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ACCEPTANCE

This dissertation, EXECUTIVE FUNCTIONING IN THE PRESENCE OF SLEEP DISORDERED BREATHING, by AMY MICHELLE SUTTON, was prepared under the direction of the candidate's Dissertation Advisory Committee. It is accepted by the committee members in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the College of Education, Georgia State University.

This Dissertation Advisory Committee and the student's Department Chair, as representatives of the faculty, certify that this dissertation has met all standards of excellence and scholarship as determined by the faculty. The Dean of the College of Education concurs.

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Abstract

EXECUTIVE FUNCTION IN THE PRESENCE OF
SLEEP-DISORDERED BREATHING
by
Amy M. Sutton

The purpose of the study was to investigate whether sleep-disordered breathing (SDB) impairs executive functioning in children. Additionally, the study sought to identify the executive functions at risk in SDB and the contribution of daytime sleepiness. SDB represents a spectrum of upper airway conditions that can be mild, such as snoring, or severe, such as obstructive sleep apnea (OSA). Children with these problems may present with excessive sleepiness, failure to thrive, and a variety of cognitive and behavioral dysfunctions including impaired executive functioning. Beebe and Gozal (2002) developed a theoretical model to explain the impact of sleepiness and hypoxia on executive functioning. This model provided a framework to examine links between the medical disorder and the neuropsychological consequences. Twenty-seven children with suspected SDB were tested with polysomnography (PSG) and a neuropsychological battery. Parents completed subjective measures of cognitive function and sleep symptoms. The children were ages 8 to 18 and had no congenital or acquired brain damage. They were matched for age and gender with 21 healthy controls. The executive function protocol included subtests from the Delis-Kaplan Executive Function System (D-KEFS), the digit span subtest from the Wechsler Intelligence Scale for Children (WISC-IV), the Tower of London-II-Drexel University (TOL-II), the Behavioral Rating

Inventory of Executive Functioning (BRIEF), and the Conners' Continuous Performance Test (CPT-II). Statistical analysis was performed using 2 statistical software packages, SAS and NCSS. Regression analysis was used to evaluate all variables. Due to significant group differences in socio-economic status (SES), SES was included as a covariate, along with IQ. No group differences in IQ were found. Significantly less robust executive function in children with SDB was identified in the domains of cognitive flexibility and impulsivity. Additionally, poorer executive planning and overall inattentiveness was also associated with SDB. Level of significance was set at 0.05 and trends ($0.05 < p < 0.10$) were acknowledged. Other areas of executive function, including working memory, behavioral and emotional inhibition, and processing speed were not associated with SDB. Moreover, academic functioning was significantly lower in children with SDB, although the differences can be shared equally with SDB, SES and IQ.

EXECUTIVE FUNCTIONING IN THE PRESENCE OF SLEEP DISORDERED BREATHING

By

Amy M. Sutton

A Dissertation

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ABBREVIATIONS

AD/HD	Attention Deficit/Hyperactivity Disorder
OSA	Obstructive Sleep Apnea
PSG	Polysomnography
SDB	Sleep Disordered Breathing
SES	Socioeconomic Status

CHAPTER 1

THE EFFECTS OF SLEEP-DISORDERED BREATHING ON EXECUTIVE FUNCTIONING IN CHILDHOOD: A REVIEW OF THE LITERATURE

Sleep and respiratory disturbances resulting from ineffective nighttime breathing patterns are known to cause significant cognitive and behavioral changes in adults and children. Sleep-disordered breathing (SDB) represents a spectrum of upper airway conditions that can be mild such as snoring (without oxygen desaturations) or severe such as obstructive sleep apnea (OSA). The study of SDB and resulting deficits has become of great interest in both adult and pediatric literature due to the rising prominence of individuals affected by the disorder. More importantly, a significant body of evidence indicated the serious cognitive and behavioral repercussions of this condition (Bass et al., 2004). The empirical research emerging from a collaboration of pulmonology and neuropsychology has related general intellectual functioning, attention, memory, executive function, and motor function to consequences of SDB (Decary, Rouleau, & Montplaisir, 2000). It has been observed that more severe forms of SDB, such as OSA, will produce more harmful physiological and neurocognitive sequelae (Lewin, Rosen, England, & Dahl, 2002). Research in this domain has focused predominantly on the consequences of SDB, reversibility of symptoms, and identifying the contribution of poor oxygenation versus sleepiness on neurocognitive outcomes. Different physiological processes are

thought to be involved in the cognitive changes with the most notable being sleep disruption causing excessive daytime sleepiness and lack of oxygen to the brain causing anoxic/hypoxic brain injury (Beebe & Gozal, 2002). Research involving treatment modalities in adults and children has demonstrated, however, recovery of many of the cognitive deficits following a treatment intervention (Ali, Pitson, & Stradling, 1996; Dahloff et al., 2002; Engleman & Martin, 1994; Feuerstein, Naegele, Pepin, & Levy, 1997; Friedman et al., 2003; Gozal, 1998; Montgomery-Downs, Crabtree, & Gozal, 2005). The main goal of this literature review is to pool the empirical and conceptual findings in both adult and pediatric literature as it relates to neurocognitive changes in the presence of SDB. Specifically, the review will provide a framework for examining a less investigated, yet emerging domain, the impact of SDB on executive functioning in children.

Physiology of Sleep-Disordered Breathing

Individuals with a respiratory sleep disorder are not readily recognized in the general population as symptoms occur primarily during the night. The daytime symptoms of the disorder are also not as easily identified, due primarily to the fact that they mimic symptoms or problems of other illnesses or mental challenges. Children, for example, may demonstrate behaviors similar to that of a child with attention-deficit/hyperactivity disorder (AD/HD) (Chervin, Ruzicka, Archbold, & Dillon, 2005; Gottlieb et al., 2003) while adults may present with fatigue, depression, and mood fluctuations (Flemons & Tsai, 1997). Despite the decreased visibility, the prevalence of SDB is wide-reaching with snoring occurring in 18%-20% of infants, 7%-13% of children ages 2-8, and 3%-5% of children over 8 (Hunt, 2004). OSA is

estimated to affect 2-3% of all children (Gottlieb et al., 2003). Similarly, the prevalence of OSA in the general adult population is approximately 4% (Decary et al., 2000).

SDB may interfere with normal body processes causing sleep disruption and changes in blood gas exchange, such as hypoxemia (low oxygen levels) and hypercarbia (high carbon dioxide levels). This occurs through periods of nighttime apnea (absence of airflow) or hypopnea (reduction of airflow). Apneas and hypopneas lasting at least ten seconds despite adequate respiratory effort qualify the individual as having the more severe form of SDB, obstructive sleep apnea (Gale & Hopkins, 2004). In general, SDB and OSA occur due to an increase in upper airway resistance while sleeping. This resistance makes natural breathing and normal respiratory patterns difficult, leading to increased respiratory effort, blood gas abnormalities, and sleep disturbances (Gozal, 2000). It can change sleep patterns causing the patient to have shortened sleep cycles and difficulty entering the deeper, restorative stages of sleep (Sanchez, Bermudez, & Buela-Casal, 2003). Thus, daytime sleepiness or somnolence is an expected physiological response to SDB. Impaired respiration leads to an imbalance of oxygen and carbon dioxide in the blood. Poorly oxygenated blood is insufficient to nourish the highly sensitive cells of the nervous system. This deprivation of nutrients can lead to nervous system cellular injuries, which typically do not recover. Although the spells of chemical imbalance are normally short and followed by adequate oxygenation, the accumulation of brief and frequent episodes can eventually lead to cell death or injury (Gale & Hopkins, 2004). Other consequences for adults include cardiovascular disease, cerebrovascular disease,

pulmonary hypertension, and cardiac arrhythmias (Cohen-Zion et al., 2001). Small children may develop a failure to thrive as well as cardiovascular disease (Hunt, 2004; Perkin, 1999).

SDB and OSA may present in an otherwise healthy child or adult or it may be comorbid with another diagnosis. Risk factors for adults include obesity, hormone abnormalities, nasal congestion such as allergic rhinitis, and having a genetic predisposition (Beebe & Gozal, 2002; Young, Skatrud, & Peppard, 2004). Adenotonsillar hypertrophy is the most common cause for children with SDB; however, other origins include obesity and craniofacial abnormalities (Hunt, 2004). Persons with SDB are typically referred by their primary physician to a pulmonologist for diagnosis and treatment of SDB. Diagnosis is achieved using polysomnography, a sleep test performed in a lab where measures of oxygenation, arousal, and breathing pattern are recorded. Polysomnography (PSG) is typically performed throughout a full night with the patient attached to several monitors. The test includes an electroencephalogram (EEG) to monitor brain wave activity, an electromyogram (EMG) to monitor selected muscle activity, and an electrooculogram (EOG) to monitor eye movement. Airflow through the mouth and nose is measured as well as end title carbon dioxide and the oxygen saturation in the blood. Electrocardiogram (ECG) leads are used to monitor the heart rate or rhythm changes and sensors attached to the torso measure chest and abdominal wall movement. Finally, the sounds produced while sleeping, such as snoring, are recorded and included in the final evaluation. With all of this data, the technicians and pulmonologist are able to determine the effectiveness of nighttime breathing and the

need for any type of intervention. The highly sensitive equipment used during a PSG allows the practitioners to identify even the most elusive signs. Many children experience symptoms of OSA for years prior to diagnosis due to subtlety of symptoms or underreporting to care providers (Blunden, Lushington, Kennedy, Martin, & Dawson, 2000).

Unlike adults, the most common cause for childhood OSA is enlarged tonsils and adenoids (Hunt, 2004). Therefore, the preferred treatment for symptomatic OSA is the removal of the tonsils and adenoids (adenotonsillectomy) thereby opening the restricted airway and allowing for effective nighttime breathing (Montgomery-Downs et al., 2005). The first choice treatment for adults is the use of continuous positive airway pressure (CPAP). This treatment involves a mask worn at night, which provides a continuous flow of air with pressure higher than that of the environment. CPAP is occasionally used in lieu of surgery for treating children with OSA (Beebe & Gozal, 2002). In tandem, adults may undergo a similar surgical procedure as children, which involves the removal of excess tissue in the upper airway such as part of the soft palate, the tonsils and adenoids, and uvula (uvulopalatopharyngoplasty or UPPP) (Dahloff et al., 2002).

Executive Function and the Prefrontal Cortex

Research on and conceptualization of how the brain works has evolved over many decades and has been adapted to incorporate a more detailed exploration of localization of function and the complex integration of brain activity. One aspect of this evolution is the proposal of “basic” versus “executive” functions. The brain has been described as being comprised of various networks of systems, dependent on the

activities of different brain regions, to produce a complex human ability capable of integrating copious amounts of information (language, reading, spatial reasoning, etc.) (Damasio, 1991; Shallice & Burgess, 1991; Stuss, 1987). Although these systems work together to produce the appearance of an integrated whole, each may be viewed as a distinct system when operating within its specialization, especially when handling rote experiences (Williamson, Scott, & Adams, 1996).

When the aforementioned systems are faced with a novel situation, an appropriate response must be evaluated, considering outcomes and consequences, and chosen as the best course. Since a preexisting blueprint for this situation does not exist, it requires creativity, problem solving, and analysis. This type of mental processing is deemed "executive functions" and is associated with the prefrontal cortex located in the frontal lobe of the human brain (Damasio, 1991; Stuss, 1987). Although many definitions of executive function exist and include all possible executive activities, Stuss (1987) proposed the following concise definition: Executive function is the ability "to extract and use information from the posterior brain systems, and to anticipate, select, plan, experiment, modify, and act on such information in novel situations" (p. 175). Another definition by Lezak, Howieson, & Loring (2004) proposed that "executive functions consist of those capacities that enable a person to engage successfully in independent, purposive, self-serving behavior" (p. 35). One group of brain activities thought to suffer in the presence of chronic, intermittent hypoxia is executive functions. Whether this phenomenon occurs due to actual cellular damage or external factors (i.e. sleepiness), the consequences impact activities of daily living, academics, and social functioning.

Due to the predominant location in the brain where executive function is said to occur, the terms “executive function” and “frontal lobe function” have often been used interchangeably. Initial localization of the executive functions is typically associated with Luria (1972) based on his findings of deficits in patients with obvious frontal lobe damage. Researchers have utilized functional imaging to demonstrate the activation of the prefrontal cortex during activities identified as executive functioning. Therefore, the concept of executive functioning cannot be discussed independent of its anatomical localization, the frontal lobes.

The frontal lobes are typically accredited with the highest level of cognitive functioning and thought formation (Fuster, 1989). They are located in the anterior half of the cerebral hemisphere and separated caudally by the central sulcus and hemispherically by the lateral sulcus. The frontal lobes are further divided into three primary regions: the motor cortex, the premotor cortex, and the prefrontal cortex (Zilles, 1990). Deeper below the brain surface is a fourth frontal region known as the paralimbic or limbic area. Of these four regions, the prefrontal cortex is the latest structure to develop prenatally and comprises the largest area of the frontal lobe (Johnson, 1997). The prefrontal cortex is the portion of the frontal lobe that is considered primarily responsible for executive functioning. Similar to the frontal lobe, the prefrontal cortex is also divided into distinct regions. These three main regions include the dorsolateral prefrontal cortex, the orbitofrontal cortex, and the anterior cingulate cortex. Each area is believed to be responsible for different aspects of executive function although most of the prefrontal lobe activities require the input from at least two, if not all, of its regions (Powell & Voeller, 2004).

The dorsolateral prefrontal cortex, or circuit, is located in the upper lateral portion of the prefrontal cortex and receives inputs from the posterior parietal lobe and the superior temporal lobe (Kolb & Whishaw, 1996). There are several main functions of the dorsolateral prefrontal cortex including regulation and integration of cognitive activities, such as maintaining attention and shifting cognitive set smoothly when necessary (Powell & Voeller, 2004). Working memory, or the ability to hold information available in memory and manipulate that information to achieve a goal, is another primary function of the dorsolateral region. In combination, these activities produce higher-level skills such as organization, problem solving, and learning. Thus, damage to this region may cause individuals to have poor information processing, attentional deficits, and impaired working memory. Additionally, they may also have difficulty setting and maintaining a goal activity (Lezak et al., 2004).

Directly below the dorsolateral region lies the orbitofrontal cortex, which receives inputs from the temporal lobe and the amygdala. The amygdala is part of the limbic system and is partially responsible for emotional and autonomic responses (Kolb & Whishaw, 1996). The orbitofrontal cortex is, therefore, an important factor in the modulation of interactive behavior. Social behaviors such as empathy, morality, self-restraint, and behavior monitoring are regulated by this area of the prefrontal cortex (Powell & Voeller, 2004). Individuals suffering damage to the orbitofrontal cortex may suffer severe personality changes, despite demonstrating otherwise intact cognition. They may lose their “people skills” and present as disinhibited, emotionally labile, aggressive, and impulsive. In general, the ability to evaluate the future consequences of present actions is impaired (Lezak et al., 2004).

The third division of the prefrontal cortex is the anterior cingulate region, located deep in the cortex on the medial sides between the hemispheres. This region is typically considered a part of the limbic system, more so than the orbitofrontal cortex, with the central roles of attention, arousal, and emotion (Powell & Voeller, 2004). Other responsibilities include divided attention, error detection, initiation of appropriate behaviors, and motivation. Apathy, lack of motivation, indifference, poor attention, depression, and blunted body movement are typical manifestations of an injury to the anterior cingulate region of the prefrontal cortex (Lezak et al., 2004). Both the orbitofrontal cortex and the anterior cingulate are involved in emotional responses. Individuals with an impaired orbitofrontal region, however, present with exaggerated emotional states (i.e. aggression and labile emotions) while those with an impaired anterior cingulate would present with muted emotional states (i.e. apathy and depression).

Although the prefrontal cortex is a key anatomical structure involved in executive functioning, without the input from the rest of the brain, these higher-level activities could not exist. Thus, the connections between the structures are as important the structures themselves. The interconnected of executive functions makes localization challenging to researchers. Moreover, when examining the development of executive functions in children, the approach must be cognizant of the maturation trajectory of the frontal lobes themselves. A research study by Hudspeth and Pribham (1992) documents maturational peaks and plateaus, which continue from early childhood into adolescence. In fact, they found that development was accelerated during the age range from 7-10 years with a major advance in maturation occurring in

late adolescence. These findings support the notion that executive processes emerge initially after birth and continue throughout childhood and adolescence (Anderson, 1998).

SDB and Deficits in Adult Functioning

SDB is linked to various cognitive and behavioral disturbances in children and adults. Early research examining the cognitive impact of SDB on functioning was conducted mostly with adult participants. This research has set the stage for similar research with children. Gale and Hopkins (2004) summarized that impairments in short-term memory, general intelligence, visuospatial function, and executive function, specifically impaired vigilance and attention, are common cognitive outcomes in adults with OSA.

Various researchers have found impairments in the areas of motor speed, information processing speed, long and short-term memory, and executive function, including working memory and attention (Salorio, White, Piccirillo, Duntley, & Uhles, 2002). In a study by Greenberg, Watson, and Deptula (1987), 14 patients with sleep apnea, 10 patients with no sleep apnea but excessive daytime sleepiness, and 14 healthy controls were given a full neuropsychological battery. Although the findings supported an overall moderate cognitive impairment in 7 of 14 measures in sleep apnea patients, the most significant finding was impaired motor speed and perceptual-organizational ability. Information processing speed impairments have also been found in patients with sleep apnea. Researchers assessed 10 adults with severe OSA, 10 with moderate OSA, and 10 normals. The findings indicated that neurocognitive impairments were worse in patients with more severe OSA, as measured by levels of

hypoxemia (Bedard, Montplaisir, Richer, Rouleau, & Malo, 1991). Bedard et al. also identified impaired processing speed and long-term episodic memory among all participants with OSA. Memory impairments, both short- and long-term have been identified in several other adult studies (Findley et al., 1986; Gale & Hopkins, 2004; Naegele et al., 1995; Roehrs et al., 1995; Verstraeten, Cluydts, Pevernagie, & Hoffman, 2004). Naegele et al. (1995) found that in 17 adults with sleep apnea compared to 17 healthy adults, memory performance was lower in those with sleep apnea. On the contrary, another study reported no significant memory deficits in patients with SDB (Boland et al., 2002). A meta-analysis of the neuropsychological effects of OSA that covered research through 2001 (Beebe, Groesz, Wells, Nichols, & McGhee, 2003), analyzed the findings of 25 studies and uncovered mixed outcomes. Overall, the impact of verbal and intellectual functioning was deemed negligible while the impact on executive functioning was substantial. However, the findings regarding memory, visual, and motor functioning, were inconclusive. Although some studies reported significant differences, other studies did not find any differences in these particular domains.

Impaired executive function, in contrast, has been consistently noted in studies of adults with OSA, with only few exceptions. Since many of these studies examined various cognitive functions, executive function was often explored as a whole rather than teasing out individual aspects of executive function (i.e. planning and organization). Those that parceled out various aspects of executive function tended to focus on attention and working memory. Decreased attentional capacity in adults with sleep apnea has been documented in several studies that employed correlations

between attention and vigilance testing to conclude that the poor attention is related more to the daytime sleepiness than to hypoxic episodes while sleeping (Bedard et al., 1991; Verstraeten et al., 2004). Researchers assessed working memory in adults with OSA and found that working memory suffers, along with other aspects of executive function, when compared to normal controls (Naegele et al., 1995). Additional findings were reported in studies that suggested that in the presence of SDB, it can be expected that executive function will be impaired (Feuerstein et al., 1997; Gale & Hopkins, 2004; Gottlieb et al., 2004). However, Verstraeten et al. (2004) contradicted these findings and reported reduced short-term memory, processing time, and attentional capacity. No differences in other types of executive function were noted (Verstraeten et al., 2004).

Despite these cognitive changes, interventions such as CPAP and adenotonsillectomy have proven to be effective in both the treatment of SDB and the reversal of most cognitive and behavioral symptoms. Numerous researchers have assessed the effectiveness of interventions and determined relevant deficits that persisted after successful treatment. Complete normalization of nighttime breathing may be expected with the typical treatment of OSA such as adenotonsilectomy or CPAP. The neurocognitive and neurobehavioral symptoms, however, may not resolve or may only partially resolve (Beebe & Gozal, 2002). Numerous adult studies have demonstrated the improvements in cognition, sleepiness, and behavior following treatment with surgery or CPAP (e.g. Dahlof et al., 2002; Lojander, Kajaste, Maasilta, & Partinen, 1999; Meurice, Marc, & Series, 1996; Sanchez et al., 2003). Naegele et al. (1998) and Feuerstein et al. (1997) found that all executive function impairments

returned to baseline following treatment with CPAP, however short-term memory impairments persisted despite treatment. Memory and verbal fluency deficits also continued following treatment with CPAP in yet another study, although sleepiness, mood, general cognitive performance, mental flexability, and attention significantly improved (Engleman & Martin, 1994). Similarly, Gale and Hopkins (2004) compared 20 adults with severe OSA to 20 adults with carbon monoxide poisoning. The findings suggested that CPAP was effective in improving executive function, however, memory remained unchanged. In a study by Naegele et al. (1998), participants showed improvements across all tests of executive functioning following treatment with CPAP. In contrast, two well-controlled studies found no difference in cognitive performance following treatment with CPAP or adenotonsillectomy (Lojander et al., 1999; Monasterio et al., 2001). In light of all studies conducted on pre and post-intervention, the general expectation is that, regardless of treatment choice, intervention improves most, but not all, outcomes.

SDB and Deficits in Child Functioning

To date, few studies have examined the short and long-term impact of SDB and OSA on children. Specifically, children with SDB may present with excessive sleepiness, failure to thrive, and a variety of cognitive and behavioral dysfunctions (e.g. Bass et al., 2004; Gottlieb et al., 2003; Hunt, 2004) including impaired intellectual ability, memory, academics, executive functions, and behavior. A meta-analysis of the research on the cognitive impact of chronic and intermittent hypoxia presented a clear association between sleep apnea and development, behavior, and

academics in children (Bass et al., 2004). Additionally, children with OSA have showed impaired learning and executive function (Hunt, 2004).

The cognitive deficits in children with SDB have been demonstrated in the literature to include general intelligence (Blunden at al., 2000; Friedman et al., 2003; Montgomery-Downs et al., 2005), memory (Gottlieb et al., 2004), and phonological awareness (O'Brien et al., 2004). In 2003, Friedman et al. tested 39 children diagnosed with OSA ages 5-9 and 20 healthy controls using an intelligence test. They found that while children with OSA had overall lower scores than the controls, there was no correlation between severity and performance. It is not surprising, then, that children who suffered from SDB also demonstrated poor academic performance. In a study involving first grade children, academic performance was clearly lower for children with SDB than for healthy children (Gozal, 1998). In a later study, Gozal and Pope (2001) evaluated the performance of 1,588 seventh and eighth grade students. The children who had experienced snoring when they were younger exhibited poorer academic performance than children who did not snore in early childhood. These findings supported the notion that children who experience early cognitive and academic delays, despite later resolution, may continue to remain behind academically. Additionally, the study looked only at children who snored, a mild form of SDB, which supports the growing belief that the SDB diagnosis need not be as severe as OSA to cause significant cognitive changes in the individual.

In addition to cognitive dysfunction, children with SDB exhibit behavioral deficits including hyperactivity and inattention, both of which are part of executive functioning, indicating the involvement of the frontal lobe (Gottlieb et al., 2004).

These behaviors often resemble AD/HD but seem clearly linked to SDB (Gottlieb et al., 2003). In a study using parent report, mild AD/HD symptoms were consistently reported in children with SDB. The appearance of AD/HD symptoms may potentially delay accurate diagnosis and treatment of SDB (O'Brien et al., 2003). A recent prospective study found that snoring is predictive of hyperactivity when SDB goes untreated (Chervin et al., 2005). These children were assessed at a four-year follow up after the initial survey for the presence or absence of SDB symptoms. Those with SDB demonstrated a significant amount of hyperactivity compared to children without SDB symptoms. Bass et al.'s (2004) meta-analysis showed the majority of research on children with SDB found impaired behavior, specifically defined as AD/HD symptoms, impaired attention, and hyperactivity. The pattern in the literature also suggested that the behavioral outcomes of SDB, inattention and hyperactivity, are similar to AD/HD but require completely different treatment modalities, such as neurostimulants versus adenotonsillectomy, for successful resolution of the behaviors. Aside from behavior and attention, other aspects of executive function in children have also been shown to suffer in the presence of SDB. Gottlieb et al. (2004) tested 205 5-year-old children with the executive function core of the NEPSY. He found lower scores across all subtests in children with SDB including Visual and Auditory Attention and the Tower. This finding implicates problems in both attention as well as planning abilities. A second study by O'Brien et al. (2004) duplicated Gottlieb et al's findings, also using the NEPSY executive function core. These conclusions remain preliminary, however, as there exists a paucity of studies evaluating the impact of SDB on the executive functioning of children.

As with adults, children diagnosed with SDB or OSA are typically referred for treatment. Following the intervention, usually adenotonsillectomy but occasionally CPAP, sleep patterns improve (Ali et al., 1996) and most cognitive, academic, and behavioral deficits return to normal (Ali et al., 1996; Friedman et al., 2003; Goldstein et al., 2000; Gozal, 1998; Montgomery-Downs et al., 2005). Ali et al. (1996) found that children with moderate SDB as well as children who snore demonstrated improvements in hyperactivity. Again, indicating that snorers need as much consideration as those with more severe forms of SDB. The Montgomery-Downs et al. (2005) study did identify some residual deficits on the NEPSY following adenotonsillectomy in the areas of sentence repetition and phonological processing. Overall, very few researchers have investigated the degree of improvement in cognitive function following an intervention especially in the domain of executive functions. Permanent impairment of executive function is possible due to sleep disturbance during critical developmental years (Gottlieb, 2005). There is no evidence as to whether one treatment modality is more efficacious than another type.

Sleepiness vs. Cellular Injury

It is evident that SDB impacts cognition and some aspects of behavior. However, one aspect of the domain remains unclear. The cognitive and behavioral outcomes of SDB can be attributed to general sleepiness, which is to be expected when sleep is continuously disrupted over a long period of time (Blunden et al., 2000). It can also be attributed to the effects of hypoxia, which causes actual physiologic damage to sensitive parts of the brain (Beebe & Gozal, 2002; Gozal, Wang, & Pope, 2001). Through the use of imaging, some researchers have identified

actual tissue damage, supporting the consequence of hypoxia (Gale & Hopkins, 2004). Gozal et al. (2001) found that excessive daytime sleepiness in children with OSA is less common and is more likely to develop in obese children. In adults, Lojander et al. (1999) found that following treatment for OSA, daytime sleepiness did not correlate with cognitive function. Contrary to these findings, other studies indicated that sleepiness is the primary cause of declining cognition (e.g. Cohen-Zion, et al., 2001; Verstraeten et al., 2004). The evidence presented for these opposing positions include the following points. In support of cellular injury, researchers argue that imaging studies of persons with OSA show cerebral atrophy (Gale & Hopkins, 2004; Macey et al., 2002). Gale and Hopkins found significant hippocampal atrophy in patients with severe OSA. Macey et al. performed MRI brain morphology on 21 patients with OSA and 21 controls. They found gray matter loss in the frontal and parietal cortex, the temporal lobe, the anterior cingulate, the hippocampus, and the cerebellum in the patients with OSA. Researchers supporting cellular damage also argue that although most cognitive functions return to normal following treatment, some deficits do persist (i.e. memory) (Feuerstein et al., 1997; Gale & Hopkins, 2004; Naegele et al., 1998) indicating permanent, non-reversible brain damage. Finally, some studies have shown that sleepiness ratings do not always correlate with decreased cognitive scores (Gozal et al., 2001; Lojander, 1999). In support of sleepiness as the cause for deficits, researchers have cited the normalization of cognition after treatment in both children and adults. Additionally, they have called attention to studies that demonstrate a correlation between sleepiness and cognitive decline (Engleman & Martin, 1994; Cohen-Zion et al., 2001). Currently, no concrete

evidence regarding cellular damage versus sleepiness demonstrates the importance of one more than another. The cognitive and behavioral outcomes are most likely due to intermittent hypoxia in addition to sleep fragmentation (Gale & Hopkins, 2004).

A Theoretical Model of SDB

Recently, researchers in the area of SDB and cognitive function have begun to address the role of the frontal lobe and executive functioning on behavior and cognitive performance. Although most of the reported deficits related to SDB can be attributed to an executive function, very little research has been conducted exclusively on executive function and SDB. Gottlieb et al. (2004) identified poorer executive functioning in children with SDB, regardless of severity. The ability of children to maintain attention and inhibit hyperactive behaviors is another aspect of executive function (Slomine et al., 2002) and as previously described, is often impaired in children with SDB. Blunden et al. (2004) found impaired attention using the continuous performance task (CPT-II) in children with symptoms of snoring or mild OSA. An overall weakness in the studies of SDB and executive function among children is the minimal consideration of the nature of executive function and the complexity of the prefrontal cortex.

To accurately assess executive function in children, multiple factors should be considered, including the child's age, developmental milestones, and specifying the particular aspect of executive function to be measured. Executive functions are relatively weak in younger children, thus difficult to measure, and do not typically come "on-line" until the child is approximately six years old (Anderson, 2001). This development continues through childhood and into young adulthood (Hudspeth &

Pribham, 1992). Hence, different assessment instruments are used with children and adults. As previously discussed, each subdivision of the prefrontal cortex has specific functions which should be considered when assessing frontal lobe function and drawing conclusions.

In response to the growing interest in the area of executive function and SDB, Beebe and Gozal (2002) developed a theoretical model to explain the impact of sleepiness and hypoxia on executive functioning and resulting behaviors. In general, the model provided the framework for researchers to examine the links between the medical disorder and the neuropsychological consequences. Beebe and Gozal propose that both sleep disruption and cellular imbalance (hypercarbia and hypoxia) contribute to prefrontal cortical dysfunction via disruption of the restorative sleep process and the disruption of chemical homeostasis. They highlighted the executive dysfunctions that are commonly seen including disinhibition, set shifting, self-regulation, working memory, analysis, and contextual memory. All of these dysfunctions contribute to adverse daytime effects. To strengthen the acceptance of this theory, future studies should choose assessment tools that evaluate these executive dysfunctions, as well as assess for the contribution of sleepiness and cellular imbalance. Including a measure of sleepiness and brain imaging studies would be invaluable to this effect.

In summary, the impact of SDB and OSA on children is a relevant concern and the focus of emerging research studies. The physiology of SDB includes both sleep disturbances and blood gas abnormalities, which impair cognitive function. Treatments such as adenotonsillectomy and CPAP have been shown to restore most,

but not all, of the deficits resulting from the condition. Various researchers that have examined adults and children with SDB identified the aspects of cognition sensitive to sleep apnea including intellectual ability, memory, psychological functioning, behavior, and executive functioning. No conclusive evidence has demonstrated whether these impairments are related more to sleepiness or cellular injury, however the evidence does seem to imply the contribution of both pathological processes. Based on this concept, a theoretical model was developed that incorporates both concerns and resulting deficits. Future studies should consider the long and short-term consequences of SDB on executive functioning. The effects of treatment on executive function in children are another critical area of research that may provide practitioners with practical information to help make decisions and promote early identification of children with SDB.

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CHAPTER 2

EXECUTIVE FUNCTIONING IN THE PRESENCE OF SLEEP-DISORDERED BREATHING

Sleep-disordered breathing (SDB) in children is receiving increasing attention, not only due to the large percentage of children affected, but also because of a growing body of evidence indicating the serious cognitive and behavioral repercussions of this condition (Bass et al., 2004). SDB represents a spectrum of upper airway conditions that can be mild, such as snoring (without oxygen desaturations), or severe, such as obstructive sleep apnea (OSA). The prevalence of SDB is wide-reaching. Evidence suggests that snoring occurs in 18%-20% of infants, 7%-13% of children ages 2-8, and 3%-5% of children over 8 (Hunt, 2004). OSA is estimated to affect 2-3% of all children (Gottlieb et al., 2003). Research in this domain has focused predominantly on the consequences of SDB, reversibility of symptoms, and identifying the contribution of poor oxygenation versus sleepiness on neurocognitive outcomes. Children with these problems may present with excessive sleepiness, failure to thrive, and a variety of cognitive and behavioral dysfunctions including impaired executive functioning (e.g. Bass et al., 2004; Hunt, 2004; Gottlieb et al., 2003). The purpose of this study was to investigate whether SDB impairs executive functioning in children and if so, which particular executive functions are at risk in SDB. In addition, the investigator aimed to determine specific measures that are sensitive to these deficits.

SDB may interfere with normal body processes, which may cause sleep disruption and changes in blood gas exchange, such as hypoxemia (low oxygen levels) and hypercarbia (high carbon dioxide levels). This occurs through periods of nighttime apnea (absence of airflow) or hypopnea (reduction of airflow) lasting at least 10 seconds despite adequate respiratory effort (Gale & Hopkins, 2004). Often children are referred by their pediatrician to a pulmonologist for diagnosis and treatment of SDB. Diagnosis is achieved using polysomnography (PSG), a sleep test performed in a lab where measures of sleep cycles, oxygenation, arousal, and breathing patterns are recorded. Adenotonsillar hypertrophy, enlarged tonsils and adenoids, is the most common cause of SDB in children but other origins include obesity and craniofacial abnormalities (Hunt, 2004). Therefore, the preferred treatment for symptomatic OSA is the removal of the tonsils and adenoids (adenotonsillectomy), thereby opening the restricted airway and allowing for effective nighttime breathing. Many children experience symptoms of OSA for years prior to diagnosis and treatment due to subtlety of symptoms or underreporting to care providers (Blunden, Lushington, Kennedy, Martin, & Dawson, 2000).

SDB is linked to various cognitive and behavioral disturbances in both children and adults. Gale and Hopkins (2004) summarized data suggesting that impairments in short-term memory, general intelligence, visuospatial function, and executive function, specifically impaired vigilance and attention, are common cognitive outcomes in adults with OSA. With regard to children, a meta-analysis of the research on the cognitive impact of chronic and intermittent hypoxia presents a clear association between SDB and development, behavior, and academics difficulties

(Bass et al., 2004). Additionally, children with OSA show impaired learning and executive function (Hunt, 2004). Children with SDB, including those identified as snorers, have lower academic performance indicative of the potential link between the influence of SDB and learning (Gozal & Pope, 2001; Gozal, 1998). Gottlieb et al. (2004) found significant differences in memory, executive function, and general intelligence between children with SDB regardless of OSA diagnosis and normal controls. Attention, memory, and general intelligence were found to be impaired in a study that compared children who snore with healthy controls (Blunden et al., 2000). This supports the growing notion that the SDB diagnosis does not have to be as severe as OSA to cause significant cognitive changes in the individual.

In addition to cognitive dysfunction, children with SDB often exhibit behavioral deficits including hyperactivity and inattention, both of which are part of executive functioning, indicating the involvement of the frontal lobe (Gottlieb et al., 2004). These behaviors often resemble Attention-Deficit/Hyperactivity Disorder (AD/HD) but seem clearly linked to SDB (Gottlieb et al., 2003). In a study using parent report, mild AD/HD symptoms were consistently reported in children with SDB. The appearance of AD/HD symptoms may potentially delay accurate diagnosis and treatment of SDB (O'Brien et al., 2003). A recent prospective study found that snoring is predictive of hyperactivity when SDB goes untreated (Chervin, Ruzicka, Archbold, & Dillon, 2005). These children were assessed for the presence or absence of SDB symptoms using an initial survey and were also assessed four years later. Those with SDB demonstrated a significant amount of hyperactivity compared to children without SDB symptoms. Bass et al.'s meta-analysis (2004) shows the

majority of research on children with SDB found impaired behavior, specifically defined as AD/HD symptoms, impaired attention, and hyperactivity. The pattern in the literature suggested that the behavioral outcomes of SDB, inattention and hyperactivity are similar to AD/HD, but required completely different treatment modalities, such as neurostimulants versus adenotonsillectomy, for successful resolution of the behaviors.

Based on the previous research, it is evident that SDB impacts cognition and some aspects of behavior. However, one aspect of the domain remains unclear. The cognitive and behavioral outcomes of SDB can be attributed to general sleepiness, which is to be expected when sleep is continuously disrupted over a long period of time (Blunden et al., 2000). It can also be attributed to the effects of hypoxia, causing actual physiologic damage to sensitive parts of the brain (Beebe & Gozal, 2002; Gozal, Wang, & Pope, 2001). Through the use of imaging, some studies have identified actual tissue damage, supporting the consequence of hypoxia (Gale & Hopkins, 2004; Macey et al., 2002). Gozal et al. (2001) found that excessive daytime sleepiness in children with OSA is less common and is more likely to develop in obese children. In adults, Lojander (1999) found that following treatment for OSA, daytime sleepiness did not correlate with cognitive function. Contrary to these findings, other researchers indicated that sleepiness is the primary cause of declining cognition (e.g. Cohen-Zion, et al., 2001; Verstraeten, Cluydts, Pevernagie, & Hoffman, 2004). Although no concrete evidence demonstrates the importance of one more than another, the cognitive and behavioral outcomes are most likely due to intermittent hypoxia in addition to sleep fragmentation (Gale & Hopkins, 2004).

The latest research on SDB and cognitive function has begun to address the role of the frontal lobe and executive functioning on behavior and cognitive performance. Although many of the reported deficits related to SDB can be attributed to executive dysfunction, little research has focused exclusively on executive function and SDB. Gottlieb et al. (2004) identified inferior executive functioning in children with SDB, regardless of severity. The ability to maintain attention and inhibit hyperactive behaviors is another aspect of executive function (Slomine et al., 2002) and as previously described, is impaired in children with SDB. Blunden et al. (2000) found impaired attention using the continuous performance task (CPT-II) in children with symptoms of snoring or mild OSA. There are few theoretical or practical explanations as to how SDB impairs executive function. In response, Beebe and Gozal (2002) developed a theoretical model to explain the impact of sleepiness and hypoxia on executive functioning and resulting behaviors. In general, the model provides the framework for researchers to examine the links between the medical disorder and the neuropsychological consequences. Beebe and Gozal propose that both sleep disruption and cellular imbalance (hypercarbia and hypoxia) contribute to prefrontal cortical dysfunction via disruption of the restorative sleep process and the disruption of chemical homeostasis. They highlight executive dysfunctions that are commonly seen including disinhibition, set shifting, self-regulation, working memory, analysis, and contextual memory. All of these dysfunctions contribute to adverse daytime effects. This study was based, in part, on Beebe and Gozal's theory, using the constructs in the research design.

Complete normalization of nighttime breathing may be expected with the typical treatment of OSA such as adenotonsilectomy or Continuous Positive Airway Pressure (CPAP), a treatment involving a mask worn at night, which provides a continuous flow of air with pressure higher than that of the environment. The neurocognitive and neurobehavioral symptoms, however, may not resolve or may only partially resolve after several months following the treatment onset (Beebe & Gozal, 2002). Numerous adult studies have demonstrated improvements in cognition, sleepiness, and behavior following treatment with surgery or CPAP (e.g. Lojander, et al., 1999; Dahlof et al., 2002; Sanchez, Bermudez, & Buelo-Casal, 2003; Meurice, Marc, & Series, 1996). Naegele et al. (1998) and Feuerstein, Naegele, Pepin, and Levy (1997) found that all executive function impairments returned to baseline following several months of treatment with CPAP, however short-term memory impairments persisted despite treatment. Fewer studies have been conducted with children but even preliminary findings show a similar pattern of recovery (Rains, 1995). Montgomery-Downs, Crabtree, and Gozal (2005) tested the cognitive function of pre-school children before and after adenotonsillectomy. The findings confirmed that cognitive function returned to normal following treatment. Despite significant evidence of recovery following treatment, not all symptoms may improve or completely normalize (Beebe & Gozal, 2002). Permanent impairment of executive function is possible due to sleep disturbance during critical developmental years (Gottlieb, 2005). While the adult literature has begun to assess neuropsychological test findings, this study will be one of the first to evaluate patients diagnosed with

sleep-disordered breathing in a systematic way to better understand the neurofunctional and neuroanatomical effects on the prefrontal cortex.

Method

Participants

Twenty-seven children, referred to a sleep lab by a pulmonologist for suspected SDB, were tested with PSG and a neuropsychological battery. The children selected as participants for this study ranged from ages 8 to 18. The participants were matched for age, gender, and socioeconomic status (SES) with 21 healthy controls. Children were included for this study if at least one parent and the child were fluent in English and both child and parent were literate. The child must not have been diagnosed with a cognitive impairment such as IQ less than 70, dyslexia, or any form of brain injury (congenital or acquired). Children with significant physical impairments, which interfere with task performance were also excluded (i.e. Cerebral Palsy, tetraplegia, etc.). Study participants were referred from the pulmonology clinic at Children's Healthcare of Atlanta involved in the Sleep Study Lab. If the child met all inclusionary criteria, they advanced to the consent process. Children were admitted as controls if their Pediatric Sleep Questionnaire results were normal and they had not been diagnosed with a developmental disability (IQ < 70), brain injury, or any other cognitive dysfunction. Children diagnosed with or showing symptoms of AD/HD were also included in this study due to the previously described research findings that suggest that children with OSA are at a higher risk for being diagnosed with AD/HD. All controls were recruited from a convenience population including siblings of study participants and children of hospital employees.

Each potential participant was evaluated based on the exclusionary and inclusionary criteria. If the patient scheduled for a sleep study met these criteria, the family was contacted and informed about the study. An initial screening was conducted to determine whether the family was interested in participating along with a description of the research process, including the neuropsychological tests needed. A financial reimbursement of $20 for time and effort was volunteered at that time. Once the patient and parent arrived for testing, an informed-consent form was explained and signed. Although none of the children were withdrawn from the study, the parents had the option to withdraw and continue with the PSG as originally planned without any further testing.

Instruments

The assessment battery consisted of objective tests which measured intelligence, academic achievement, and executive functioning. The total time needed for completion was approximately 1.5-2 hours. Additionally, parent report measures were used to assess sleepiness and sleep hygiene, behaviors and executive functioning in the home and school environments. Parent report measures were completed while the child was undergoing testing. Table 1 presents the instruments used and the domains measured.

Assessment of intelligence. A measure of intelligence was obtained using the two-subtest version of the Wechsler Abbreviated Scale of Intelligence (WASI), which was devised to quickly and accurately estimate one's intellectual functioning (Wechsler, 1999). The two-subtest WASI provides a Full Scale IQ score by measuring an individual's abilities in verbal and nonverbal domains, using the

Vocabulary and Matrix Reasoning subtests, respectively. The Vocabulary subtest is a 42-item task that requires the examinee to name pictures and orally define pictorially and orally represented words. It provides a measure of one's expressive vocabulary, verbal knowledge, and fund of information. The Matrix Reasoning subtest assesses an individual's ability to complete a series of 35 incomplete grid patterns by choosing the correct response from five possible choices. This subtest is a measure of one's ability in nonverbal fluid reasoning. The WASI can be used with individuals between the ages of 6 and 89, and administration of the two-subtest version takes about 15 minutes to complete. The utility of the WASI has been demonstrated in both reliability and validity studies. With regard to reliability, a coefficient of 0.96 has been established for the full scale IQ (FSIQ) score. Further, both content and concurrent validity have been demonstrated. The WASI FSIQ score has also been shown to correlate highly (greater than 0.90) with the FSIQ scales of the Wechsler Intelligence Scale for Children-III and IV (Wechsler, 1999).

Academic achievement. To evaluate academic skills, the Woodcock-Johnson Tests of Achievement Battery (WJ-III) is a solid and well-validated choice. The full battery includes 22 tests in the areas of reading, mathematics, written language, oral language, and academic knowledge. To establish a baseline academic composite, the Academic Skills index was chosen, which includes the Letter-Word Identification, Calculation, and Spelling subtests. Letter-Word Identification requires the examinee to read a list of words and pronounce them correctly. The participants are not required to know the definition of the words. The Calculation subtest incorporates a variety of math problems for the participant to answer using paper and pencil without time

Table 1

Testing Protocol

Measure	Domain
Wechsler Abbreviated Scale of Intelligence	Intellectual Capability
Woodcock Johnson Tests of Achievement	Academic Skill
Measures of Executive Functioning	
DKEFS Verbal Fluency	Verbal Cognitive Flexibility
DKEFS Color-Word Interference	Inhibition/Impulsivity Cognitive Flexibility
DKEFS Trail Making Test	Visual Cognitive Flexibility
WISC-IV-IV Digit Span	Working Memory
Drexel Tower of London-II	Planning, Inhibition, Initiation, Processing Speed
Conners' Continuous Performance Test	Attention/Impulsivity
Parent Self-Report	
BASC-2	Social, Mood, Behavior
BRIEF	Executive Functioning
Hollingshead	Socioeconomic Status
SDIS-C and SDIS-A	Sleep/Daytime sleepiness

restriction. Finally, the Spelling subtest is similar to a standard spelling test in which the participants write out words that are read aloud in a sentence. The WJ-III can be given to children and adults starting at age five. Due to the non-timed nature of these subtests, administration can take from 15 to 30 minutes to complete. The median reliability coefficient ranged from 0.81 to 0.94. Reliability for all clusters was 0.90 or higher. Test validity has been supported by considerable evidence including a confirmatory factor analysis. Additionally, the internal correlations of the entire battery are consistent with areas of achievement and ability/achievement clusters (Woodcock, McGrew, & Mather, 2001).

Assessment of executive function. This study utilized three subtests from the Delis-Kaplan Executive Function System (D-KEFS) Battery including the Verbal Fluency test, the Color-Word Interference test, and the Trail-Making test. All three tests are based on historically sound tests used in the last four decades. In general, the D-KEFS is a set of standardized tests that attempt to measure higher-level cognitive functions specific to the frontal lobes. It was normed on American children and adults from ages 8 to 89 years of age (Delis, Kaplan, & Kramer, 2001). The subtests were chosen based on their predictive abilities specific to the functional areas assessed in this study, namely the cortical and subcortical frontal lobe pathways (Lezak, 2004; Baron, 2003).

The D-KEFS Verbal Fluency test examines a participant's ability to generate words fluently based on phonemics and concepts (letters and categories) as well as assessing the capacity to switch from one construct to the next (switching categories). This test is considered sensitive in assessing cognitive flexibility. The participant is

asked to name as many words as possible within one minute that begins with a given letter in three trials. Next, he or she is asked to name words within a given category (i.e. animals) within one minute. Finally, the examinee is asked to switch between categories, naming an item from one category then the other category, until the end of one minute. The full subtest takes no more than 10 minutes including instructions and testing.

The D-KEFS Color-Word Interference test measures the effects of verbal interference. In particular, one's ability to inhibit a verbal response for a conflicting response is assessed. Thus, inhibition and impulsivity are the main variables considered. The test consists of four conditions, with the first section assessing ability to name color patches without written words. The second condition exposes the examinee to reading colors aloud that are presented in consistent black ink. A third condition challenges the participant to state aloud the actual ink color of a printed word and suppress the written word itself, which spells a contradictory color. Finally, in a fourth condition, the participant must switch back and forth between reading words written in conflicting colors and naming the ink colors of words that spell other colors. This final condition assesses for impulsivity and cognitive flexibility. The total test time is no more than 10 minutes.

The D-KEFS Trail-Making test assesses visual cognitive flexibility. It consists of five conditions including four tasks, which derive normative data to control for skills needed to perform the task that assess the actual executive abilities. The participant connects letters, numbers, and dots to determine visual scanning, number sequencing, letter sequencing, and motor speed abilities. The executive function test

integrates these skills and requires the participant to switch accurately and quickly between numbers and letters while connecting them with a “trail.” All five conditions of the Trail-Making test can be completed in less than 10 minutes.

Working memory involves the ability to temporarily hold information in one’s memory while manipulating that information or using the information to plan a strategy. The Wechsler Intelligence Scale for Children, fourth edition (WISC-IV), includes a subtest called Digit Span, which claims to measure this ability. In the first half of Digit Span, the participant is read a string of numbers and must recite these back to the examiner (Digit Span Forward). The second condition requires the participant to recite the numbers backwards which involves holding these digits in short-term memory and manipulating them, thus relying on working memory (Digit Span-backwards). This test can be completed in 10 to 15 minutes. The overall utility of the WISC-IV has been examined in multiple validity and reliability studies. Reliability coefficients between 0.79 and 0.90 have been identified across subtests. Correlation between the WISC-IV and other intelligence tests was performed to determine convergent validity. In particular, the Digit Span subtest correlated moderately with other measures of working memory (0.79) (Wechsler et al., 2004).

The Tower of London-II (TOL-II) is a neuropsychological test that was developed to assess higher-order problem solving and executive planning abilities. It can be used for children as well as adults and consists of three pegs and three colored beads that must be moved using a set of rules to create a prescribed pattern. The executive function measures generated by the TOL-II include executive planning, inhibition, initiation, and processing speed. The participant must move one bead at a

time, stacking no more than two beads on a peg, to reproduce the given pattern in the fewest moves possible. Internal consistency was estimated at 0.79 and test-retest reliability was acceptable at $r = 0.70$ (Schnirman, Welsh, & Retzlaff, 1998). This test can be used for individuals ages 7 to 77 years. Administration time is between 10 and 15 minutes (Shallice, 1982).

The Parent Form of the Behavioral Rating Inventory of Executive Functioning (BRIEF) is an 86-item questionnaire for parents of school-age children used to assess executive function behaviors in home and social environments (Gioia, Isquith, Guy, & Kenworthy, 2000a). It was designed to evaluate children between the ages of 5 to 18 years, and it takes approximately10-15 minutes to complete. The reliability and validity of the BRIEF have been empirically-supported. Test-retest reliability estimates of clinical scales range from 0.76 to 0.85 (Gioia, Isquith, Guy, and Kenworthy, 2000b). Further, content, convergent, and divergent validity have also been established (Gioia et al., 2000a). Parents record their children's functioning at home by indicating whether behaviors have never, sometimes, or often been problematic over the last six months. Their endorsements provide measures of eight different aspects of executive functioning on empirically-derived clinical scales, including the Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor scales. These clinical scales are combined to form two broader indices, the Behavioral Regulation index and the Metacognition index. An overall score, the Global Executive Composite (GEC) is also derived from the clinical scales, and it provides a global measure of a child's executive function behaviors.

Attention was measured with the Conners' Continuous Performance Test, second edition (CPT-II), a computerized, 14-minute, fixed interval test of visual continuous performance (Conners, 2000). The CPT-II is thought to be useful in evaluating elements of sustained attention, stimulus selection, and inhibition of irrelevant responses, and it can be used with individuals who are six years or older. Respondents are required to click the mouse when any letter except the target letter, "X," appears. The test consists of six trials, with three sub-trials, each containing 20 letter presentations. Interpretation involves measuring the number of omission and commission errors. Omission errors are failures to respond to the target letter and are suggestive of inattention. Commission errors, responses to non-target letters, are indicative of impulsivity. The test-retest reliability coefficients across scales range from 0.55 to 0.84 (Conners, 2000). The CPT-II has been found to accurately predict deficits in attention and executive function (Conners, 2000; Spreen & Strauss, 1998). Additionally, neuroimaging studies have shown the activation of the prefrontal cortex while performing a CPT task (Casey et al., 1997).

Parent self-report. The Parent Rating Scale (PRS) of the Behavior Assessment System for Children, Second Edition (BASC-2) is used to evaluate children and young adults between the ages of 2 and 25 years, and it takes approximately 10 to 20 minutes to complete. Parents rate descriptors of their children's behaviors on a four-point scale of frequency, ranging from Never (0) to Almost always (3). Parents' endorsements provide information about their children's behavior on three broad domains, Externalizing Problems, Internalizing Problems, and Adaptive Skills. Each of the broad domains is made up of primary scales that

assess specific areas of functioning, such as attention problems and functional communication. The scores obtained on the broad domains are compiled to create a broad composite, the Behavioral Symptom Index, which provides an overall measure of a child's problem behaviors. The internal consistency of the composites and scales on the PRS for ages 8-18 range from 0.73 to 0.95 while test-retest reliability ranged from 0.65 to 0.92. Factor analysis was performed on all test items and the BASC-2 was correlated with other well-established instruments, including the BRIEF and the Conners' Parent Rating Scale-Revised (Reynolds & Kamphaus, 2004). The scales that were of most interest in this study were the Behavioral Symptoms Index, as an indicator of behavioral regulation and impulsivity, the Hyperactivity scale, and the Attention Problems scale.

SES was measured by the Hollingshead Four Factor Index of Social Status. This one-page questionnaire asks the participant or participants' family member to provide the highest level of education completed and class of occupation (i.e. laborer, technical, managerial, etc.). The information is required for both parents and participant (Hollingshead, 1975). In this case, as the participants were children, the parent filled out the questionnaire based on the education and occupation of the parents and grandparents. Although the Hollingshead is frequently criticized for being oversimplified and out-dated, it is the most widely accepted measure of SES (Bornstein & Bradley, 2003).

The Sleep Disorder Inventory for Students (SDIS) was administered to parents of participants (both control and study group). This is the first known study to utilize the SDIS to evaluate the neurocognitive outcomes of SDB. The SDIS has two forms,

one for children ages 2-10, and one for children ages 11-18. This 41 or 46-question scale (depending on the age of the participant) queries parents regarding their children's sleep patterns, sleep hygiene, daytime somnolence, level of arousal, and other aspects of sleep disturbances. An overall index of sleep disturbance is determined with this instrument in addition to four specific indices of common sleep disorders. These include OSA, Periodic Limb Movement Disorder, Delayed Sleep Phase Syndrome, and Excessive Daytime Sleepiness. The overall construct validity of the instrument was evaluated via exploratory and confirmatory factor analysis. Predictive validity of the SDIS was measured by comparing SDIS results with polysomnography results. The outcomes of these studies provide strong support for the usefulness and validity of the SDIS (Luginbuehl, 2004).

Physiological measure of sleep-disordered breathing. A PSG was performed on each child in the study group and scored by registered PSG technicians. The montage included central and occipital electroencephalography, electro-oculography, submental and anterior tibial electromyography, nasal-oral thermistry, end tidal capnography, snoring microphone, electrocardiography, thoracic and abdominal excursions by piezoelectric belts, finger pulse oximetry, and continuous video recording. The signals were digitally recorded on a Nellcor Puritan Bennett Sandman system. Sleep stages were scored according to the guidelines developed by Rechtshaffen and Kales (1998). Obstructive apnea was defined as a complete cessation of airflow for at least two respiratory cycles, accompanied by continued respiratory effort. Obstructive hypopnea was determined by a 50% reduction in airflow as compared to the baseline immediately preceding the event as measured by

amplitude of thermistor or capnograph waveform, but only if this was also accompanied by desaturation of at least 4%, paradoxical respiratory effort, or an arousal. The results of the PSG were examined in conjunction with the results of the SDIS to determine the presence of SDB in the study group.

Procedure

This study was approved by the Institutional Review Boards of Georgia State University, Emory University, and Children's Healthcare of Atlanta. All procedures, risks and benefits, confidentiality issues, and the voluntary nature of participation were explained as part of the informed consent process. Signed consent was obtained from all parents of participants. Additionally, informed consent was explained in simplified terms to children between 8-10 years of age and verbal assent was obtained. Children between the ages of 11 and 15 were provided the same information and signed a written assent. Adolescents, aged 16-17, were provided the same informed consent as their parents and co-signed the consent with their parents. After participants were informed about the study and had given consent, neuropsychological testing was conducted on the evening of their scheduled PSG. Participants' parents were taken to a waiting area where they were asked to complete the parent-report assessments. Each participant was taken to a quiet testing area to complete the described battery. The participants then underwent a PSG to determine the presence and degree of SDB. The control participants underwent the neuropsychological testing but did not complete a PSG due to cost and convenience. Instead, the SDIS was used to rule out any overt SDB. If any control participant had

screened as “at-risk” on the SDIS, they would have been excluded from the study. No control participants demonstrated any sleeping problems per parental report.

The variables involved in this study include demographic information such as general intelligence, SES, and demographics of sleep. SES and IQ were used as covariates in the analysis to ensure the fewest confounding variables as possible. Sleep demographics were used to assure accurate control and study group assignment. The measures of executive functioning previously described result in the following dimensions of executive function, which are also represented in the hypotheses:

- Working memory
- Cognitive flexibility
- Inhibition
- Impulsivity and behavioral regulation
- Processing speed
- Executive planning and organization
- Attention

Due to the sizable number of variables generated by the large testing battery, some variables were eliminated and others combined into dimensions that would most accurately reflect the participants’ performance and provide the most information with a limited number of participants. These variables coincide with the theoretical foundation of the study based on Beebe & Gozal (2002). This theoretical model approached the involvement of sleep disruption and hypoxia on prefrontal dysfunction leading to the dysfunction of the executive system. The executive functions that are likely to be influenced by this condition include behavioral

inhibition, set shifting, self-regulation of affect and arousal, working memory, analysis/synthesis, and contextual memory. The instruments and associated variables were chosen to address certain aspects of these different areas of executive functioning. A confirmatory approach to the clinical questions was proposed. The following hypotheses are put forth for analysis in this study:

(1) There will be no significant difference in intellectual functioning, as measured by WASI IQ, between the study group and the control group.

(2) The neuropsychological testing results for the participants with SDB will attest to significantly poorer working memory than those manifested by the control group.

(3) The neuropsychological testing results for the participants with SDB will attest to significantly less cognitive flexibility than those manifested by the control group.

(4) The neuropsychological testing results for the participants with SDB will attest to challenges with inhibition when compared to those manifested by the control group.

(5) The neuropsychological testing results for the participants with SDB will attest to significantly more impulsivity than those manifested by the control group.

(6) The neuropsychological testing results for the participants with SDB will attest to significantly reduced processing speed than those manifested by the control group.

(7) The neuropsychological testing results for the participants with SDB will attest to challenges with planning and organization as compared to those manifested by the control group.

(8) The neuropsychological testing results for the participants with SDB will attest to significantly poorer sustained attention than those manifested by the control group.

Data Analysis

Statistical analysis was performed using the two statistical software packages, SAS and NCSS. SAS 8e, release 8.02 TS Level 02M0, was used for regression analyses and new variable definitions. NCSS 2001 was used for descriptive statistics and MANOVA. The MANOVA was used to examine the group differences with regard to IQ and SES and confirmed the equal distribution of intellectual abilities across groups. Datastep programming in SAS was used to define an overall AD/HD index based on the CPT-II results. Regression analysis was used to evaluate all variables. Due to the existence of covariates, PROC GLM in SAS was utilized with covariates specified.

A large sample size allows one to assume that the population tends to approximate the normal distribution. This generally occurs for a sample greater than 30. Because the sample size was 46, and each group still is over 20, it was deemed sufficiently large to support this assumption of normality. Without a large enough sample, only nonparametric statistical analysis would have been mandated. With a large enough sample, one can utilize either parametric or nonparametric approaches.

A nonparametric test, Kolmogoroff-Smirnoff for normality was performed on all variables. Homogeneity of variance was confirmed via nonparametric tests.

Regression analysis is a statistical method employed for examination of the relationship between predictor variables and a dependent variable. This results in an equation that can then be used to make predictions of the dependent variable by substituting values for the predictor variables. This particular parametric approach was selected because of the need to make such projections.

IQ and SES were considered potentially confounding and were therefore used as covariates. Regression analysis finds the least-squares best fit model relating a dependent variable to one or more independent variables. By forcing the acceptance of a covariate into a model, the behavior attributable to that covariate is essentially removed from the model, allowing pure assessment of the independent variables. This process applies for one or more covariates simultaneously. Level of significance was set at 0.05 and trends ($0.05 < p < 0.10$) were acknowledged. It is not common in the social sciences to accept any p-values over .05; however, due to the need for covariates and their impact on the results, the identification of trends may provide useful information to guide future studies.

Results

Of the 27 children who presented with suspicion of SDB, 20 were diagnosed with mild to moderate SDB by a pulmonologist based on the results of the PSG, medical evaluations, and significantly elevated scores on the SDIS. Another six participants were found to have significantly elevated SDIS scores despite having inconclusive PSG testing. One participant had a normal PSG and a normal SDIS and

was, therefore, eliminated from the study. The remaining 26 participants were compared to the 21 control participants, none of whom demonstrated elevated SDIS scores. In the control group, 52% (11) of the participants were female and 48% (10) were male. The study group was made up of 61% (16) males, and 39% (10) females. Racial distribution was also evenly distributed with 52% (11) of the participants Caucasian and 47% (10) African-American. No other races were represented in the control group. Caucasian participants were more prevalent in the study group, making up 65% (17). There were six African-American participants (23%) and three participants (11%) of "Other" racial identities (Latin-American and Asian-American). The average age of the control group was 12.9 and the average age of the study group was 10.8. Age differences were accounted for within the psychological tests, as all tests were normed for age and provide scores adjusted to reflect the normal distribution for a given age group. Participant demographics are summarized in Table 2. Psychological testing is commonly reported in several different forms, standard scores (WASI, TOL-II, and WJ-R), scaled scores (WISC-IV and DKEFS), and T-scores (BASC, BRIEF, and CPT-II).

SES

Socio-economic status was significantly different between the groups ($F = 10.39$, $p < .01$). The average SES score for the control group was 58.8 while the average SES score for the study group was 44.18. This was likely due to the recruitment pool available for establishing the control group. Despite the statistically significant difference in SES, when the mean SES for each group was assigned a *z*-score, both means fell within the first standard deviation, or average range ($z = -0.35$,

study group; $z = 0.53$, control group). However, due to the potentially confounding nature of this variable, SES, in addition to IQ, was used as a covariate in the overall analysis between the groups. The results of the neuropsychological tests, including control and study group means, the percentage of explained variance (R^2), and the overall F value, are presented in Tables 3, 4, and 5.

Table 2

Participant Demographics

Variable		Minimum	Maximum	Mean	SD
Age					
	Control	8	18	12.95	2.97
	Study	8	18	10.80	2.53
SES					
	Control	41.5	66	53.8	9.0
	Study	22	63.5	44.1	11.1
IQ					
	Control	71	131	108.2	13.9
	Study	76	137	107.3	15.3
SDIS Overall index					
	Control	26	54	41.4	6.5
	Study	46	77	64.7	9.2

Table 3

Neuropsychological Test Results with Covariates: IQ and SES

Models	Control Group Mean ± SD	Study Group Mean ± SD	R^2	β	F
WISC-IV DS	10.4 ± 2.4	9.2 ± 2.5	.25	.50	0.36
VF Switching	12.7 ± 2.5	10 ± 2.8	.28	.53	4.47*
VF Letter	10.7 ± 2.3	9.8 ± 2.3	.09	.30	1.64
CW Inhibition	11.3 ± 1.7	9.5 ± 3.5	.46	.67	0.73
CW Switching	11.7 ± 1.6	8 ± 3.7	.48	.69	12.12*
Trails Switching	10.5 ± 3.2	7.8 ± 4.6	.21	.45	3.65**
TOL-II Move	90.1 ± 18.6	94 ± 15.5	.14	.37	0.89
TOL-II Exec Time	97.6 ± 9.4	90.7 ± 17.1	.23	.47	2.22
TOL-II Rules	96.9 ± 16	92.6 ± 17.1	.16	.40	0.41
BASC Behavior Index	46.1 ± 5.2	55.2 ± 12.9	.25	.50	5.0*
BASC Attention	50.8 ± 8	54.6 ± 11.1	.17	.41	0.15
BASC Hyperactivity	47.5 ± 7.1	53.5 ± 12.4	.13	.36	0.21
WJ-R Academic skills	108.5 ± 9.5	98.2 ± 12.8	.65	.80	6.77*

* $p \leq 0.05$ level ** $0.05 < p < 0.10$ (trend)

Note: The models in the table show the variables adjusted for SES and IQ

Table 4

BRIEF Results with Covariates: IQ and SES

Models	Control Group Mean ± SD	Study Group Mean ± SD	R^2	β	F
Inhibition	49.4 ± 8.2	53.6 ± 10.9	.04	.20	0.88
Shift	46 ± 7.8	55.3 ± 13.6	.28	.53	4.35*
Emotional Control	45.9 ± 10.5	55.5 ± 15.6	.25	.50	2.47
Initiation	46.5 ± 7	57 ± 10.2	.30	.54	11.69*
Working Memory	51.2 ± 9.2	60.3 ± 10.9	.20	.44	5.43*
Planning/Organization	48.3 ± 9.6	57.4 ± 12.7	.15	.66	5.96*
Org. of Materials	51.2 ± 11.4	52.8 ± 10.4	.04	.20	.81
Monitor	47.5 ± 7.8	54.5 ± 12.9	.17	.41	5.38*
Behavioral Regulation	46.9 ± 8.5	55.3 ± 14.1	.24	.49	2.66**
Metacognition Index	48.8 ± 8.2	57.8 ± 12.3	.17	.41	6.74*
GEC	48.1 ± 7.4	57.5 ± 13.2	.21	.45	5.91*

* $p \leq 0.05$ level ** $0.05 < p < 0.10$ (trend)

Note: The models in the table show the variables adjusted for SES and IQ

Table 5

CPT-II Results with covariates: IQ and SES

Variable	Control Group Mean ± SD	Study Group Mean ± SD	R^2	β	F
CPT-II omission	47.2 ± 5.9	55 ± 13.2	.19	.43	2.91**
CPT-II commission	50.9 ± 9.2	55.4 ± 9.6	.25	.50	7.79*
CPT-II hit rate	44.6 ± 10.7	49.7 ± 11.2	.23	.48	.27
CPT-II variability	48.2 ± 8.7	53.5 ± 11.3	.13	.36	2.49
CPT-II overall	-	-	.41	.64	22.45*

* $p \leq 0.05$ level ** $0.05 < p < 0.10$ (trend)

Note: The models in the table show the variables adjusted for SES and IQ

Hypothesis 1: Intellectual Ability

Intellectual abilities were evenly distributed in both groups with the average IQ score for the control group of 108.2 and the study group of 107.3. A Kolmogoroff-Smirnoff test for normality was performed and found no statistically significant difference between groups ($p > .05$). These findings are consistent with the first hypothesis and indicate similar intellectual abilities in the control and study groups. Therefore, intellectual ability is unlikely to be the cause of any variability in executive functioning between the two groups.

Hypothesis 2: Working Memory

This aspect of executive function was evaluated by examining the results of the WISC-IV-IV Digit Span subtest and the working memory scale of the BRIEF. Analysis revealed no statistically significant group differences for Digit Span performance, once SES was considered. Based on parent report, however, there was a significant difference between groups in working memory observed in the home ($F_{(3, 43)} = 5.43$, $p < .05$).

Hypothesis 3: Cognitive Flexibility

All measures of cognitive flexibility in the study group were found to be significantly different or trending towards significance when compared to the control group. The results of the Verbal Fluency subtest, category switching, were significantly different between groups ($F_{(3, 43)} = 4.47$, $p < .05$). Similarly, the results of the Color Word subtest, switching, was also significant. ($F_{(3, 43)} = 12.12$, $p <.05$). The Trails subtest, switching, just missed the cutoff for significance at 0.06. The group differences, however, demonstrate a trend which might be confirmed if SES was more closely matched between the control and study group (Farah et al., 2006). The scale demonstrating parental observation of cognitive flexibility, BRIEF shift, also revealed significant group differences ($F_{(3, 43)} = 4.35$, $p <.05$).

Hypothesis 4: Inhibition

Inhibition was examined with the Color Word subtest, inhibition scale, the TOL-II, rules scale, and the BRIEF Inhibition and Emotional Modulation scales. The scales evaluating inhibition did not reveal any significant group differences.

Hypothesis 5: Impulsivity

Impulsivity was addressed via components of four different tools. The CPT-II commissions scale demonstrated significant group differences ($F_{(3, 43)} = 7.79$, $p < .01$). The Color Word switching scale also showed significant group differences ($F_{(3, 43)} = 12.12$, $p < .01$). In addition, significant group differences and trends were identified on the parent report scales, BASC Behavioral Symptoms index ($F_{(3, 43)} = 5$, $p < .05$) and BRIEF Behavioral Regulation index ($F_{(3, 43)} = 2.66$, $p = 0.1$).

Hypothesis 6: Processing Speed

The scales evaluating processing speed, TOL-II execution time, CPT-II variability, and CPT-II hit rate, did not reveal any significant group differences.

Hypothesis 7: Planning/Organization

The planning scores of the TOL-II did not show significant group differences. In contrast, the parent report scales of the BRIEF involving planning were significant. (BRIEF planning $F_{(3, 43)} = 5.96$, $p < .05$, BRIEF initiation $F_{(3, 43)} = 11.69$, $p < .01$). The BRIEF organization scale did not demonstrate any significant group differences.

Hypothesis 8: Sustained Attention

Overall CPT-II scores, in which at least one scale was elevated into the impaired range, were significantly different between groups ($F_{(3, 43)} = 22.45$, $p < .01$). The parent report scale on the BASC addressing attention, however, was not found to be significant.

Discussion

The major findings in this study were the significantly less robust executive function in children with SDB in the domains of cognitive flexibility and impulsivity. Additionally, poorer executive planning and overall inattentiveness were also associated with SDB. Moreover, other areas of executive function, including working memory, behavioral and emotional inhibition, and processing speed were not associated with SDB. It was also notable that academic functioning was significantly lower in children with SDB, although the differences can be shared equally with SES and IQ. Previous studies also report academic and learning difficulties in the presence of SDB (Gozal, 1998; Gozal & Pope, 2001). Understanding the exact origin of the differences is difficult due to the impact of attention deficits, socioeconomic variances, and intellectual potential.

Attention and SDB

In this study, children with diagnosed and suspected attention deficits were included, despite the potential interference with cognitive performance. This was due to the overlap of symptoms that are shared between children with AD/HD and those with SDB. Some scientists and practitioners suspect that children with SDB are often diagnosed prematurely with AD/HD when the problem actually stems from the SDB (Gottlieb et al., 2003). The participants in the study, who were previously diagnosed with AD/HD and prescribed medications, were asked to take their medications as usual prior to the testing. Thus, attention deficits were less detectable during testing. Despite this, a significant difference was found between the control and study groups with regard to overall attention.

Daytime Sleepiness and SDB

SDB can present as a mild condition such as snoring or a more severe condition such as OSA. Previous studies have found that even mild forms of SDB can result in cognitive impairments (Gozal & Pope, 2001; Gozal, 1998). Due to the limited number of participants and the homogeneity of PSG results, the study group was not divided into mild and severe forms of SDB. All of the study group participants were found to have mild to moderate SDB, and were then combined into one group. The majority of symptoms that were manifested included snoring, frequent arousals at night, difficulty waking in the morning, and daytime sleepiness. In the scientific realm, one of the ongoing discussions about SDB and cognition involves the contribution of sleepiness versus organic damage on executive performance (Gale & Hopkins, 2004). Although this study was not specifically designed to quantify these roles, some information can be ascertained from the SDIS. This study is one of the first to utilize the SDIS to help identify problematic sleeping as it relates to cognitive dysfunction. The SDIS measured the symptoms and degree of sleep impairment per parental report. A unique feature of this instrument is the scales measuring different types of sleep disturbance. The OSA scale assigned a value associated with the presence of OSA symptoms. The EDS (excessive daytime sleepiness) scale measured the presence of symptoms associated with sleepiness. In 8 of the 26 study cases, the OSA scale was significantly elevated while the EDS scale remained in the normal range. Of the other 18 cases, the OSA and EDS scales were in the same range (i.e. both elevated or both normal). In none of the cases was the EDS scale elevated while the OSA scale remained normal. Thus, the children in this study

with symptoms of OSA frequently lack symptoms of daytime sleepiness but children with excessive daytime sleepiness always display symptoms of OSA.

Executive Function and SDB

This study is distinguishable from previous research by the focus on executive function and the various dimensions of executive function. It was hypothesized that several aspects of executive function would significantly differ between children with SDB and children in the control group. These domains included working memory, cognitive flexibility, inhibition, impulsivity, processing speed, executive planning, organization, and attention. Each of these domains was represented by various tests, subtests, and parental report questionnaires. Those data points or scales were relegated to the different executive function domains based on the manuals for each of the tests and what the scales claim to measure. Some of the scales were relevant to more than one domain and some of the scales that resulted from the testing were not deemed relevant to this study and were therefore not included in the analysis.

Per parental report, working memory was worse in the study group, although their scores still fell within the average range of ability. The results of the WISC-IV-IV Digit Span test demonstrated no difference between the groups. Working memory was, therefore, not found to be an area of concern for the children with SDB.

Cognitive flexibility, or the ability to shift between concepts and adapt strategies to face an unknown condition, was a domain that the children with SDB found more difficult. In three of the four subtests addressing cognitive flexibility (Verbal Fluency category switching, Color Word switching, and Trails switching), the mean scores fell in the low average range for the study group while the control

group achieved scores in the average to high average range. The fourth subtest was parent reported, BRIEF shift, with study group results falling in the average range. These findings are not only clinically significant; they are also practically significant, as the difficulties in this domain dip below average. The study group also showed more impulsivity than the control group. On the objective measures of impulsivity (CPT-II commissions and Color Word switching), the study group performed significantly worse than the control group, however only on Color Word switching did the performance drop to the low average range. Per parental report (BRIEF monitoring and BASC behavior), although performance in the study group was significantly worse than the control group, the scores still fell within the average range. In this domain, clinical significance was determined, but this may lack practical utility. It is important to consider, however, that the mean IQ of the study group was at the higher end of the average range so that higher intelligence may possibly compensate in the actual scores. It is possible that children in the mid to lower average range would dip into the impaired range if the pattern seen in this study were to persist. Considering the statistical trend, further investigation in a larger group of children with more severe forms of SDB, in addition to mild to moderate SDB, might yield results that demonstrate true dysfunction rather than mere statistically significant differences.

All tests in the inhibition and processing speed domains failed to display a significant difference between groups once SES and IQ were used as covariates. In the executive planning domain, objective tests failed to identify group differences. However, per parent report, the study group displayed significantly more struggles

with problem solving and planning (BRIEF subtests). Finally, with regard to attention, overall CPT-II scores were significantly worse in the study group with 20 of the 26 children in the study group demonstrating clinically significant attention deficits. Only 6 of the 21 children in the control group exhibited an elevated scale on the CPT-II.

Prefrontal Cortex and SDB

Overall executive functioning is typically accredited to the frontal lobes of the human brain (Fuster, 1989). The frontal lobes are located in the anterior half of the cerebral hemisphere and are divided into three primary regions: the motor cortex, the premotor cortex, and the prefrontal cortex (Zilles, 1990). The prefrontal cortex is the portion of the frontal lobe that is considered primarily responsible for executive functioning. Like the frontal lobe itself, the prefrontal cortex is also divided into distinct regions. These three main regions include the dorsolateral prefrontal cortex, the orbitofrontal cortex, and the anterior cingulate cortex, and each area is believed to be responsible for different aspects of executive function (Powell & Voeller, 2004). There are several main functions of the dorsolateral prefrontal cortex including regulation and integration of cognitive activities, such as maintaining attention and shifting cognitive set smoothly when necessary (Powell & Voeller, 2004). Working memory, or the ability to hold information available in memory and manipulate that information to achieve a goal, is another primary function of the dorsolateral region. In combination, these activities produce higher-level skills such as organization, problem solving, and learning. Thus, damage to this region may cause the individual to have poor information processing, attentional deficits, and impaired working

memory. He or she may also have difficulty setting and maintaining a goal activity (Lezak et al., 2004). The second region, the orbitofrontal cortex, also has several main functions including the modulation of interactive behavior. Social behaviors such as empathy, morality, self-restraint, and behavior monitoring are regulated by this area of the prefrontal cortex (Powell & Voeller, 2004). The third division of the prefrontal cortex is the anterior cingulate region with the central roles of attention, arousal, and emotion (Powell & Voeller, 2004). Other responsibilities include divided attention, error detection, initiation of appropriate behaviors, and motivation. Based on the results of this study, the dorsolateral prefrontal cortex seems to be most affected by SDB. Maintaining attention, cognitive flexibility, and task impulsivity were the predominant areas of concern for the study group and are also aspects of cognition associated with the dorsolateral prefrontal cortex. As research increases in the area of executive function and SDB, increased emphasis should be placed on discerning the specific areas of the prefrontal cortex affected by SDB via neuropsychological testing or neuroimaging.

Study Findings and a Theoretical Model

The findings of this study provide initial support to Beebe and Gozal's (2002) model of SDB and executive function which proposes that both sleep disruption and cellular imbalance (hypercarbia and hypoxia) contribute to prefrontal cortical dysfunction via disruption of the restorative sleep process and the disruption of chemical homeostasis. Based on this model, dysfunctions that are commonly seen include disinhibition, set shifting, self-regulation, working memory, analysis, and contextual memory, all of which contribute to adverse daytime effects. Specifically,

set shifting problems, analytical challenges, and poor self-regulation were identified in this study among children with SDB. Furthermore, based on parent report, excessive sleepiness and symptoms of OSA were more frequently conveyed in the study group. To expand and provide evidence for the model, future studies should include more tests of contextual and working memory in addition to the executive function battery described in this report. Perhaps cortical thickness and studies of morphometry could address any structural changes in prefrontal cortices in future research.

Study Limitations and Future Research

Several limitations of the current study must be considered when interpreting the results. First, the heterogeneity of frontal lobe functional areas makes it difficult to correlate specific deficits with discrete frontal lobe areas. The neuropsychological battery was chosen specifically to measure different aspects of the three frontal lobe areas. Due to the apparent sensitivity of the dorsolateral prefrontal cortex to SDB, future research might choose to concentrate the test battery to only those tests measuring skills associated with that region. Perhaps future cortical thickness and morphometry studies could address any structural changes in prefrontal cortices.

Another limitation was the sample size and demographics. Due to the sampling methods and strict inclusion criteria, only 48 total participants were recruited for this study over a period of eight months. Thus, SES and racial distribution varied between the control and study groups. Due to the significant differences in SES, it was necessary to use SES as a covariate. As a result, the effects seen in the statistical analysis were somewhat diluted. Future studies would be

benefited by matching SES as closely as possible. Additionally, differences in race and its impact on executive function with SDB were not addressed in this study.

A third limitation of the study was the lack of variability in severity of SDB. Due to sample size, mild and moderate cases of SDB were examined as one group and none of the participants were found to have severe SDB. Several studies have observed the cognitive function in children with mild SDB (i.e. snoring) and found significant impairments in executive function (Gozal & Pope, 2001; Gozal, 1998). An area that needs further exploration is the impact of SDB severity on cognitive function. Such research would provide practitioners with important information about the necessity and promptness of interventions. Additionally, it would be informative and thorough if the control participants could undergo a PSG similar to the study group. This would assure that no child with SDB would enter the control group. In the current study, due to cost limitations and convenience for the control participants, baseline PSG's were not obtained. Instead, the parent report form, SDIS, was used to screen for sleep disorders.

Finally, clinicians would benefit from examining the executive function of children with SDB before and after a treatment intervention. Although it is important to understand the exact nature of the insults on cognitive function resulting from SDB, patient's families and medical practitioners are seeking practical information to guide decisions about types of intervention, promptness of intervention, and outcome expectations. Many unfortunate cases of attention impairments and executive dysfunction in otherwise healthy children might be averted if scientists continue to

investigate the impact of SDB as well as the reversibility of cognitive symptoms with appropriate treatment.

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