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REVIEW

Neurocognitive performance and behavior before and after treatment for sleep-disordered breathing in children

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Abstract: Neurocognitive and behavioral problems are increasingly reported in children with sleep-disordered breathing (SDB). The impact of treatment for SDB on neurocognition and behavior is, therefore, an issue of increasing importance. To date, there has been little consideration given to the quality of studies when reviewing associated neurocognitive and behavioral problems in children with SDB, and furthermore, there has been little systematic review of treatment outcomes. The aim of this review was to provide an up-to-date and critical review of the current literature. Findings indicate a specific pattern of neurocognitive problems in children with SDB; however, the pattern of behavioral problems is less clear. Very few studies were found to provide a rigorous investigation of posttreatment neurocognitive and behavior outcomes. Despite this, relatively consistent improvements in global intelligence, attention, and visual spatial ability are shown; however, persistent deficits in other domains are also evident. For behavior, problems of hyperactivity, aggression or conduct problems, and somatic complaints improve following treatment. In contrast, symptoms of anxiety and social problems less consistently improve. These findings should aid in the development of more targeted investigations and well-designed studies exploring both the causative mechanisms and the treatment response for neurocognitive and behavior problems in children with SDB.

Keywords: adenotonsillectomy, neurocognition, sleep-disordered breathing, children, behavior

Obstructive sleep-disordered breathing (SDB) is common in children and varies along a continuum of upper airway obstruction from primary snoring to upper airway resistance syndrome (UARS) to obstructive sleep apnea syndrome (OSAS). Primary snoring is characterized by frequent snoring without ventilatory abnormalities or obvious sleep disruption and affects 5%–10% of children. UARS differs from primary snoring in that sleep is fragmented by arousals, while the severe OSAS is characterized by hypoxia and sleep fragmentation, affecting 1%–4% of children.[1] There is now convincing evidence that SDB is associated with neurocognitive and behavioral deficits, particularly those of hyperactivity, inattention, memory, learning, executive functioning, and general cognitive capacity.[2] In contrast, there is less convincing evidence that treatment of SDB (ie, adenotonsillectomy) reverses deficits. This remains to be completely investigated, as do the correlates of SDB and their association with neurocognitive and behavioral deficits.

Charles Dickens,[3] in his book *The Posthumous Papers of the Pickwick Club*, is credited with an early description of child SDB, with the fat boy Joe often falling asleep in strange or inappropriate places and snoring when he was sleeping, as having slow perception, bizarre and aggressive behavior, being red-faced with swollen legs and

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dividing "… his time into small alternate allotments of eating and sleeping." Over 50 years later, William Osler[4] in the 1892 edition of *The Principles and Practice of Medicine* presciently described a child with suspected SDB, as responding "… slowly to questions and may be sullen and cross … The influence on the mental development is striking … It is impossible for them to fix the attention for long at a time". Similarly, William Hill[5], reporting in the British Medical Journal in 1889, noted symptoms of "… backwardness and stupidity …" in children with adenotonsillar enlargement. Despite these seminal observations, it took another 8 decades before the impact of childhood SDB on daytime cognitive performance and behavior was formally investigated by Guilleminault et al[6] in 1976. These authors reported that the majority of children with OSAS in their small sample of eight children had excessive daytime sleepiness and learning difficulties at school. Further, children attending school were reported by their teachers to be hyperactive, to be inattentive, and to have a general decrease in intellectual ability while half the children were receiving mental health intervention for "emotional problems". Despite the small sample size and lack of controls, this initial study demonstrated that children with SDB have substantive behavior and cognitive performance deficits – a finding that was largely overlooked for the next 2 decades. In 1982, Guilleminault et al[7] published a report of 25 snoring children who on nocturnal polysomnography (PSG) did not meet the criteria for OSAS, but demonstrated significantly increased esophageal pressure during sleep when compared with controls, suggesting UARS. Notably, these children were hyperactive (48%), aggressive (40%), withdrawn (40%), and clumsy (44%). All the school-aged children in remedial education programs were reported to have learning problems (40%). Further, eight children were on methylphenidate treatment for hyperactivity, and 19 children had a current or previous referral to a psychiatrist or psychologist. Although only the second investigation in this area, this study indicated that even mild forms of SDB may be associated with significant behavioral and cognitive sequelae.

Until the mid-1990s, there was little additional research examining cognitive and behavior sequelae in children with SDB, with the focus only returning in the early 2000s. A series of reviews undertaken between 2001 and 2006[2,8–12] have consistently identified cognitive deficits in attention, memory and learning, and general intelligence, and behavioral problems of attention, hyperactivity, and aggression, with the later reviews also including anxiety, depression, and emotional instability. However, the deficits identified in these earlier studies reflect the focus of researchers, with several domains notably absent or underexplored from examination such as sensorimotor function, language skills, and visuospatial ability. The early reviews also revealed substantial methodological limitations in the field, including inadequate sampling methods; inappropriate or inadequate statistical analysis; small sample sizes; lack of control data; inadequate methods for diagnosis of SDB status; and a failure to consider potential confounders such as socioeconomic and demographic status, obesity, family history, chronicity of disease, age, gender, comorbid disorders, ethnicity, parental education, and other environmental factors. An especially important limitation is the failure by most studies to consider the interplay between SDB, hyperactive behavior, and ADHD, the delineation of which appears to be vital in helping to clarify the unique role SDB plays in the development of hyperactive behavior.[13]

A critical review of the literature

Given the recent increase in research investigating the cognitive and behavioral deficits among children with SDB and the many limitations evident in this research, it is important that strict evaluation guidelines be established. A parallel need has emerged in the adult OSAS field resulting in rigorous exclusion criteria, which has enabled better characterization of the pattern of cognitive domains impacted by OSAS and identification of those cognitive domains that improve with treatment. For example, Aloia et al[14] excluded studies specifically recruiting non-OSAS participants, without verification of OSAS by PSG; recruiting medical populations with OSAS, including children or adolescents and exclusively patients with central sleep apnea; and assessing a single cognitive domain or using nonvalidated instruments. In doing so, a clear pattern of spared global intelligence, but impaired attention, executive functioning, memory, and psychomotor functioning, was characterized in OSAS adults, with treatment response in all domains except in psychomotor functioning. Imposing similar exclusions and critically reviewing the current child-based literature are also likely to clarify the pattern of neurocognitive and behavioral problems and treatment response in children with SDB.

Data for the current review included empirical studies published in peer-reviewed journals up until November 2009. A literature search using PubMed and PsychInfo online databases was made using combinations of the following search terms: sleep, children, snoring, apnea, cognition, neurocognition, cognitive, behavior, and behavioral. Existing reference lists from the published studies were also reviewed to identify

additional relevant studies. Studies with no English version, book chapters, review articles, dissertations, abstracts, letters to the editor, and any nondata analytic reports were excluded. Initially, 95 studies were identified for consideration (see Appendix A). To provide a more critical review of the literature, studies were included only if they met the following criteria:

1. SDB status was verified by overnight laboratory or home-based multichannel PSG [including at least oximetry, airflow, electrocardiogram, thoracic and abdominal movements, and video monitoring in the absence of electroencephalogram (EEG)].
2. Special medical populations with SDB were excluded (such as those with Down's syndrome or Pierre Robin sequence).
3. Study participants aged over 18 years were excluded.
4. Validated measures of neurocognitive performance (excluding school grades) and behavior were used.
5. Data of control group or standardized normative data were used while reporting group performance (except when reporting the association between SDB severity and performance).

To facilitate a better understanding of the contribution of SDB to neurocognitive and, likewise, behavioral deficits, these two broad areas have been separately examined. Twenty-eight studies that report neurocognitive findings (Table 1) and 21 reporting behavioral findings (Table 2) with 12 overlapping studies were included. In addition, we further separated the studies into those that have examined the association between SDB severity and neurocognition (n = 13; Table 3) and between SDB and behavior (n = 12; Table 4), with seven overlapping studies.

Neurocognitive performance deficits in children with SDB

A summary of neurocognitive domains assessed by studies meeting this review's criteria is presented in Table 1. All studies report one or more neurocognitive deficits in children with SDB, with the frequency of affected domains ranging from 40% for verbal intelligence to 71% for attention. The most frequently assessed domain was intelligence (including global, verbal, and nonverbal intelligence; 24 studies) and the least sensorimotor functioning (six studies). Most studies report significant deficits in intelligence, attention, and executive function and less commonly deficits in memory, visual–spatial ability, language skills, and sensorimotor functions. Notably, there does not appear to be a dose-response effect, with the magnitude of deficits comparable in primary snoring and OSAS.

Despite 13 of 20 studies reporting that global intelligence scores were significantly lower in children with SDB compared with controls, mean scores for children with SDB in 11 of these studies were within the normal range and less than one standard deviation below the mean in only two studies.[10,15] In addition, a number of studies report the mean global intelligence scores in control groups at or above the upper limit of the normal range.[16–19] It could be argued that a recruitment bias in control samples may force the difference observed in these studies; however, performance in these control samples is consistent with that of healthy children in other large studies.[20] The pattern of findings for global intelligence parallels those for other neurocognitive domains, with the performance reduced in children with SDB but generally in the normal range. Of the two exceptions that report substantively reduced global intelligence quotient (IQ) scores, one study exclusively recruited children with low socioeconomic standing, while the second included children with severe SDB symptoms. Compared with children from high socioeconomic status (SES), children with low SES have worse neurocognitive performance when sleep is disturbed, but similar performance when sleep is undisturbed.[21] Low SES is also associated with an increased risk for behavioral and neurocognitive deficits among children with SDB.[22,23] Taken together, these results suggest an interaction between SDB and SES, which may place subgroups of children at higher risk for neurocognitive and behavioral impairment. The results also highlight the problems of evaluating neurocognitive performance and the need to control for confounds, such as SES, in analyses.

In addition to deficits in intelligence, majority of studies also report that children with SDB have reduced executive function characterized by problems with planning and strategizing, but not with inhibition.[10,18,24–27] This suggests a specific pattern of executive dysfunction among children with SDB and distinct to findings in ADHD, where deficits in inhibition are considered to be a core feature.[28] The final area of consistently reduced performance in children with SDB is attention. A primary deficit in attentional capacity has been proposed to underlie both lower and higher order neurocognitive deficits in adults with OSAS.[29] It is considered that attentional capacity is sensitive to sleep fragmentation and likely to be evident across the SDB spectrum. In addition, attentional capacity is considered to underpin higher order neurocognitive processes such as executive functioning. Despite the appeal of these hypotheses, the magnitude of

Table 1 Comparisons of neurocognitive function between children with and without SDB

Authors	Global intelligence	Verbal intelligence	Nonverbal intelligence	Memory	Attention	Executive function	Language	Visual spatial	Sensorimotor
Rhodes et al[45]	+	NA	NA	+	NA	NA	NA	NA	NA
Blunden et al[31]	+	+	+	+	+	NA	NA	NA	NA
Owens et al[46,*]	o	o	NA	o	+	+	o	o	+
Hansen and Vandenberg[47,*]	NA	NA	NA	o	+	NA	NA	NA	NA
Lewin et al[19]	o	o	o	NA	NA	NA	NA	NA	NA
Friedman et al[16]	+	o	NA	+	NA	NA	NA	o	NA
Kaemingk et al[48]	o	o	o	+	NA	NA	o	NA	NA
Archbold et al[49,*]	o	NA	NA	o	+	o	o	NA	NA
Beebe et al[24]	o	NA	NA	o	o	+	NA	NA	NA
Gottlieb et al[17]	+	o	+	+	+	+	NA	NA	NA
Kennedy et al[50]	+	+	o	+	+	NA	NA	NA	NA
O'Brien et al[27]	+	o	+	o	+	+	+	o	NA
O'Brien et al[51]	+	+	o	+	o	o	+	+	NA
O'Brien et al[26]	+	+	+	o	+	o	+	+	NA
Montgomery-Downs et al[15]	+	NA	NA	NA	NA	NA	o	NA	NA
Chervin et al[43]	NA	NA	NA	NA	+	NA	NA	NA	NA
Galland et al[32]	NA	NA	NA	NA	+	NA	NA	NA	NA
Halbower et al[52]	+	NA	NA	o	o	+	NA	o	o
Hill et al[33]	o	o	o	NA	+	+	NA	o	NA
Kurnatowski et al[34]	NA	NA	NA	+	+	+	+	+	+
Li et al[53,a]	NA	NA	NA	NA	+	NA	NA	NA	NA
Ziliotto et al[54]	NA	NA	NA	+	NA	NA	NA	NA	NA
Gozal et al[55]	+	NA	NA	NA	NA	NA	NA	NA	NA
Uema et al[56]	NA	NA	NA	+	o	NA	NA	NA	NA
Calhoun et al[57]	o	o	+	o	o	o	NA	o	NA
Giordani et al[25]	NA	o	NA	+[a]	+	o	o	+	o
Gozal et al[58]	+	+	o	o	o	+	+	o	o
Kohler et al[18]	+	+	+	+[b]	+[c]	+	+	+	+
Studies showing impairment in children with SDB	13/20 (65%)	6/15 (40%)	6/12 (50%)	12/21 (57.1%)	15/21 (71.4%)	9/14 (64.3%)	6/11 (54.5%)	5/12 (41.7%)	3/6 (50%)

[a]Compared to standardized norms only.
[b]Giordani et al[25] report deficits in recall of dot patterns but not for recall of faces, verbal stories, or words.
[c]Kohler et al[18] report deficits in recall of verbal stories but not recall of faces or words.
[d]Kohler et al[18] report deficits in visual but not auditory attention.
Note: "+" indicates significant deficits in SDB children shown and "o" indicates significant deficits in SDB children not shown.
Abbreviation: NA, not assessed.

Table 2 Association of neurocognitive function with SDB severity among children

Authors	Global intelligence	Verbal intelligence	Nonverbal intelligence	Memory	Attention	Executive function	Language	Visual spatial	Sensorimotor
Rhodes et al[45]	NA	NA	NA	+	NA	NA	o	NA	NA
Lewin et al[19]	o	+	o	NA	NA	NA	NA	NA	NA
Kaemingk et al[48]	+	o	+	+	NA	NA	+	NA	NA
Archbold et al[49]	NA	NA	NA	NA	NA	+	NA	NA	NA
Beebe et al[24]	o	NA	NA	o	+	+	NA	NA	NA
Kennedy et al[50]	+	+	+	+	o	NA	NA	NA	NA
O'Brien et al[27]	+	o	+	o	+	+	o	o	NA
Chervin et al[43]	NA	NA	NA	NA	o	NA	NA	NA	NA
Galland et al[32]	NA	NA	NA	NA	o	NA	NA	NA	NA
Li et al[53]	NA	NA	NA	NA	+	NA	NA	NA	NA
Suratt et al[59]	+	o	NA	o	o	NA	NA	o	NA
Calhoun et al[57]	o	o	o	o	o	o	NA	o	NA
Kohler et al[18]	o	o	o	o	o	o	o	o	o
Studies showing association between neurocognition and SDB severity	4/8 (50%)	2/7 (28.6%)	3/6 (50%)	3/8 (37.5%)	3/9 (33.3%)	3/5 (60%)	1/4 (25%)	0/4 (0%)	0/1 (0%)

Note: "+" indicates significant association shown and "o" indicates significant association not shown. Associations in the abovementioned studies were determined using a range of statistical techniques including Pearson correlations, Spearman's rho correlations, linear regression, logistic regression, and analysis of variance. Due to the limited number of studies and variation in sleep measures reported, SDB severity represents measures of hypoxia and/or respiratory-related arousals and/or frequency of respiratory events.
Abbreviation: NA, not assessed.

neurocognitive deficits is generally comparable in children with mild SDB (primary snoring) and children with severe SDB (OSAS).[18] In the few cases of a difference between SDB groups and contrary to expectations, children with primary snoring generally perform worse than children with OSAS.[25] As a corollary, a similar pattern of finding regarding SDB severity to those reported for neurocognitive functioning is evident in behavioral functioning.[30] Attentional deficits in children with SDB are typically for visual not auditory, and while generalization is limited due to the variation of tests used on balance SDB children have problems with maintaining sustained visual attention.[10,17,18,24,26,27,31–34] As attention deficits have been found to mediate deficits in other neurocognitive functions among adults with SDB,[29] it will be important for future research to investigate the interaction between attention and executive functioning as this may explain deficits in other neurocognitive domains.

Associations between SDB severity and neurocognitive performance

Only a small number of studies have examined the association between SDB severity and neurocognitive performance, and the majority of these have failed to demonstrate a significant dose-response association (Table 2). The only finding with any consistency is the reported significant associations between increased SDB severities with reduced executive function (3 of 5 studies). Examination of the studies revealed no obvious factors to explain why some studies have reported significant and others nonsignificant correlations.

The lack of significant associations raises concerns about the assumption of a temporal relationship between SDB severity and neurocognitive performance. Because of the relative difficulty in testing neurocognitive functioning in young children, SDB studies are typically restricted to children >5 years. However, the incidence of SDB symptoms peaks in preschool children,[35] suggesting that children with SDB are likely to have been symptomatic for longer periods before testing. As such, it is possible that neurocognitive deficits secondary to SDB may develop in early life explaining the lack of correlation between SDB severity and neurocognitive measures found later in life. This suggests that the relationship may be more related to the age of disease onset or disease duration rather than the current SDB severity. Cumulative effects or earlier point of insult during a period of rapid neural development may result in greater severity and a range of deficits.

Table 3 Comparisons of daytime behavior between children with and without SDB

Authors	Inattention	Hyperactivity	Anxiety	Depression	Aggression/ oppositional	Social problems	Withdrawn	Somatic complaints
Blunden et al[31]	o	NA	o	o	o	o	o	o
Owens et al[46,*]	o	o	o	NA	o	NA	NA	+
Lewin et al[19]	o	NA	+	+	o	+	o	+
Gottlieb et al[60]	+	o	NA	NA	NA	NA	NA	NA
Kaemingk et al[48]	o	o	NA	NA	NA	NA	NA	NA
Kohyama et al[61]	+	NA	+	+	o	+	+	+
Beebe et al[24]	o	+	o	o	+	NA	NA	NA
Crabtree et al[62]	NA	NA	NA	+	NA	+	NA	NA
Melendres et al[41]	NA	+	NA	NA	NA	NA	NA	NA
O'Brien et al[27]	o	o	o	o	o	o	o	o
O'Brien et al[51]	+	o	o	NA	o	o	NA	o
O'Brien et al[26]	+	+	+	+	o	+	+	NA
Mulvaney et al[63]	+	o	o	o	+	+	o	o
Chervin et al[43]	NA	+	NA	NA	NA	NA	NA	NA
Galland et al[32,*]	+	+	o	+	+	o	o	+
Mitchell and Kelly[64,*]	NA	o	NA	o	o	NA	NA	+
Suratt et al[59]	o	o	o	NA	o	o	NA	o
Constantin et al[65,*]	o	o	NA	NA	o	NA	NA	NA
Dillon et al[66]	o	o	o	o	+	NA	NA	NA
Giordani et al[25]	+[b]	+	o[a]	NA	+[a]	+[a]	NA	o[b]
Zhao et al[30]	o	o	+	+	+	+	+	+
Studies showing impairment in children with SDB	7/17 (41.2%)	6/16 (37.5%)	4/14 (28.6%)	6/12 (50%)	6/16 (37.5%)	7/12 (58.3%)	3/8 (37.5%)	6/12 (50.0%)

Note: "+" indicates more problems in SDB children shown and "o" indicates more problems in SDB children not shown.
[a]Compared to standardized norms only; [b]Personal communication with author and unpublished analyses.
Abbreviation: NA, not assessed.

The contention that neurocognitive deficits may occur shortly after birth in infants with SDB is supported by at least two studies. Montgomery-Downs and Gozal[36] reported that in 35 healthy infants (mean age = 8.2 months), higher snoring-associated arousal scores were associated with lower neurocognitive development scores ($r = -0.43$). Of note, however, is that Montgomery-Downs and Gozal's study neither did include infants with OSAS in the sample nor did they differentiate between nonsnoring controls and primary snorers in their analyses, thus limiting the examination of any dose effect in the association between SDB severity and severity of neurocognitive deficits. Hunt et al[37] examined the relationship between cardiorespiratory events (ie, oximetry-defined apnea) and neurocognition at 2 years of age in a combined sample of 256 healthy infants with a history of apparent life-threatening events and their siblings. Infants with ≥5 compared with <1 "apnoeic/bradycardic" events per hour had lower mental development scores. Additional analysis of the correlations between SDB severity and neurocognitive performance by our group[18] in 46 children with SDB has revealed that correlations were stronger and significant in children aged 3–4 years, but not in 5–7 and 8–12 year olds (see Figure 1). In sum, these studies support the hypothesis that SDB in early infancy results in measurable developmental deficits.

Problematic behavior in children with SDB

In general, less than half the studies report increased problematic behavior in children with SDB (Table 3). The most frequently reported problematic behaviors were somatic complaints, depression, and social problems. This is in contrast to the widely held belief that hyperactivity, aggression or oppositional behavior, and inattention are predominant in children with SDB. The inconsistency in results combined

Table 4 Association of behavior with SDB severity among children

Authors	Attention	Hyperactivity	Anxiety	Depression	Aggression/ conduct	Social problems	Withdrawn	Somatic complaints
Lewin et al[19]	o	NA	o	o	o	o	o	o
Kohyama et al[61]	o	NA	o	o	o	o	o	o
Beebe et al[24]	+	+	o	+	+	NA	NA	NA
Crabtree et al[62]	NA	NA	NA	o	NA	o	NA	NA
Melendres et al[41]	NA	o	NA	NA	NA	NA	NA	NA
O'Brien et al[27]	o	o	o	o	o	o	o	o
Chervin et al[43]	o	o	NA	NA	NA	NA	NA	NA
Galland et al[32]	o	o	o	o	o	o	o	o
Li et al[53]	NA	o	o	o	o	o	o	o
Suratt et al[59]	o	o	o	NA	o	o	NA	o
Dillon et al[66]	o	o	o	o	+	NA	NA	NA
Zhao et al[30]	o	o	+	+	+	+	+	+
Studies showing association between behavior and SDB severity	1/9 (11.1%)	1/9 (11.1%)	1/9 (11.1%)	2/9 (22.2%)	3/9 (33.3%)	1/8 (12.5%)	1/6 (16.7%)	1/7 (14.3%)

Note: "+" indicates significant association shown and "o" indicates significant association not shown. Associations in the abovementioned studies were determined using a range of statistical techniques including Pearson correlations, Spearman's rho correlations, linear regression, logistic regression, and analysis of variance. Due to the limited number of studies and variation in sleep measures reported, SDB severity represents measures of hypoxia and/or respiratory-related arousals and/or frequency of respiratory events.
Abbreviation: NA, not assessed.

with the results of this review suggests that problematic behavior in children with SDB may be better explained by comorbid sleep problems.[38] The incidence of comorbid sleep disorders in children with SDB (eg, sleep walking and night terrors) is high.[39,40] This raises the importance of controlling the effect of comorbid sleep problems on behavior in future studies.

There is some evidence that children with SDB are sleepier than controls, which may contribute to increased problematic behavior. Melendres et al[41] administered the Epworth Sleepiness Scale to measure the level of daytime sleepiness in 108 children with suspected SDB and 72 controls matched for age, gender, race, and SES. Children with suspected SDB were rated as sleepier and more hyperactive than controls; however, no difference in sleepiness scores was found between the children with primary snoring versus OSAS. It is noteworthy that the Epworth Sleepiness Scale is reported not to correlate with objective measures of sleepiness in children with SDB,[42] raising the need for validation of an age-specific sleepiness scale before conclusions about such results can be drawn. Chervin et al[43] used the Multiple Sleep Latency Test (MSLT) in 78 children with SDB before and after adenotonsillectomy and compared results with those of 27 controls of similar demographic status from an unrelated hospital clinic. The MSLT is reported to be sensitive to sleepiness in children from 3 years of age.[44] Chervin's group found that children scheduled for adenotonsillectomy demonstrated increased SDB severity and reduced MSLT times before surgery on the day following PSG, indicating increased sleepiness.

Associations between SDB severity and problematic behavior

As with neurocognition, there is little evidence of an association between SDB severity and problematic behavior (Table 4). Only three of 12 studies report any significant association, with all three reporting that SDB severity was associated with increased aggression or oppositional behavior and two studies reporting that SDB severity was associated with increased depression. This suggests the possibility of a third factor such as sleepiness modulating the association between SDB and behavior. The two previously mentioned studies assessing sleepiness in children with SDB report significant linear correlations between SDB severity and sleepiness.[41,43] Both these studies examined only a limited range of other behaviors (confined to measures of attention and hyperactivity); however, no associations of problematic behavior and SDB severity were reported.

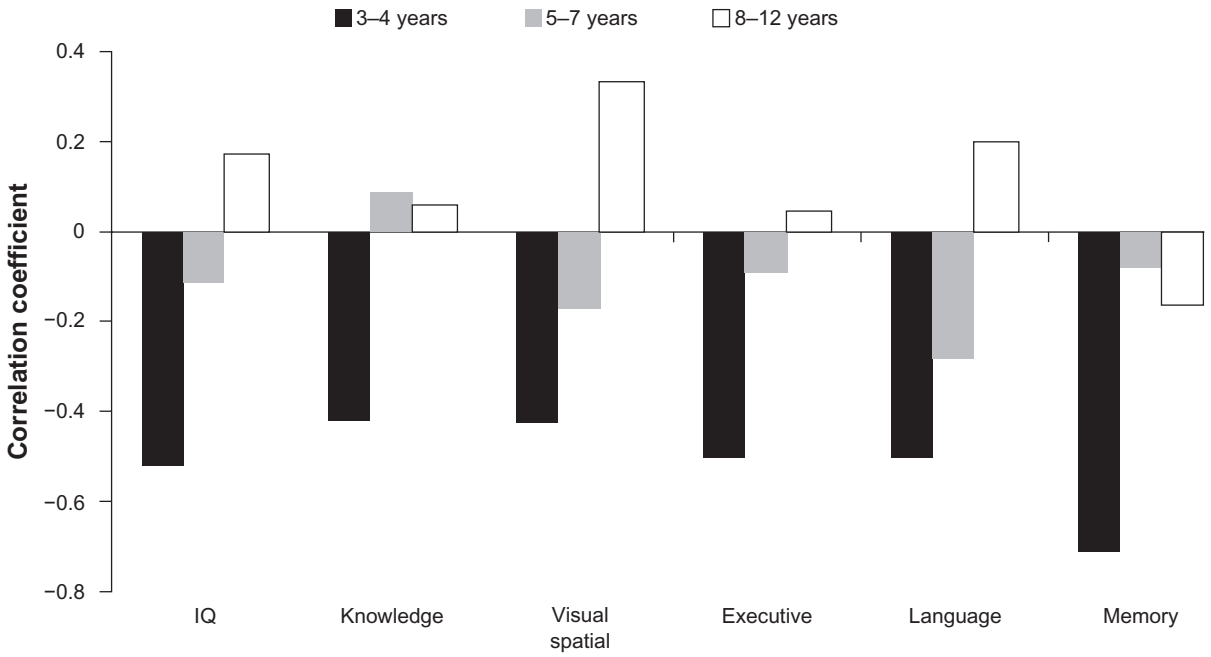

Figure 1 Pearson bivariate correlations (*r*) between SDB severity (obstructive apnea and hypopnea index) and neurocognitive performance domains among children with SDB at different ages (n = 18 for 3–4 years, n = 13 for 4–7 years, and n = 13 for 8–12 years). For further details on study design and results see Kohler et al.[18]

Effects of treatment on neurocognition and behavior

Given the daytime decrements outlined earlier, there is currently great interest in demonstrating that treatment of childhood SDB reverses not only the nocturnal ventilator abnormalities but also the behavioral and neurocognitive deficits. Our review identified 30 treatment studies: 27 adenotonsillectomy studies (including two studies that compared tonsillectomy with intracapsular tonsillectomy or tonsillotomy), two tracheotomy studies, and one study that used unspecified surgery and continuous positive airway pressure (Appendix B). The impact of treatments other than adenotonsillectomy on neurocognitive and behavioral functions in children is largely unknown and is an area deserving further study. Overall, the treatment (by adenotonsillectomy) is reported to improve attention, memory, and school performance and reduce hyperactivity, aggression or oppositional behavior, inattention, somatic complaints, and anxiety.

Neurocognitive performance after treatment for SDB

One of the early proponents of adenotonsillectomy for childhood OSAS was William Osler who in 1919 said, "If the tonsils are large and the general state is evidently influenced by them they should be at once removed";[67] however, it was not until the 1970s that researchers began examining its effect on neurocognitive functioning. Early studies of treatment for SDB in children are anecdotal in nature, but all report improved neurocognitive and behavioral functioning. For example, in the landmark study by Guilleminault et al[6] adenotonsillectomy reduced daytime sleepiness and improved school performance in all eight children and normalized academic performance in three of five children experiencing learning difficulties. In 1982, Guilleminault et al[7] again demonstrated that adenotonsillectomy led to improved school performance in all cases 3 months postsurgery. Before treatment, all children with SDB were placed in remedial school classes and only two remained in these classes for 6 months after treatment. Tiredness was also reduced as measured by MSLT scores. In the same year, Brouillette et al[68] reported five of 22 children with SDB, behavioral disturbance, excessive sleepiness, and developmental delay. All demonstrated improved daytime functioning following surgical treatment.

From 1990 to 1996, results from a series of studies conducted at the Osler Chest Unit in Oxford demonstrated improved questionnaire-based reports of attention and vigilance, following either adenotonsillectomy for SDB or spontaneous resolution of snoring.[69–71] In 1998, Gozal[72] confirmed the benefits of adenotonsillectomy in a large sample of children recruited from a community rather than a hospital's sleep clinic. In an innovative study, he examined the academic performance in 297 first-grade children who ranked in the lowest 10% of their class and identified

54 children with SDB (confirmed by overnight oximetry and monitoring of transcutaneous partial pressure of carbon dioxide). Of this subset, 24 underwent adenotonsillectomy and by second grade demonstrated improved academic performance compared with both untreated children and children without evidence of SDB, but who also performed in the lowest 10% of their class. Two years later, another group reported improved daytime sleepiness and school performance among 45 children aged 2.5–15.5 years, following removal of adenoids and/or tonsils for OSAS confirmed by PSG.[73] A number of reviews have since confirmed the benefits of adenotonsillectomy as a treatment for upper airway obstruction, estimating that ventilatory function is normalized in on average 66% to 83% of cases following surgery[74,75] and, likewise, postadenotonsillectomy gains in neurocognitive and behavioral performance.[76,77] However encouraging, the interpretation of the literature needs to be treated with caution as few studies have adequately addressed methodological limitations especially assessing children with PSG at follow-up and lack of control data. As outlined in recent studies, it is estimated that up to 33% of children on average continue to obstruct postadenotonsillectomy, potentially confounding postoperative comparisons. As well, without a control group it is difficult to exclude learning effects, which may explain treatment gains, particularly if there is a short time between testing. After applying the strict criteria described earlier, we were able to include only two studies examining the impact of adenotonsillectomy on neurocognitive function[18,43] and two studies examining the impact on behavior[43,66] in this review. Below is a brief discussion on relevant treatment studies, followed by the results of this review for neurocognitive and behavior functions.

A range of neurocognitive and behavior functions were assessed by Owens et al[46] in 18 children with OSAS. Eight of these children subsequently underwent adenotonsillectomy and were reassessed 6–12 months postsurgery. Tests of executive function (verbal fluency) were improved following surgery. Although no significant change in general neurocognitive ability, language skill, memory, visual perception, motor ability, or behavior was observed, effect sizes were reported to be large for tests of attention and visual-motor ability. Hansen and Vandenberg[47] examined another small group of children with OSAS and demonstrated that memory performance was improved 5 months after treatment. Improvements in visual attention and general neurocognitive performance approached statistical significance in this study; however, auditory attention (which was rated as impaired in comparison to normative data before treatment) remained unchanged. In 2003, Friedman et al[16] assessed neurocognitive function using standardized tests in 39 children with OSAS compared with 20 controls. Twenty-seven children with OSAS and 14 controls were reassessed 6–10 months after adenotonsillectomy. Significant improvement was seen in treated children for perceptual ability, concept formation, verbal and spatial memory, analytical thinking, and total intelligence. No improvement was seen for vocabulary and memory for numbers. Avior et al[79] assessed attention in 19 children with SDB before and 2 months after adenotonsillectomy. Attention improved in all except one participant postoperatively, demonstrating that neurocognitive changes may occur within the first 2 months after treatment; however, the potential impact of a learning effect needs to be considered.

In the first study to examine preschool children, Harvey et al[80] assessed mental ability in 24 children with OSAS before and 6 months after adenotonsillectomy. Results were compared with 15 age- and gender-matched children with OSAS but who did not receive any intervention. Adenotonsillectomy did not result in any change in mental ability scores and no between-group differences were observed, raising questions about the optimal timing of treatment to prevent daytime deficits. In 2005, Montgomery-Downs et al[15] compared data from 19 preschool children with OSAS to 19 matched nonsnoring controls on measures of general intellectual ability, language development, and memory at baseline and 3–6 months postadenotonsillectomy for those with OSAS. At baseline, general intellectual ability was lower in OSAS children and improved in 16 children postoperatively. No group differences were found pre- or postsurgery for measures of memory and language; however, executive function performance was impaired in OSAS subjects both before and after treatment. Combined, these results suggest that general neurocognitive ability and executive deficits are evident among preschool-aged children with OSAS, and some of these deficits may not be remediated 3–6 following treatment.

Galland et al[32] report objective measures of sustained attention and parental reports of behavior in 61 children with suspected SDB pre- and 3-months postsurgery. Visual continuous performance testing revealed increased inattention and impulsivity among children before surgery and significant improvement following adenotonsillectomy. In contrast, performance on an auditory continuous performance test showed no significant deviation from normative data and no change postsurgery. Similarly, Li et al[53] assessed attention and impulsivity among 40 children with suspected SDB before

and 6 months following adenotonsillectomy. Response time and indications of ADHD were improved postoperatively; however, there was no significant association between change in SDB severity and change in test scores. In an assessment of cerebral blood flow and neurocognition in children with mild SDB compared with controls, Hogan et al[81] found some evidence of improved processing speed and visual attention among children with SDB; however, measures of executive function remained in deficit postadenotonsillectomy. Using anecdotal parental report of neurocognitive performance and behavior, Moré et al[82] found a large proportion of parents of 44 children with SDB reported resolved problems of speech delay, poor school performance, poor concentration, and poor memory. More recently, Lundeborg et al[83] reported that language deficits (phonological processing) were improved following both tonsillectomy and partial resection (tonsillotomy) in preschool-aged children with SDB; however, deficits compared with controls were still evident at 6 months following treatment.

In one of only two studies to meet the inclusion criteria set for this review, Chervin et al[43] compared measures of behavioral hyperactivity, psychiatric morbidity, sleepiness, and test of attention between 78 children scheduled for adenotonsillectomy and 27 children for unrelated surgery (77 vs 23 at follow-up). One year after surgery, children who underwent adenotonsillectomy demonstrated improvement in attention deficits and reduction in sleepiness to levels equivalent to controls. No association between attention and any PSG variable was observed; however, sleepiness (as assessed on MSLT) was significantly associated with multiple indications of SDB, including apnea index and oxygen saturation nadir. Controls in this study included cases demonstrating clinically significant levels of SDB, and these results may, therefore, not truly represent the differential neurocognitive and behavioral aspects of children with and without SDB. In contrast, in the only other study meeting the inclusion criteria, Kohler et al[18] found wide-ranging neurocognitive deficits primarily in global intelligence; planning; working memory; and memory for narrative, visual attention, and language development among 44 children with SDB both at baseline and 6 months following adenotonsillectomy compared with 48 controls. It may be that deficits take longer than 6 months to normalize, but these findings raise concerns regarding the permanency of deficits.

Despite the pattern of treatment response for a number of neurocognitive performance domains in children with SDB, residual deficits in memory, executive functioning, and language development are also evident. In addition, only two studies met the strict inclusion criteria used in this review (which emphasized valid assessment of SDB severity, neurocognitive performance, and inclusion of control data at baseline and follow-up assessments), themselves presenting contrasting results. Clearly, further well-controlled treatment studies are required before informed decisions about treatment efficacy for remediating neurocognitive deficits can be made.

Behavior after treatment for SDB

Although commonly reported in the positive, relatively few studies have examined whether problematic behavior is reduced in children with SDB following treatment. In 1982, Guilleminault et al[7] reported that the behavior improved 3-months postadenotonsillectomy and by 6 months none of the eight children with SDB previously taking methylphenidate for hyperactivity were still medicated. Brouillette et al[68] also reported reduced hyperactivity, reduced aggression, and reduced daytime sleepiness following surgical treatment for SDB among five children. Goldstein et al[84,85] demonstrated in a combined cohort of 79 children that adenotonsillectomy improved anxiety, depression, thought problems, and total problematic behavior; however, reports of improvements in withdrawn behavior, somatic complaints, and attention problems were inconsistent. Mitchell and Kelly[64] assessed behavior in 23 children with OSAS and reported postadenotonsillectomy improvements at 6 months and again at 9–18 months in aggression, hyperactivity, somatic complaints, depression, and atypicality. Galland et al[32] report in 61 children with SDB that adenotonsillectomy reduced hyperactivity, aggression, depression, somatic complaints, attention problems, and composite scores for internalizing, externalizing, and total problems. Roemmich et al[86] report reduced hyperactivity in 54 children with OSAS 12 months postadenotonsillectomy. Apart from problems of aggressive behavior, Li et al[53] also report in 40 children with SDB substantial reduction in a broad range of internalizing and externalizing behavior problems 6 months following adenotonsillectomy. Wei et al[87,88] completed a 6-month and a 2.4- to 3.6-year follow-up of 71 and 44 children with SDB, respectively, and reported postadenotonsillectomy improvement in inattention, hyperactivity, and oppositional behavior. Moré et al[82] report that aggressiveness and hyperactivity were reduced 9 months after adenotonsillectomy, while Ericsson et al[89] report reduced somatic complaints following either tonsillotomy or tonsillectomy in 67 children with SDB; mixed results for symptoms of aggression, anxiety, inattention, and social problems; and no change for withdrawn behavior and thought

problems. In contrast, Constantin et al[65] report no gains postadenotonsillectomy compared with retrospective ratings of behavior. Tran et al[78] compared behavior in 42 children pre- and postadenotonsillectomy for OSAS and 41 children undergoing unrelated surgery. The authors report that children with OSAS demonstrated a greater improvement than controls in thought problems, somatic complaints, internalizing behaviors, and total behavioral problems. Despite the encouraging results, and similar to the caveats noted for the neurocognitive studies, relatively few of the studies examining the impact of adenotonsillectomy on behavior have included PSG and control data at follow-up.

Both studies to assess behavior response to treatment and meet the inclusion criteria in this review are from the same sample of children. Chervin et al[43] found that before adenotonsillectomy, 78 children with SDB were rated as more hyperactive and more likely to have attention-deficit or hyperactivity disorder compared with 23 controls. One year after surgery, children who underwent adenotonsillectomy demonstrated hyperactivity levels equivalent to controls. Dillon et al[66] found reduced oppositional behavior in children with SDB, but found problems with anxiety and depression following treatment.

Largely consistent with previous reviews, reductions in hyperactivity, aggression or oppositional behavior, and somatic complaints seem evident following treatment for SDB. There is also some evidence to suggest that the closely-related symptoms of depression and withdrawn behavior are reduced posttreatment. In contrast, the evidence that parentally reported inattention and anxiety improves after treatment is less convincing.

Possible mechanisms

It is generally believed that the neurocognitive and behavioral deficits seen in children with OSAS are due to intermittent nocturnal hypoxia or fragmentation of sleep and that the failure to normalize these daytime deficits postadenotonsillectomy is secondary to the failure either to adequately correct fragmentation or hypoxia or to correct a persisting neurological dysfunction. A major difficulty for research in this area is that there is little correlation between the findings on PSG, such as cortical arousals and apnea or hypopnea indices, and changes in neurocognition or behavior.[90] In addition, as daytime deficits are seen in children with mild upper airway obstruction, it is likely that explanatory polysomnographic changes will be subtle. The investigation of the etiology of these neurocognitive and behavioral deficits, therefore, requires a focus on more sensitive methods of evaluating sleep fragmentation and the effects of intermittent hypoxia on cerebral molecular structure and function.

As fragmentation of sleep by upper airway obstruction-induced arousals is less frequent in childhood OSAS, attention has been focused on more detailed evaluation of their sleeping EEG. The cyclic alternating pattern (CAP) is a measure of sleep microstructure, quantifying phasic EEG activity across the night to derive an estimate of sleep stability and fragmentation.[91] A1 phase frequency of CAP (a protective reaction of the sleeping brain) has been shown to be reduced in children with SDB[92] and A2 phases (mild cortical activation) increased among children with OSAS compared with controls.[93] A rebound in A1 indices was observed among children with OSAS 1 year after rapid maxillary expander treatment; however, other measures such as A2 frequency remained unchanged.[94] The functional significance of these differences is yet to be determined as is the association with neurocognitive performance and behavior. An initial study in children with Asperger syndrome has found strong correlations between neurocognitive performance, behavior, and a number of CAP indices, providing encouraging results for future investigation in children with SDB.[95]

Chervin et al[96] quantified variations in EEG power frequencies with the respiratory cycle in children with SDB [called the "respiratory cycle – related EEG changes" (RCREC)]. Changes in RCREC were associated with subjective sleepiness in children with SDB,[97] and postoperative changes in RCREC correlated more strongly with changes in daytime sleepiness and attention compared with changes in apnea and hypopnea frequency.[98] This suggests that more detailed evaluation of sleeping EEG recordings in children using these new methods may yield new information on the association between functional EEG changes and daytime deficits.

Intermittent hypoxia results in oxidative stress and induces a proinflammatory response. In animal models this leads to apoptosis and disorganization in cerebral regions which underpin learning and memory. Neuroimaging studies in adults with SDB demonstrate a range of cerebral abnormalities including reduced hippocampal volume; frontal white matter abnormalities among SDB patients at greater risk of vascular disease; changes to motor, sensory, and autonomic control regions of the brain during wakefulness; absence of prefrontal activation in association with poor working memory performance; and compensatory recruitment of brain regions during a verbal learning test.[99–102] In addition, cerebral blood flow is altered during sleep and wakefulness among adults with OSAS compared with controls.[103,104]

Elevated levels of inflammatory cytokines (proteins known to mediate inflammation, brain injury repair, neural development, and autoimmune response) and reactive oxygen species in response to hypoxia and/or sleep fragmentation have been demonstrated in adults with SDB.[105–107] Studies among adults with OSAS also suggest that the upregulation of cytokines is associated with symptoms of depression, fatigue, and daytime sleepiness.[106] Increased inflammatory markers among children with SDB have been reported in some studies[108–112] but not others.[113,114] Rodent models suggest that increased oxidative stress and upregulation of proinflammatory cytokines and inducible nitric oxide synthase (iNOS) are important contributors to both hippocampal and cortical apoptosis.[115–117] Zhan et al[118] recently demonstrated that the pharmacological inhibition of iNOS or genetic ablation of the enzyme in mice was associated with markedly reduced brain oxidative injury. Also, using a rodent model, animals exposed to intermittent hypoxia have been shown to demonstrate increased oxidative stress within neural tissue and reduced spatial learning compared with animals exposed to room air only or those exposed to intermittent hypoxic conditions but receiving antioxidants to prevent oxidative cellular damage.[119]

These findings have led to interest in the evaluation of the neurochemical and structural changes in OSAS, particularly in structures such as the hippocampus and prefrontal cortex, which underpin many of the functional neurobehavioral deficits shown. Using voxel-based morphometry, Macey et al[120] demonstrated changes in gray matter concentration across multiple brain regions including the hippocampus and frontal cortex in 21 adults with OSAS compared with controls, a finding supported by Morrell et al[121] who reported a loss of gray matter concentration in the left hippocampus of seven adults with OSAS. A more recent study from Macey et al[122] outlined extensive white matter changes particularly in brain regions previously shown to be functionally or anatomically affected in adults with OSAS (hippocampus and amygdala, frontal, parietal, and temporal cortices). Thus, there is evolving and compelling evidence that brain structure is altered in adults with OSAS. The picture is less clear in children as few such studies have been completed.

Using proton magnetic resonance spectroscopic imaging, Halbower et al[52] in a subset of six children with severe OSAS (mean OAHI, 37.8), demonstrated a significant decrease of the mean neuronal metabolite ratio *N*-acetyl aspartate/choline in both the left hippocampus and the right frontal cortex, indicating metabolic disturbance and possible neuronal loss. The authors speculate that untreated OSAS could permanently alter the child's developmental and academic potential. Hill et al[33] demonstrated increased cerebral blood flow velocity in children with SDB, possibly indicating increased cerebral blood flow secondary to increased metabolic demand and/or narrowing of blood vessels. Although values were not directly associated with SDB severity or executive function performance and processing speed, differences between SDB children and controls for performance on neuropsychological tasks were reduced when controlling for blood flow velocity. Following treatment, the same group was able to demonstrate a reduction in cerebral blood flow among children with SDB. This occurred despite continued deficits in executive functioning.[81]

A recent series of studies has postulated that individual differences in systemic inflammatory response to hypoxia (and/or sleep fragmentation) may explain differential outcomes to SDB in children.[55,58,123] Levels of the inflammatory marker, high-sensitivity C-reactive protein (hsCRP), were higher among children with OSAS compared with both controls and snorers, while global neurocognitive ability was reduced in the OSAS group. Of note, a subgroup of snoring children with reduced neurocognitive scores also demonstrated elevated hsCRP levels. Furthermore, children with OSAS and lower neurocognitive scores demonstrated elevated hsCRP levels compared with matched children with OSAS and normal neurocognitive scores.[55] A second study found lower plasma concentrations of the neuroprotective insulin-like growth factor-1 in children with OSAS and neurocognitive deficits compared with children with OSAS and normal neurocognitive functioning.[58] Although at least one study has shown improvement in inflammatory markers among children with SDB following treatment,[124] it is not known whether related improvements in neurocognitive function follow. Finally, apparent individual susceptibility may, at least in part, be genetically determined. A familial aggregation of SDB in children has been reported, suggesting increased SDB risk to be at least in part a heritable trait.[125,126] Recently, the chromosomal region containing the apolipoprotein E (*ApoE*) gene has been implicated as a disease susceptibility locus for SDB.[127] This result has been confirmed in child SDB[123,128] and, in addition, it was found that children with both SDB and neurocognitive deficits demonstrated greatest expression of the *ApoE* ε4 allele (presumably resulting in reduced neuroprotection). Investigation of the genetic underpinnings of SDB is extremely limited to date, and hence, further studies mapping target gene regions are required.

Irrespective of the specific causal pathway of neurocognitive and behavioral deficits in children with SDB, the age of SDB onset is a potential moderator of residual deficits. Cumulative effects or earlier point of insult during a period of rapid neural development may result in greater severity and range of deficits. Studies of cortical maturation suggest that the neuronal overproduction and subsequent pruning throughout childhood develop in parallel to a range of neurocognitive milestones.[129–131] Neuronal insults in childhood are assumed to result in less structural and functional deficits compared with adults due to the brain's ability to compensate or modify by taking advantage of such neuronal overproduction and subsequent alternate synaptic pathways. Proponents of this idea point to the evidence from good outcomes for children with focal neuronal insults.[132,133] Others argue that this same increased interconnectivity combined with brain immaturity and limited established neurocognitive skills may place younger children at increased risk of functional and cumulative deficits following brain insults.[134] In the latter case, it is considered that unless a certain function is learned during a critical or sensitive period of development, the function in question will be permanently lost or disadvantaged. Chugani[135] has demonstrated that dramatic increases in brain metabolism occur between the ages of 1 and 4 years and that the high levels of metabolism are maintained up until 9–10 years. The author suggest that repeated activation of certain neuronal circuits during this period (by practice at tasks dependent on such circuits) results in stabilization of those circuits and that attempts after this time may be too late for promotion of such stabilization. One would expect that this period of increased metabolic activity represents the overlay of multiple pathways each subserving different neurocognitive functions. Coincident with this, we see an increased potential for plasticity, together supporting efforts to stabilize specific functions while the opportunity exists. Disruption of processes important for neuronal metabolism among children with SDB by increased inflammation, vascular responsiveness, and reduced opportunity for consolidation of learning may lead to long-term deficits depending on the timing of illness and treatment.

In addition to the timing of SDB onset and treatment, interindividual differences in cortical development may cause additional variation in the timing of sensitive periods for specific neurocognitive domains and subsequent vulnerability for neurocognitive deficits. Cortical growth has been shown to follow varying trajectories in children with different levels of intelligence.[136] It is suggested that due to the later structural and metabolic maturation of the frontal and prefrontal cortex in more intelligent children and the prolonged phase of this maturation, an extended critical period of neurocognitive development might be afforded to such children. Consistent with this notion, Mahone et al[137] found that children with ADHD and above-average IQ scores performed no worse on tests of executive function than controls with an equivalent IQ. In contrast, children with ADHD and average IQ scores demonstrated worse performance compared with IQ equivalent controls. Adults with SDB and high intelligence demonstrated attention and alertness performance equivalent to high-intelligence controls. In contrast, patients with average intelligence demonstrated reduced attention and alertness performance compared with average-intelligence controls.[138] High intelligence may serve to prevent clinical impairment by providing greater reserve of neurocognitive function to compensate for neuronal insults, and in doing so suggests that increased neuronal plasticity plays an important part within the context of sensitive periods of neurocognitive development. This is yet to be evaluated among children with SDB.

Conclusion

Our critical review of neurocognition and behavior in children with SDB before and after treatment suggests firstly that before treatment, children with any degree of SDB demonstrate neurocognitive impairment compared with controls or standardized norms. This impairment is most apparent for domains highly dependent on frontal – cortical processes including executive function, attention, subsequent general intellectual ability, and to a lesser extent language development. However, compared with control samples the reductions in general intelligence are typically within the normal range. Associations with SDB severity support the concept of a direct impact of SDB on frontal cortical functions as SDB severity was most consistently correlated with reduced executive function; however, the role of nonspecific sleep disruption and the potential mediating role of attention and/or executive deficits are yet to be investigated among children with SDB. Secondly, the pattern of behavioral problems among children with SDB is less clear. A number of studies report problematic behavior in children with SDB; however, such problems are evident in less than half of the studies included. In contrast to the previous reports, evidence from well-conducted studies does not indicate inattentiveness and hyperactivity to be more prevalent than other problematic behaviors such as depression, somatic complaints, and social problems. Significant associations between behavior and SDB severity are evident in a very few studies, suggesting

that other mediating factors related to general sleep disruption such as daytime sleepiness are at play in regulating behavior among children with SDB.

Of the treatment studies to date, the majority assess treatment effects among primary school-aged children with little follow-up data extending beyond 1 year. In addition, only a very small number of studies assess preschool-aged children, a period of life deemed critical in neurocognitive development. The key finding from treatment studies is that very few studies provide follow-up PSG to quantify posttreatment SDB severity, and similarly few studies include control data at both baseline and follow-up time points, making it difficult to establish clear patterns of treatment response. From the wider literature, neurocognitive performance improvements in global intelligence, attention, and visual–spatial ability are relatively consistent. In contrast, deficits in language and short-term memory appear to persist. Little data are available to determine whether improvements in executive deficits are likely. For behavior, problems of hyperactivity, aggression or conduct problems, and somatic complaints improve following adenotonsillectomy. In contrast, symptoms of anxiety and reported social problems do not appear to improve. Despite the reported behavior improvements, baseline reports often suggest no clinically significant problem.

The characterization of the pattern of neurocognitive deficits and problematic behavior in children with SDB provided by this review will aid in the development of more targeted investigations and well-designed studies exploring both the causative mechanisms and the treatment response. A number of theoretical models have been put forward, which require substantiation in well-designed studies if we are to delineate the pathways linking SDB to neurocognitive deficits and to understand the failure in some cases for neurocognitive deficits to resolve with treatment. In addition, the timing of intervention in children and consideration of individual development may also contribute to variations in treatment efficacy. Given the high prevalence of child SDB reported in the community and the potential long-term impact on the quality of life and health, and an individual's academic and occupational success, further investigations and development of effective strategies to identify the symptoms early and prevent residual deficits are needed.

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Appendix

Appendix A Summary of published studies investigating neurocognitive performance and behavior in children with SDB

Authors	Population	SDB/snoring measure	Neurocognitive dysfunction	Behavioral dysfunction	Note
Guilleminault et al[6]	8 OSAS (5–14 y)	PSG	Academic difficulties	Emotional disturbance, hyperactive, sleepiness	Anecdotal reports only
Guilleminault et al[139]	24 OSAS, 26 OSAS secondary to medical problem, 22 controls (all 1–16 y)	Esophageal pressure, PSG	Academic difficulties, language	Aggression, hyperactive, inattentive, sleepiness, withdrawn	Anecdotal reports only
Brouillette et al[68]	22 OSAS (3–5 y)	Daytime PSG	Not reported	General behavior, sleepiness	Anecdotal reports and unspecified measures
Guilleminault et al[7]	25 snorers, 25 controls (all 2–14 y)	Esophageal pressure, PSG	Academic difficulties	Aggressive, hyperactive, sleepiness, withdrawn	Anecdotal reports only
Weissbluth et al[140]	71 behavior, academic, an development problems (6.2 ± 3.5 y); 355 controls (5.8 ± 3.1 y)	Questionnaire	Academic difficulties	Hyperactive, inattentive	No PSG, nonvalidated behavior measure
Brouillette et al[141]	23 OSAS (3.8 ± 2.4 y), 46 controls (4.0 ± 2.3 y)	PSG, questionnaire	NA	Sleepiness, withdrawn	PSG in OSAS group only, nonvalidated behavior measure
Stradling et al[71]	61 snorers (4.7 ± 1.7 y), 31 controls (4.7 ± 1.7 y)	Home oximetry and video, questionnaire	NA	Aggressive, hyperactive	Nonvalidated behavior measure
Ali et al[142]	782 from health registrar – 66 SDB, 66 controls (all aged 4–5 y)	Home oximetry and video, questionnaire	NA	Aggressive, hyperactive, inattentive	Nonvalidated behavior measure
Carskadon et al[143]	29 children with adenotonsillar hypertrophy (8.7 ± 3.0 y)	Questionnaire	NA	Disruptive	Nonvalidated behavior measure, no control group
Ali et al[69]	507 from health registrar (all aged 6.5–7.5 y) – 56 snorers	Questionnaire	NA	Hyperactive, sleepiness	
Rhodes et al[45]	5 patients with OSAS (12.9 ± 2.1 y), 9 clinical patients with no OSAS (13.5 ± 1.5 y)	PSG	Learning, memory	NA	All subjects were obese
Ali et al[70]	12 SDB (5–12 y), 11 snorers (6–12 y), 10 controls (6–12 y)	Questionnaire, home nocturnal oximetry and video	No between-group differences (IQ, attention, response speed)	Aggressive, hyperactive, inattentive	
Guilleminault et al[144]	411 sleep clinic patients (birth to 12 y)	Esophageal pressure, PSG	NA	Oppositional	Nonvalidated behavior measure
Chervin et al[145]	27 ADHD patients (9.5 ± 3.7 y), 116 non-ADHD patients (8.9 ± 4.7 y)	Questionnaire	NA	Hyperactive, inattention	Groups defined by ADHD symptom, nonvalidated behavior measure
Owens-Stively et al[146]	23 OSAS (age not reported)	PSG	Attention	Impulsivity and inattentiveness compared with moderate/severe OSA, mild OSA more severe hyperactivity	No control group
Gozal[72]	297 first grade children with poor academic performance (177 controls, 66 primary snorers, 30 nontreated SDB, and 24 treated SDB)	Home oximetry and $TcCO_2$, questionnaire	Academic performance	NA	

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Appendix A (*Continued*)

Authors	Population	SDB/snoring measure	Neurocognitive dysfunction	Behavioral dysfunction	Note
Owens et al[147]	100 OSAS (8.9 ± 4.7 y) vs 52 behavioral sleep problems	PSG	NA	OSAS patients displayed less problematic behavior compared with children with behavioral sleep problems	Snoring evident in the group with behavioral sleep problems
Harvey et al[80]	56 SDB (2.9 ± 1.3 y)	PSG	Not reported	Not reported	28% neurologically abnormal
Blunden et al[31]	16 snorers (7.2, 5–10 y), 16 controls (7.7, 5–10 y)	PSG (n = 26), questionnaire	Attention, IQ, memory	No differences between groups	Groups not matched for SES
Ferreira et al[148]	976 children (8.1 ± 1.5 y) from community (8.8% habitual snorers)	Questionnaire	NA	Irritability, sleepiness	
Goldstein et al[85]	36 snorers (4.6, 2–10 y)	Questionnaire, physical examination	NA	Externalizing	No control group
Kelmanson[149]	200 infants—71 snorers/noisy breathing (3.0 ± 1.0 mo)	Questionnaire	NA	Negative mood	Nonvalidated sleep measure
Owens et al[46]	18 OSAS (7.3 ± 2.0 y)	PSG	No difference between mild and moderate OSAS	Learning problems, somatic complaints, no difference between mild and moderate OSAS	No control group
Richards and Ferdman[73]	45 OSAS post-AT (2.5–15.5 y)	PSG, questionnaire	School performance	Sleepiness	Retrospective review, no control group
Brunetti et al[150]	895 school students (7.3 y, 3–11 y) – 44 habitual snorers (4.9%)	Questionnaire, limited home PSG (n = 34), laboratory PSG (n = 12)	Academic performance	Hyperactive	
Chervin and Archbold[151]	113 sleep clinical patients (9.9 ± 4.0 y) – 59 SDB, 54 non-SDB	PSG	NA	No reported associations	Non-SDB group included primary snorers
Gozal and Pope[152]	797 low-performing students, 791 high-performing students (all 13–14 y)	Questionnaire	Snoring more likely amongst low-performing students	NA	
Hansen and Vandenberg[47]	7 OSAS (7.3 ± 2.0 y), 7 narcoleptics (7.3 ± 2.0 y)	PSG	Attention	NA	No control group
Smedje et al[153]	635 children (84 ± 5 mo) from community (9.3% habitual snorers)	Questionnaire	NA	No reported associations	
Stein et al[154]	472 children (4–12 y) from pediatric clinic (23% snored >1 night/wk)	Questionnaire	NA	Social problems, somatic complaints	
Chervin and Archbold[151]	866 children attending clinics (6.8 ± 3.2 y), 139 habitual snorers	Questionnaire	NA	Snoring associated with hyperactivity	
Goldstein et al[84]	64 children awaiting AT (7.3 ± 2.0 y)	Questionnaire, physical examination	NA	All behaviors within clinical range	No control group
Lewin et al[19]	12 severe OSAS (6.6 ± 1.5 y), 16 mild OSAS (7.6 ± 3.0 y), 10 controls (6.9 ± 1.1 y)	PSG (OSAS only), questionnaire	Information processing, verbal IQ (associations and group differences reported for severe OSAS group and controls only)	Internalizing problems, somatic complaints, externalizing problems, anxiety/depression, social problems in mild OSAS group only	No PSG in control group

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Appendix A (*Continued*)

Authors	Population	SDB/snoring measure	Neurocognitive dysfunction	Behavioral dysfunction	Note
Castronovo et al[156]	447 children (4.1 ± 0.9 y) from community, 154 habitual snorers	Questionnaire, limited home PSG (n = 241)	NA	Irritable	Nonvalidated behavior measure
Chervin et al[22]	146 school children (9.3 ± 0.4 y)	Questionnaire	Teacher reports of performance but not objective test scores	NA	
Chervin et al[157]	872 children attending clinics (6.7 ± 3.2 y)	Questionnaire	NA	Aggression, conduct problems	
Freidman et al[16]	39 OSAS (6.8 ± 0.2 y), 20 controls (7.4 ± 1.4 y)	PSG (OSAS only), questionnaire	Analytic thinking, auditory-visual integration, general intelligence, memory	NA	No PSG in control group
Gottlieb et al[60]	3,019 children (all 5 y, 362 habitual snorers)	Questionnaire	NA	Aggression, hyperactive, inattentive, sleepiness	
Kaemingk et al[48]	149 school children (8.4 ± 1.7 y), 77 AHI ≥ 5	PSG	Memory	None found	
Kohyama et al[61]	32 SDB (5.6, 4–9 y), 137 controls (5.3, 4–6 y)	PSG (SDB only)	NA	Anxiety, inattention, social problems, somatic complaints, thought problems, withdrawn	No sleep assessment for controls
Montgomery-Downs et al[23]	746 developmentally or financially disadvantaged children (4.2 ± 0.53 y)	Questionnaire	School performance	Hyperactivity, sleepiness	High percentage on nonresponders
O'Brien et al[13]	71 children with ADHD symptoms, 39 controls (all 5–7 y)	PSG, questionnaire	No reported effects	OSAS and snoring are more prevalent when ADHD symptoms are mild	Groups defined by ADHD symptoms, limited analysis of contribution of OSAS
Shin et al[158]	3,871 high-school students (16.8 y), 433 habitual snorers	Questionnaire	School grades	Sleepiness	Nonvalidated sleep and behavior measure
Urschitz et al[159, 160]	1,144 school children (9.6 ± 0.7 y), 114 habitual snorers	Questionnaire, home nocturnal oximetry	Mathematical, science, and spelling performance	Attention, hyperactive, sleepiness	
Archbold et al[49]	12 children scheduled for AT (9.0 ± 0.85 y)	PSG	Sustained attention, vigilance	NA	No control group
Avior et al[79]	19 OSAS (8.0 y, range 5–14 y)	Questionnaire, adenotonsillar hypertrophy	Attention	Attention	No control group
Beebe et al[24]	32 SDB (6.7 ± 0.5 y), 17 controls (6.7 ± 0.5 y)	PSG (SDB only), questionnaire	Verbal fluency	Aggression, conduct problems, hyperactive	Psychostimulants use amongst controls, no PSG for control
Crabtree et al[62]	85 SDB (10.1 ± 1.5 y), 35 controls (9.6 ± 0.9 y)	PSG, questionnaire	NA	Depression, social problems	
Ersu et al[161]	2,147 school students (8.5 ± 1.3 y), 151 habitual snorers	Questionnaire	NA	Hyperactive, sleepiness	
Gottlieb et al[17]	61 SDB, 144 controls (all 5 y)	Questionnaire, PSG (n = 180)	Attention, executive function, hand–eye coordination, IQ, memory	ADHD symptoms, inattention	

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Appendix A (*Continued*)

Authors	Population	SDB/snoring measure	Neurocognitive dysfunction	Behavioral dysfunction	Note
Huang et al[162]	88 ADHD (8.5 ± 1.9 y, 50 with OSA), 27 controls (9.0 ± 2.0 y)	PSG, questionnaire	Response time	Hyperactive	
Kaditis et al[163]	3,680 school students (1–18 y, median age 9.8 y), 154 habitual snorers	PSG (n = 70), questionnaire	NA	Sleepiness	
Kennedy et al[50]	13 snorers (7.0 ± 4.0 y), 13 controls (7.0 ± 4.0 y)	PSG	Attention, IQ, memory, verbal	NA	
Melendres et al[41]	108 SDB (7.0 ± 4.0 y), 72 controls (8.0 ± 4.0 y)	PSG (SDB only), questionnaire	NA	Hyperactive, sleepiness	
O'Brien et al[27]	35 SDB (6.7 ± 0.6 y), 35 controls (6.7 ± 0.5 y)	PSG, questionnaire	Executive function, phonological processing, visual attention	No differences between groups	Testing on morning after PSG
O'Brien et al[51]	49 high sleep pressure score (SPS) (6.7 ± 0.5 y), 150 low SPS (6.7 ± 0.5 y)	PSG, questionnaire	Language, verbal IQ, visuospatial, memory	Inattention	Low SPS also displayed significant obstruction
O'Brien et al[26]	87 snorers (6.6 ± 0.5 y), 31 controls (6.8 ± 0.4 y)	PSG, questionnaire	Language, visual attention, visuospatial	Anxiety, delinquency, depression, hyperactive, inattention, social problems, withdrawn	
Rosen et al[164]	162 SDB (9.5 ± 0.9 y), 667 controls (9.5 ± 0.8 y)	Limited PSG, questionnaire	NA	Aggressive, emotionally labile, hyperactive, oppositional, social problems, somatic complaints	Inclusion in SDB group could be based on parental report only
Arman et al[165]	96 habitual snorers (9.3 ± 1.4 y), 190 controls (9.4 ± 1.2 y)	Questionnaire	NA	ADHD symptoms, conduct problems, inattention, oppositional, sleepiness	
Blunden et al[166]	11 snorers (9.4 ± 1.2 y), 9 snorers + behavioral sleep problems (9.4 ± 1.2 y), 13 behavioral sleep problems (9.4 ± 1.2 y), 31 controls (9.4 ± 1.2 y)	Questionnaire	Attention, verbal IQ	Externalizing, internalizing	
Carvalho et al[167]	79 SDB (9.4 ± 1.2 y), 468 nonrespiratory sleep disorders (9.4 ± 1.2 y), 633 controls (9.4 ± 1.2 y)	Questionnaire	Visual–motor ability	NA	
Chervin[168]	229 children from clinics (10.6 ± 3.1 y), 28 habitual snorers	Questionnaire	NA	Hyperactive	
Goodwin et al[169]	480 school students (9.4 ± 1.2 y), 115 SDB (RDI ≥ 1)	Unattended home PSG	Learning problems	Sleepiness	Nonvalidated behavior measure
Montgomery-Downs et al[15]	19 OSAS (4.2 ± 0.8 y), 19 controls (4.3 ± 0.7 y)	PSG, questionnaire	IQ, verbal fluency	NA	
Mulvaney et al[63]	403 school students (9.4 ± 1.2 y), 63 SDB, 340 controls	Unattended home PSG	NA	ADHD symptoms, aggressive, emotional lability, inattention, oppositional, social problems, thought problems	Controls displayed significant respiratory disturbance

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Appendix A (*Continued*)

Authors	Population	SDB/snoring measure	Neurocognitive dysfunction	Behavioral dysfunction	Note
Sogut et al[170]	1,198 school children (8.1 ± 1.9 y), 39 habitual snorers	PSG (28 snorers), questionnaire	School grades	Sleepiness	Nonvalidated behavior measure
Tran et al[78]	42 children scheduled for AT (5.8 ± 2.5 y), 41 children scheduled for unrelated surgery (7.3 ± 3.8 y)	PSG (AT group only)	NA	Presurgery comparisons not made, but all mean scores within normal range for both groups	No PSG for control
Urschitz et al[171]	995 school students (9.6 ± 0.7 y, 99 habitual snorers)	Questionnaire, home nocturnal oximetry	Mathematical ability	NA	
Chervin et al[43]	78 children scheduled for adenotonsillectomy (8.1 ± 1.8 y), 27 controls (9.3 ± 2.0 y)	Esophageal pressure, PSG, questionnaire	Attention	ADHD symptoms, hyperactive, sleepiness	Some controls demonstrated SDB
Emancipator et al[172]	164 SDB (9.4 ± 0.8 y), 671 non-SDB (9.4 ± 0.8 y), all children from community sample	Limited PSG, questionnaire	Executive function, information processing, language comprehension, verbal problem solving	NA	
Galland et al[32]	61 children scheduled for adenotonsillectomy (7.0 ± 2.0 y)	Limited PSG, questionnaire	Attention, impulsivity	Aggression, depression, hyperactive, inattention, somatic complaints	No control group
Halbower et al[52]	19 OSAS (10.0 ± 2.5 y), 12 controls (9.8 ± 2.6 y)	PSG	Executive function, IQ	NA	5/19 OSAS children had ADHD diagnosis
Hill et al[33]	21 scheduled for adenotonsillectomy (5.5 ± 1.3 y), 17 controls (5.5 ± 1.4 y)	PSG (SDB only), questionnaire	Attention, processing speed	NA	No PSG for control
Kurnatowski et al[34]	117 SDB (9.4 ± 1.2 y), 104 controls (9.4 ± 1.2 y)	PSG	Attention, executive function, memory, verbal comprehension, visuospatial	NA	30% controls demonstrated snoring
Li et al[53]	40 referred for adenotonsillar hypertrophy (8.4 ± 1.6 y)	PSG	Attention	No association with SDB severity	No control group
Mitchell and Kelly[64]	23 OSAS (9.4 ± 1.2 y)	PSG	NA	Somatic complaints	No control group
Suratt et al[59]	114 with adenotonsillar hypertrophy (8.5 ± 1.9 y)	PSG, questionnaire	Verbal reasoning, vocabulary	Somatic complaints	No control group
Ziliotto et al[54]	10 oral breathing and SDB (7.6 y), 10 oral breathing and SDB (8.1 y), 10 controls (7.5 y)	PSG (oral breathing groups only)	Memory for sounds (auditory processing)	NA	No PSG for control
Constantin et al[65]	138 sleep clinic patients (5.5 ± 3.0 y)	PSG	NA	No difference between OSAS and non-OSAS	Retrospective behavior assessment, no control group
Dillon et al[66]	78 children scheduled for adenotonsillectomy (8.1 ± 1.8 y), 27 controls (9.3 ± 2.0 y)	PSG	NA	ADHD symptoms, oppositional	Some controls demonstrated SDB

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Appendix A (*Continued*)

Authors	Population	SDB/snoring measure	Neurocognitive dysfunction	Behavioral dysfunction	Note
Gozal et al[55]	102 OSAS (6.4 ± 0.4 y), 103 snorers (6.6 ± 0.3 y), 73 controls (6.3 ± 0.3 y)	PSG, questionnaire	Global cognitive ability	NA	Specific cognitive domains not specified
Hiscock et al[173]	4,983 communities (4.7 ± 0.2 y)	Questionnaire	Verbal ability	Conduct problems	
Uema et al[56]	24 OSAS, 37 primary snorers, 20 controls (all 6–12 y)	PSG	Verbal memory	NA	Deficits in both OSAS and primary snorers
Wei et al[88]	117 referred for adenotonsillectomy (6.5 ± 1.8 y)	Questionnaire	NA	ADHD-type behavior, inattention, oppositional	No control group, no comparison with standard norms
Giordani et al[25]	40 OSAS scheduled for adenotonsillectomy (7.8 ± 1.8 y), 38 non-OSAS scheduled for adenotonsillectomy (8.4 ± 1.8 y), 26 controls (9.2 ± 2.0 y)	PSG	OSAS: attention, mathematical ability, visual memory, visuospatial; non-OSAS: mathematical ability,visual memory, visuospatial	Externalizing, hyperactivity, internalizing	Controls from unrelated surgery clinic
Karpinski et al[174]	39 preschool students (4.3 ± 0.6 y)	Questionnaire	Executive function	NA	Only 6 snoring children
Moré et al[82]	73 snorers (4.6 ± 2.0 y)	Questionnaire, PSG (61 children)	Memory	Aggression	No control group, no comparison with standard norms
Zhao et al[30]	403 communities (8.3 ± 1.6 y)	Unattended home PSG	NA	Aggression/ oppositional, social problems, somatic complaints	Deficits irrespective of hypoxia severity
Aronen et al[175]	43 snorers (4.9 ± 1.1 y), 46 controls (4.8 ± 1.1 y)	Questionnaire	Auditory attention, language development, verbal ability	Anxiety, emotional lability	Not all children included in analyses of language and attention
Calhoun et al[57]	571 communities (413 controls, 8.7 ± 1.6 y; 158 SDB, 8.7 ± 1.7 y)	PSG	Nonverbal IQ (snoring + OSA vs nonsnoring + no OSA)	NA	
Ericsson et al[89]	67 referred for tonsillar hypertrophy (all 4.5–5.5 y)	None	NA	Internalizing	No control group, no measure of SDB
Gozal et al[58]	87 OSAS (6.4 ± 0.5 y), 52 controls (6.1 ± 0.4 y)	PSG	Executive function, language development, mathematical ability, verbal ability	NA	
Kohler et al[18]	44 SDB (6.6 ± 2.6 y), 48 controls (7.7 ± 2.6 y)	PSG	Executive function, IQ, language development, sensorimotor, verbal memory, visuospatial	NA	
Lundeborg et al[83]	67 referred for tonsillar hypertrophy (4.8 ± 0.4 y), 47 controls (4.8 ± 0.4 y)	None	Language development (phonological processing)	NA	No measure of SDB

Abbreviations: AT, adenotonsillectomy; SDB, sleep-disordered breathing; OSAS, obstructive sleep apnea syndrome; PSG, polysomnography; $TcCO_2$, transcutaneous CO_2 monitoring; IQ, intelligence quotient; NA, not assessed.

Appendix B Summary of published studies investigating changes in neurocognitive performance and behavior following treatment for SDB amongst children

Study	Baseline population	Follow-up population	SDB measure	Intervention	Follow-up period	Neurocognitive effects	Behavior effects
Guilleminault et al[6]	8 OSAS	7 OSAS	PSG	AT (n = 5), tracheotomy (n = 2)	3 and 6 wk (AT), 22 and 28 mo (tracheotomy)	↑School performance	↓Daytime sleepiness
Brouillette et al[68]	22 OSAS	22 OSAS	Daytime or nighttime PSG	Adenoidectomy and/or tonsillectomy (n = 11), tracheotomy (n = 11)	Not specified	NA	↓Daytime sleepiness and ↓behavioral disturbance (n = 5)
Guilleminault et al[7]	25 snorers, 25 controls	25 snorers	PSG, esophageal pressure	AT (snoring only)	12 mo	↑School performance (by 3 mo), ↑attention (n = 5)	↓Hyperactivity (by 6 mo), ↓daytime sleepiness (n = 5)
Stradling et al[71]	61 snorers, 31 controls	58 snorers, 31 controls	Oximetry, video (26 snorers and 27 controls)	AT (snoring only)	6 mo	NA	↓Hyperactivity and ↓aggression/ rebelliousness
Ali et al[70]	12 SDB, 11 snorers, 10 controls	12 SDB, 11 snorers, 10 controls	Oximetry, video	AT (SDB and snoring only)	3–4 mo	SDB: ↑vigilance, no difference in impulsivity; snoring: no difference in impulsivity	SDB: ↓aggression, inattention and hyperactivity; snoring: ↓Hyperactivity
Gozal[72]	120 SDB, 177 controls	120 SDB, 177 controls	Oximetry, $TcCO_2$	AT (24 SDB only)	15 mo	↑Academic performance in treated SDB children	NA
Harvey et al[80]	56 SDB	42 SDB	PSG	AT (24 SDB only)	6 mo	No change in mental development	NA
Goldstein et al[85]	36 SDB	15 SDB	Questionnaire	AT	3 mo	NA	↓Internalizing, withdrawn and somatic complaints, anxiety, depression, inattention and hyperactivity
Owens et al[46]	18 OSAS	8 OSAS	PSG	AT	~7 mo	↑Executive function, ↑motor skills; no change in IQ, language, memory, visual perception/ motor ability	No change in internalizing, externalizing, and somatic complaints, attention, anxiety, hyperactivity
Richards and Ferdman[73]	NA	45 OSAS	PSG, questionnaire	AT	6–18 mo	Poor school performance despite treatment	Daytime sleepiness despite treatment
Hansen and Vandenberg[47]	7 OSAS, 7 narcoleptics	7 OSAS, 7 narcoleptics	PSG	Unspecified surgery and CPAP (OSAS only)	Not specified	↑Memory, ↑visual attention; no change in verbal attention	NA
Goldstein et al[84]	64 OSAS	64 OSAS	Clinical history, physical examination	AT	3 mo	NA	↓Internalizing, externalizing, withdrawn, and somatic complaints, anxiety, depression, inattention and aggression

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Appendix B (*Continued*)

Study	Baseline population	Follow-up population	SDB measure	Intervention	Follow-up period	Neurocognitive effects	Behavior effects
Friedman et al[16]	39 OSAS, 20 controls	27 OSAS, 14 controls	PSG (OSAS only), questionnaire	AT (OSAS only)	6–10 mo	↑Analytic thinking, perceptual ability, visuospatial ability, intelligence, verbal memory; no change in vocabulary and memory for numbers	NA
Avior et al[79]	19 OSAS	19 OSAS	Questionnaire, physical examination	AT	2 mo	↑Attention	↑Attention
Montgomery-Downs et al[15]	19 OSAS, 19 controls	19 OSAS	PSG, questionnaire	AT (OSAS only)	3–6 mo	↑IQ; no change for language development	NA
Tran et al[78]	42 OSAS, 41 controls	42 OSAS, 41 controls	PSG (OSAS only)	AT (OSAS only)	3 mo	NA	↓Internalizing, thought problems and somatic complaints; no change in externalizing and withdrawn behavior, inattention, aggression, anxiety or depression
Chervin et al[43]	78 SDB, 27 controls	77 SDB, 23 controls	PSG	AT	12 mo	↑Attention	↓Hyperactivity and sleepiness
Galland et al[32]	61 suspected SDB or tonsillitis	61 suspected SDB or tonsillitis	Limited PSG, questionnaire	AT	3 mo	↑Visual attention; no change for auditory attention	↓Internalizing, externalizing and somatic complaints, inattention, hyperactivity, aggression and anxiety
Li et al[53]	40 suspected SDB	40 suspected SDB	PSG	AT	6 mo	↑Attention	↓Internalizing, externalizing and somatic complaints, inattention, depression, hyperactivity and anxiety; no change in aggression
Mitchell and Kelly[64]	23 OSAS	23 OSAS	PSG	AT	6 mo and 9–18 mo	NA	↓Internalizing, externalizing and somatic complaints, depression, hyperactivity and aggression
Roemmich et al[86]	54 OSAS	54 OSAS	PSG	AT	12 mo	NA	↓Hyperactivity
Constantin et al[65]	94 SDB	94 SDB	PSG	AT (n = 54)	~4 y (retrospective reports only)	NA	No change in oppositional behavior, inattention and hyperactivity
Dillon et al[66]	79 SDB, 27 controls	78 SDB, 23 controls	PSG	AT	12 mo	NA	↓Oppositional behavior; however, differences still evident post-AT; no change in anxiety and depression; ↓inattention and hyperactivity no greater than for controls

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Appendix B (*Continued*)

Study	Baseline population	Follow-up population	SDB measure	Intervention	Follow-up period	Neurocognitive effects	Behavior effects
Wei et al[88]	117 SDB	71 SDB	Questionnaire	AT	6 mo	NA	↓Inattention, hyperactivity and oppositional behavior
Hogan et al[81]	19 SDB, 14 controls	19 SDB, 14 controls	PSG (SDB, baseline only), oximetry and questionnaire (n = 16 SDB, baseline and follow-up)	AT	11 mo (SDB), 13 mo (control), $P < 0.001$	↑Processing speed; trend for ↑ in visual attention; no change for executive function	NA
Moré et al[82]	73 SDB	44 SDB	PSG (n = 29), questionnaire	AT	9 mo	↑Concentration, memory, school performance and ↓speech delay (parent report only)	↓Aggressiveness and hyperactivity
Ericsson et al[89]	67 SDB	67 SDB	Clinical examination	TE (n = 32), TT (n = 35)	6 mo	NA	TE: ↓somatic complaints, anxiety, inattention, social problems (no change in withdrawn behavior, aggression, thought problems); TT: ↓somatic complaints, aggression (no change in withdrawn behavior, anxiety, inattention, social and thought problems)
Lundeborg et al[83]	67 SDB, 47 controls	64 SDB, 31 controls	Clinical examination	TE (n = 32), TT (n = 35)	6 mo	↑Language development; however, deficits still evident posttreatment	NA
Kohler et al[18]	44 SDB, 48 controls	44 SDB, 48 controls	PSG	AT	6 mo	↑Visuospatial ability, however, deficits still evident posttreatment; no change in IQ, executive function, attention, language development, sensorimotor function and memory	NA
Wei et al[87]	71 SDB	44 SDB	Questionnaire	AT	2.4–3.6 y	NA	↓Inattention, hyperactivity, and oppositional behavior; no change in ADHD symptoms

Abbreviations: AT, adenotonsillectomy; SDB, sleep-disordered breathing; OSAS, obstructive sleep apnea syndrome; PSG, polysomnography; $TcCO_2$, transcutaneous CO_2 monitoring; TE, tonsillectomy; TT, intracapsular tonsillectomy/tonsillotomy; IQ, intelligence quotient; NA, not assessed.