P, Pituch KJ, Dahl RE, Guilleminault C. Inattention, hyperactivity, and symptoms of sleep-disordered breathing. Pediatrics 2002;109:449–456.
22. Ali NJ, Pitson D, Stradlin JR. Natural history of snoring and related behaviour problems between the ages of 4 and 7 years. Arch Dis Child 1994;71:74–76.
23. Ali NJ, Pitson DJ, Stradling JR. Snoring, sleep disturbance, and behaviour in 4–5 year olds. Arch Dis Child 1993;68:360–366.
24. Rudnick EF, Mitchell RB. Behavior and obstructive sleep apnea in children: is obesity a factor? Laryngoscope 2007;117:1463–1466.
25. Constantin E, Kermack A, Nixon GM, Tidmarsh L, Ducharme FM, Brouillette RT. Adenotonsillectomy improves sleep, breathing, and quality of life but not behavior. Arch Otolaryngol Head Neck Surg 2007;133:216–222.

26. Baldassari CM, Mitchell RB, Schubert C, Rudnick EF. Pediatric obstructive sleep apnea and quality of life: a meta-analysis. Proc Am Thorac Soc 2008;5:274–282.
27. Owens J. The ADHD and sleep conundrum: a review. J Dev Behav Pediatr 2005;26:312–322.
28. Dillon JE, Blunden S, Ruzicka DL, Guire KE, Champine D, Weatherly RA, Hodges EK, Giordani BJ, Chervin RD. DSM-IV diagnoses and obstructive sleep apnea in children before and 1 year after adenotonsillectomy. J Am Acad Child Adolesc Psychiatry 2007;46:1425–1436.
29. Li HY, Huang YS, Chen NH, Fang TJ, Lee LA. Impact of adenotonsillectomy on behavior in children with sleep-disordered breathing. Laryngoscope 2006;116:1142–1147.
30. Karpinski AC, Scullin MH, Montgomery-Downs HE. Risk for sleep-disordered breathing and executive function in preschoolers. Sleep Med 2008;9:418–425.
31. Bao G, Guilleminault C. Upper airway resistance syndrome–one decade later. Curr Opin Pulm Med 2004;10:461–467.
32. Kalra M, Pal P, Kaushal R, Amin RS, Dolan LM, Fitz K, Kumar S, Sheng X, Guha S, Mallik J, Deka R, Chakraborty R. Association of ApoE genetic variants with obstructive sleep apnea in children. Sleep Med 2008;9:260–265.
33. Gottlieb DJ, DeStefano AL, Foley DJ, Mignot E, Redline S, Givelber RJ, Young T. APOE epsilon4 is associated with obstructive sleep apnea/hypopnes: the sleep heart health study. Neurology 2004;63:664–668.
34. Gozal D, Capdevila OS, Kheirandish-Gozal L, Crabtree VM. APOE epsilon 4 allele, cognitive dysfunction, and obstructive sleep apnea in children. Neurology 2007;69:243–249.
35. Blunden SL, Beebe DW. The contribution of intermittent hypoxia, sleep debt and sleep disruption to daytime performance deficits in children: consideration of respiratory and non-respiratory sleep disorders. Sleep Med Rev 2006;10:109–118.
36. Suratt PM, Barth JT, Diamond R, D'Andrea L, Nikova M, Perriello VA Jr, Carskadon MA, Rembold C. Reduced time in bed and obstructive sleep-disordered breathing in children are associated with cognitive impairment. Pediatrics 2007;119:320–329.
37. Patel SR, Hu FB. Short sleep duration and weight gain: a systematic review. Obesity (Silver Spring) 2008;16:643–653.
38. Rhodes SK, Shimoda KC, Waid LR, O'Neil PM, Oexmann MJ, Collop NA, Willi SM. Neurocognitive deficits in morbidly obese children with obstructive sleep apnea. J Pediatr 1995;127:741–744.
39. Owens J, Mehlenbeck R, Lee J, King M. Behavioral outcomes in children with sleep disordered breathing: impact of weight, sleep duration, and co-morbid sleep disorders. Arch Pediatr Adolesc Med 2008;162:313–321.
40. Mitchell RB, Kelly J. Behavioral changes in children with mild sleep-disordered breathing or obstructive sleep apnea after adenotonsillectomy. Laryngoscope 2007;117:1685–1688.
41. Ali NJ, Pitson D, Stradlin JR. Sleep disordered breathing; effects of adenotonsillectomy on behavior and psychological function. Eur J Pediatr 1996;155:156.
42. Wei JL, Mayo MS, Smith HJ, Reese M, Weatherly RA. Improved behavior and sleep after adenotonsillectomy in children with sleep-disordered breathing. Curr Opin Pulm Med 2007;13:505–509.
43. Mitchell RB. Adenotonsillectomy for obstructive sleep apnea in children: outcome evaluated by pre- and postoperative polysomnography. Laryngoscope 2007;117:1844–1854.
44. Chervin RD, Ruzicka DL, Giordani BJ, Weatherly RA, Dillon JE, Hodges EK, Marcus CL, Guire KE. Sleep-disordered breathing, behavior, and cognition in children before and after adenotonsillectomy. Pediatrics 2006;117:769–778.
45. Avior G, Fishman G, Leor A, Sivan Y, Kaysar N, Derowe A. The effect of tonsillectomy and adenoidectomy on inattention and impulsivity as measured by the test of variables of attention (TOVA) in children with obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg 2004;131:367–371.
46. Díez-Montiel A, de Diego JI, Prim MP, Martín-Martínez MA, Pérez-Fernández E, Rabanal I. Quality of life after surgical treatment of children with obstructive sleep apnea: long-term results. Int J Pediatr Otorhinolaryngol 2006;70:1575–1579.
47. Friedman BC, Hendeles-Amitai A, Kozminsky E, Leiberman A, Friger M, Tarasiuk A, Tal A. Adenotonsillectomy improves neurocognitive function in children with obstructive sleep apnea syndrome. Sleep 2003;26:999–1005.
48. Galland BC, Dawes PJ, Tripp EG, Taylor BJ. Changes in behavior and attentional capacity after adenotonsillectomy. Pediatr Res 2006;59:711–716.
49. Goldstein NA, Post JC, Rosenfeld RM, Campbell TF. Impact of tonsillectomy and adenoidectomy on child behavior. Arch Otolaryngol Head Neck Surg 2000;126:494–498.
50. Montgomery-Downs HE, Crabtree VM, Gozal D. Cognition, sleep, and respiration in at-risk children treated for obstructive sleep apnoea. Eur Respir J 2005;25:336–342.
51. Mitchell RB, Kelly J. Outcome of adenotonsillectomy for severe obstructive sleep apnea in children. Int J Pediatr Otorhinolaryngol 2004;68:1375–1379.
52. Garetz SL. Behavior, cognition, and quality of life after adenotonsillectomy for pediatric sleep-disordered breathing: summary of the literature. Otolaryngol Head Neck Surg 2008; 138:S19–S26.
53. Katz ES, Lutz J, Black C, Marcus CL. Pulse transit time as a measure of arousal and respiratory effort in children with sleep-disordered breathing. Pediatr Res 2003;53:580–588.
54. Kheirandish-Gozal L, Miano S, Bruni O, Ferri R, Pagani J, Villa MP, Gozal D. Reduced NREM sleep instability in children with sleep disordered breathing. Sleep 2007;30:450–457.
55. Bass JL, Corwin M, Gozal D, Moore C, Nishida H, Parker S, Schonwald A, Wilker RE, Stehle S, Kinane TB. The effect of chronic or intermittent hypoxia on cognition in childhood: a review of the evidence. Pediatrics 2004;114:805–816.
56. Gozal D, Serpero LD, Sans Capdevila O, Kheirandish-Gozal L. Systemic inflammation in non-obese children with obstructive sleep apnea. Sleep Med 2008;9:254–259.
57. Gozal D, Crabtree VM, Sans Capdevila O, Witcher LA, Kheirandish-Gozal L. C-reactive protein, obstructive sleep apnea, and cognitive dysfunction in school-aged children. Am J Respir Crit Care Med 2007;176:188–193.
58. Li M, Chan H, Yin J, So H, Ng SK, Chan IH, Lam CW, Wing YK, Ng PC. C-reactive protein in children with obstructive sleep apnea and the effects of treatment. Pediatr Pulmonol 2008;43:34–40.
59. Gozal D, Sans Capdevila O, Crabtree VM, Serpero LD, Witcher LA, Kheirandish-Gozal L. Plasma IGF-1 levels and cognitive dysfunction in children with obstructive sleep apnea. Otolaryngol Head Neck Surg 2008;138:265–273.
60. Gozal D, Kheirandish-Gozal L, Serpero LD, Sans Capdevila O, Dayyat E. Obstructive sleep apnea and endothelial function in school-aged non-obese children: effect of adenotonsillectomy. Circulation 2007;116:2307–2314.
61. Dollman J, Ridley K, Olds T, Lowe E. Trends in the duration of school-day sleep among 10- to 15-year-old South Australians between 1985 and 2004. Acta Paediatr 2007;96:1011–1014.
62. Nixon GM, Thompson JM, Han DY, Becroft DM, Clark PM, Robinson E, Waldie KE, Wild CJ, Black PN, Mitchell EA. Short sleep duration in middle childhood: risk factors and consequences. Sleep 2008;31:71–78.