NEUROCOGNITION AND ACADEMIC ACHIEVEMENT IN SCHOOL-AGED CHILDREN WITH OBSTRUCTIVE SLEEP APNEA AND DEPRESSIVE SYMPTOMS

By

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ABSTRACT

The current study investigated the relationship between obstructive sleep apnea (OSA) and depressive symptoms on neuropsychological functioning and academic achievement in a sample of ethnically diverse school-aged children in the Southwest United States. A total of 38 participants aged 6 – 12 were studied as part of an ongoing randomized clinical trial (SleepCATS) investigating the neurocognitive impact of continuous positive airway pressure therapy (CPAP) on neurobehavioral outcomes. Children were identified as having primary snoring, mild OSA, or Moderate-Severe OSA based on in-lab nocturnal polysomnography and were assessed for depressive symptoms using the parent report of the Child Behavior Checklist (CBCL). Neuropsychological testing was conducted using the Cambridge Automated Neuropsychological Test Battery (CANTAB) to assess executive functioning, working memory, and motor control. The Grooved Pegboard Test (GPT) was used to assess fine motor speed and dexterity and academic achievement was assessed on the Woodcock-Johnson Test of Academic Achievement Third Edition (WJ-ACH III). The study identified 39% of the sample as having clinical depressive symptoms and mean depressive symptoms for the sample was nearly one standard deviation above the norms. Multivariate analysis of covariance models (MANCOVA) were used to determine differences in neuropsychological test performance by neurocognitive constructs. Results from the study found significant main effects for OSA severity on the CANTAB Spatial Span Test and a significant interaction of off clinical depressive symptoms and OSA severity on the Applied Problems test of the WJ ACH III. When groups were compared between children with primary snoring and OSA (Mild and Moderate-Severe combined) there were no longer significant effects for academic achievement or working memory, however, there was a significant main effect for motor control on the CANTAB with children with OSA.
exhibiting lower performance compared to those with primary snoring. The results from this study suggest children with moderate-severe OSA may exhibit increased difficulties in working memory and fine-motor control, and also have increased difficulties with academic math achievement when children with moderate-severe OSA also have depressive symptoms. These findings suggest children with higher severities of OSA may experience increased learning and academic challenges, which may be further exacerbated when accompanied by depression.
Chapter 1

Introduction

This first chapter will define and provide a general overview of obstructive sleep apnea (OSA), and potential theoretical factors associated with neurocognitive morbidity in children with OSA. Particular emphasis will be placed on the effects OSA and depression have on cognition and academic performance in children and adolescents. This chapter also provides a statement of the problem, the rationale and purpose, as well as the specific aims and hypotheses for the present study. Definitions of pertinent key terms as it applies to the literature will also be defined.

OSA

OSA is a pervasive sleep-related breathing disorder (SRBD) affecting up to 3% of school-aged children that is characterized by intermittent collapse of the upper respiratory airway that prevents ventilation and interrupts typical sleep patterns (Rosen et al, 2003; ATS, 1996). Repeated upper airway obstructions result in complete cessation of airflow (apneas) or partial reductions in airflow (hypopneas). As a direct result of these repeated obstructions in the respiratory airway, oxygen saturation of the blood is reduced resulting in hypoxemia and hypercarbia, with repeated arousals during sleep also being observed. The culmination of these events during sleep have repeatedly been found to be associated with a plethora of adverse neurobehavioral problems ranging from deficits in neurocognition and attention (Beebe, 2006), daytime somnolence (Ali, Pitson, & Stradling, 1993), overall reduced quality of life (Tran, Nguyen, Weedon, & Goldstein, 2005) as well as compromised academic performance in typical (Gozal, 1998; Gozal & Pope, 2001; Guilleminault, Winkle, Korobkin, & Simmons, 1982;
Perfect, Archbold, Goodwin, Levine-Donnerstein, & Quan, 2013; Weissbluth, Davis, Poncher, & Reiff, 1983) and overweight children (Beebe, Ris, Kramer, Long, & Amin, 2010).

In addition to the many areas of neurobehavioral functioning that are directly impacted by respiratory obstructions, OSA has also been associated with numerous psychomedical comorbidities and poorer physical health status. Specifically, if untreated, OSA has been associated with increased risk for diabetes (Botros et al., 2009), cardiovascular manifestations (Kwok, Ng, & Chan, 2008), increased blood pressure (Marcus, Green, & Carrol, 1998), higher body mass index (BMI) and obesity (Verhulst, van Gaal, de Backer, & Desager, 2008), asthma, failure to thrive (Freezer, Bucens, & Robertson, 1995; Lind & Lundell, 1982), stroke, and overall increased mortality rates (Yaggi et al., 2005) compared to those without OSA. Recent evidence from adult populations have also begun to reveal that OSA is comorbid with clinical affective symptoms of anxiety and depression (Vaudeputte & Weerd, 2003; Wheaton, Perry, Chapman, & Croft, 2012), which could further exacerbate the neurobehavioral morbidity caused from OSA symptomology.

Although OSA has been estimated to approach a 3% prevalence rate in school-aged children, higher rates have been reported for milder forms of SRBDs. Primary snoring (PS) is the mildest form of SRBD and has been estimated to occur in up to 12% of the youth population (Ferreira et al., 2000). Defined by the presence of auditory perception of snorting noises during sleep, PS has been observed to result in fewer neurobehavioral deficits than OSA, yet alterations in sleep architecture and cognition have been found (O’Brien et al., 2004). Upper airway resistance syndrome (UARS) is also on the SRBD continuum and is defined by increasingly negative intrathoracic pressures during inspiration. Similar to OSA, this leads to arousals, sleep fragmentation, and altered sleep architecture (Guilleminault et al., 1982). Although UARS is
observed in the absence of apneas, hypopneas, or hypoxemia, those with UARS appear to
demonstrate similar neurobehavioral deficits as those with OSA. Obstructive hypoventilation
(OH) may also arise as a SRBD, particularly in those who are obese. This condition often results
in significant hypercarbia and may closely resemble OSA during nocturnal sleep.

During the course of early development OSA is more prevalent amongst those born
premature (Rosen et al., 2003), those who have neuromuscular diseases and craniofacial
abnormalities (Gislason & Benediktsdottir, 1995), and those who are overweight or obese
(Redline et al., 1999). To that end, treatment of OSA in early childhood years is generally
effective. In fact, treatment of adenotonsillar hypertrophy; the most common cause of OSA in
childhood (Green & Carrol, 1997; Owens, 1998), has been amenable in approximately 50 to 70%
of all cases. Despite this, many children are not cured through this procedure and may be more
resistant to this treatment if they are obese (Mitchell & Kelly, 2007), have genetic predisposition
to OSA, experience asthmatic episodes (Bhattacharjee et al., 2010) or have structural craniofacial
abnormality (Hoeve, Joosten, & van den Berg, 1999; Rosen, Muckle, Goding, Mahowald, &
Ullevig, 1994). Cases such as these may require additional behavioral management such as
weight loss or positive airway pressure (PAP) therapy for treatment.

**Executive Dysfunction Model of OSA**

In order to understand the mechanisms in which neurobehavioral deficits occur as a result
of OSA, Beebe and Gozal (2002) suggested a theoretical model of “executive dysfunction” in
which cognitive and behavioral manifestations occur due to OSA. Through their model, they
proposed that OSA affects neurobehavioral functioning through multiple functions that together
compound the deficits observed from having OSA. Specifically, the model proposes that OSA
leads to sleep disruption and blood gas abnormalities that prevent restorative processes in brain
due to sleep interruption as well as direct cellular impact on the brain. They postulate that glial viability and metabolite abnormalities including the desaturation of oxygen and excess carbon dioxide in the blood supplied to the brain may be primarily responsible for these outcomes. In addition, the model proposes that the primary manifestation of the cellular impact occurs within the developmentally sensitive prefrontal cortex and hippocampus that are sensitive to desaturation of oxygen in small blood vessels. Consistent with these hypotheses is the fact that much of the neurobehavioral impact exceeds deficits observed purely by daytime somnolence and the majority of deficits observed in those with OSA are in the area of executive functioning that is largely mediated by the prefrontal cortical regions. In particular, the model proposes that the executive dysfunction is characterized by deficits in specific domains; set shifting, working memory, analysis, contextual memory, self-regulation, arousal, as well as behavioral inhibition.

Independently, OSA in children has been empirically found to be associated with neurocognitive deficits in verbal skills and phonological processing (Blunden, Lushington, Kennedy, Martin, & Dawson, 2000; Blunden, Lushington, Lorenzen, Martin, Kennedy, 2005; Emancipator et al., 2006; Kurnatowski, Putynski, Lapienis, & Kowalska, 2006; O’Brien et al., 2004; Rhodes et al., 1995), visuospatial problem solving and construction (Blunden, et al., 2000; Friedman et al., 2003; Kurnatowski, Putynski, Lapienis, & Kowalska, 2006; O’Brien et al., 2004; O’Brien, et al., 2004a), visual and verbal learning and memory (Blunden et al., 2000; Friedman et al., 2003; Kurnatowski, et al., 2006; O’Brien et al., 2004a; Rhodes et al., 1995), working memory, inhibition, selective attention and vigilance (Archbold, Giordani, Ruzicka, & Chervin, 2004; Blunden et al., 2000; Avior, et al., 2004; Blunden et al., 2005; Huang et al., 2004; O’Brien, et al., 2004a; Owens, Spriito, Marcotte, McGuinn, & Berkelhammer, 2000), planning (O’Brien, et al., 2004), processing speed (Lewin, Rosen, England, & Dahl, 2002), and abstraction and
analysis (Emancipator et al., 2006). Although typically average, limited evidence also suggests children with OSA may have lower global intellectual abilities, with the majority of these findings appearing in preschool children (Beebe, 2006; Montgomery-Downs, Jones, Molfese, & Gozal, 2003, Montgomery-Downs, Crabtree, & Gozal, 2005).

Depression

Amongst the notable comorbidities associated with OSA that may have a significant impact on neurocognition, is the presence of depressive symptoms. Unlike OSA, depression is routinely assessed by psychologists as part of a comprehensive neuropsychological evaluation. Characterized by fatigue, psychomotor retardation, diminished concentration and interest in activities, and feelings of worthlessness (DSM-V; American Psychiatric Association, 2013), depressive symptoms commonly appear during childhood and early adolescence. Epidemiological studies of childhood depression provide diverse estimates of prevalence rates depending on criteria for classifying depressive disorders in childhood, however, there appears to be strong evidence that prevalence of depressive disorders increase from childhood through early to late adolescence. Less than 1% of preschool children demonstrate symptoms of major depressive disorder (MDD; Kashani, & Carlson, 1987), whereas rates in prepubertal children and adolescents range from .03 to 2.5% (Costello, et al., 1996; Fleming, & Offord, 1990; Keenan, Hipwell, Duax, Stouthamer-Loeber, & Loeber, 2004). Rates of depression increase significantly for adolescents, with estimates ranging from .4 to 6.4% with a significantly higher proportion of females experiencing depression during adolescence (Fleming, & Offord, 1990; Hoffman, Baldwin, & Cerbone, 2003).

Similar to OSA, depressive symptoms have been linked to many areas of neurobehavioral morbidity including altered neurocognition, academic performance, and sleep parameters.
Independently, depressive symptoms in children have been found to be associated with deficits in frontal mediated tasks of working memory (Gunther, Holtkamp, Jolles, Herpertz-Dahlmann, & Konrad, 2006; Matthews, Coghill, & Rhodes, 2008; Osborn, & Meador, 1990), problem solving (Lundy et al., 2010; Emerson, Mollet, & Harrison, 2005), attention, processing speed, encoding and learning, memory and retrieval (Lundy et al, 2010; Gunther et al., 2006; Horan, Pogge, Borgar, Stokes, & Harvey, 1997; Lauer et al., 1994), and metamemory (Lauer et al., 1994). Decreased response time (Ladouceur, Dahl, & Williamson, 2005), psychomotor-speed (Rapport, Denney, Chung, & Hustace, 2001; Matthews, Coghill, & Rhodes, 2008; Kovacs, & Goldston, 1991), and motor coordination (Lundy et al., 2010; McClure, Rogeness, & Thompson, 1997) have also been observed. Although global intellectual quotients (IQ) during school-aged years are typically intact, there is some evidence that increasing depressive symptomology may be associated with lower overall IQ scores in school-aged children and adolescents (Lundy et al., 2010; Lefkowitz, & Tesiny, 1985; McClure et al., 1997). Still, it should be noted that fluid visuospatial perception and reasoning skills have been observed to be lower in those with depressive symptoms (McClure et al., 1997), and some have demonstrated associations with reduced language skills and depressive symptoms (Lundy, et al, 2010).

Despite typically intact overall intelligence, children with depressive symptoms who do not have a primary learning disability (LD) have demonstrated poorer academic performance and skills compared to those without depression. Many of these academic performance deficits may be due to the behavioral manifestations of inattention and hyperactivity within the classroom as a result of the child’s depressive state (McClure et al., 1997; Hodges, & Plow, 1990; Muris, Van Der Pennen, Sigmond, & Mayer, 2008; Livingston, Stark, Jennings & Haak, 1996; Cole, Martin, Powers, & Truglio, 1996), but motivation and poor concentration may also contribute to these
behavioral manifestations (Kovacs, & Goldston, 1991; Cole, Martin, Powers, & Truglio, 1996; Edelsohn, Ialongo, Werthamer-Larsson, Crockett, & Kellam, 1992). Specific academic performance has been comparatively lower in tests of spelling, mathematics (Lundy et al, 2010), academic knowledge (Hodges, & Plow, 1990), and reading skills (Vincenzi, 1987). To date, extremely limited studies have investigated the interplay OSA and depression may have on cognition or academic performance in school-aged children.

Summary

Despite the presence of an ever growing body of pediatric sleep medicine literature investigating the neurobehavioral deficits in pediatric OSA in the past 20 years, there has been a significant paucity of research aimed at exploring the complex interaction that having OSA and comorbid depressive symptoms might have on neurobehavioral functioning in school-aged children. The state of the current literature appears to provide strong evidence that OSA and depression each contribute to significant neurocognitive deficits, notable academic deficits, and discrepant alterations in sleep parameters have been reported. There is also evidence to suggest that increasing severity of OSA and increasing depressive symptoms may be associated with increased neurobehavioral deficits compared to milder forms of each disease. Evidence from neurobiological studies of OSA and depression have consistently confirmed neural and functional alterations in the brain that appear to be consistent with the nature of psychometric test deficits observed in frontal-lobe mediated tasks. To that end, no published study to date has attempted to investigate neurocognitive and academic performance deficits in school-aged children with OSA and comorbid depressive symptoms.
Overview of Proposed Study

Using data being collected as part of an ongoing clinical trial investigating the neurobehavioral outcomes of children undergoing PAP therapy for treatment of OSA, baseline participants from the trial were used to assess how severity of OSA and clinical depressive symptoms contribute to performance on measures of neurocognition and academic performance. Children underwent a neuropsychological test battery assessing neuropsychological and academic domains. Parents also reported on behavior and depressive symptoms of their children and all children underwent in-lab PSG following an adaptation night to obtain objective psychophysiological sleep parameters.

Significance

The current study addresses how the presence of OSA and comorbid depressive symptoms affects neurocognition and academic performance in school-aged children. Provided the significant impact that having OSA and depression has on neurocognition and subsequent academic performance ensures that the current study will have far reaching implications for school psychologists. First, the present study is one of only a few to add to the significant paucity of research investigating academic performance in children with OSA. Secondly, the present study is the first to my knowledge to assess the interaction having OSA and depressive symptoms has on neurocognition and academic performance in school-aged children. Although school psychologists are not typically involved in the direct assessment of children with sleep disorders, school psychologists do routinely assess for depression and may be inclined to screen for OSA. In addition, school psychologists are well qualified to implement and facilitate behavioral interventions for treating OSA, such as weight management or positive airway pressure adherence protocols. Moreover, if children with depressive symptoms and OSA
demonstrate significant deficits above and beyond those typically manifested in depression alone, children qualifying for special educational services inside school settings may be better placed under the category of other health impairment (OHI) rather than for emotional or behavioral disturbances. Overall, it is believed that the current study will have far-reaching implications for guiding assessment, intervention, and policies for school-based, medical health, and sleep medicine settings.

**Purpose, Research Questions, and Hypotheses**

The purpose of the current study was to investigate neurocognition and academic performance in children with OSA, and examine how depressive symptoms contribute to alterations in these outcomes. Specifically the current study aimed to investigate the relationship OSA and concurrent presence of depressive symptoms has on neurocognition and academic achievement. The study investigated if having a higher RDI and increasing depressive symptoms contributed to neurocognitive and academic morbidity. The following questions were investigated:

1. Do children with mild or moderate/severe OSA (RDI 1.5 ≤ 5 vs. > 5) and mild vs. clinical depressive symptoms (CBCL-Anxious/Depressed or Withdrawn/Depressed T ≥ 63) experience reduced neurocognitive performance compared to children without sleep apnea?
   a. **Hypothesis 1a**: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures of working memory.
   b. **Hypothesis 1b**: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures of planning.
c. Hypothesis 1c: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures of fine motor speed.

d. Hypothesis 1d: There will be a main effect on severity of OSA with those with Moderate-Severe OSA performing lower on measures of working memory compared to those without OSA.

e. Hypothesis 1e: There will be a main effect on severity of OSA with those with Moderate-Severe OSA performing lower on measures of attention/vigilance compared to those without OSA.

f. Hypothesis 1f: There will be an interaction between clinical depressive symptoms and OSA severity on tasks of working memory, with those who have Moderate Severe OSA and clinical depressive symptoms exhibiting lower performance than all other groups.

2. Do children with mild or moderate/severe OSA (RDI 1.5 ≤ 5 vs. > 5) and mild vs. clinical depressive symptoms (CBCL-Anxious/Depressed or Withdrawn/Depressed T ≥ 63) experience reduced academic achievement compared to those without sleep apnea?

a. Hypothesis 2a: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures Applied Problems.

b. Hypothesis 2b: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures Reading Fluency.
c. Hypothesis 2c: There will be an interaction effect between presence of clinical depressive symptoms and severity of OSA for Applied Problems, with those who have Moderate-Severe OSA and clinical depressive symptoms exhibiting lower performance than all other groups.

d. Hypothesis 2d: There will be no significant main effect or interaction effects between groups on measures of Letter Word Identification, Understanding Directions, Brief Achievement, or parent reported academic performance.
Pertinent Key Terms

Hypercarbia- Increase in carbon dioxide in the blood

Hyoxemia- Reduction in blood oxygen saturation to small vessels

Obstructive sleep apnea (OSA) - Characterized by intermittent complete or partial collapse of the respiratory airway, snoring, apneic pauses, and arousals

Sleep Related Breathing Disorder (SDBD) - Characterizes the continuum of nocturnal breathing disorders that range from PS, UARS, obstructive hypoventilation (OH), and OSA

Primary Snoring (PS) - An attempt to breathe that is limited by upper airway resistance but does is not accompanied by an apnea, hypopnea, hypoxemia, or significant arousals. Observed via self-report of chronic snoring or validated via PSG

Upper Airway Resistance Syndrome (UARS) - Characterized by negative intrathoracic pressure during inspiration that is accompanied by arousals. Snoring and increased respiratory effort without a decrease in airflow are common

Daytime Somnolence/Excessive Daytime Sleepiness (EDS) – Subjective experience of being fatigued during the day or falling asleep during typical daytime activities (watching TV, riding in a car, lying down after eating). Objective assessment includes the use of a multiple sleep latency test (MSLT) or maintenance of wakefulness test (MWT)

Preschool Children – Preschool children will be defined as children between the ages of 0 to 6, or those who have not yet initiated K-12 schooling

School-Aged Children – School-aged children will be defined as the time between the ages of 6 to 12 or those children who are in grades K through 6th

Adolescents – Adolescents will be primarily used to define those who are between the ages of 10 – 25 years of age
Youth – The term “youth” will be used to describe children and adolescents when the age range includes those who are of school-aged but who also span into the age of adolescence

**Apnea Hypopnea Index (AHI)** - Total number of apneic and hypopneic respiratory events per hour of sleep

**Respiratory Disturbance Index (RDI)** - Total number of apneic and hypopneic respiratory events per hour of sleep with the inclusion of respiratory event related arousals (RERAs) included in the index

**Apnea** - Discrete pauses in breathing with duration of 10 seconds or more, or two or more breath cycles in youth

**Hypopnea** - A partial collapse of the respiratory airway that that leads to a 30 to 50% reduction in airflow

**Mild OSA** - Defined in children as an AHI or RDI greater than 1.5 events per hour of sleep but less than five events

**Moderate OSA** - Defined in children as having an AHI or RDI greater than 5 and less than 10 events per hour

**Severe OSA** - Defined in children as having an AHI or RDI greater than 10 events or more per hour of sleep

**Obstructive Apnea** - Complete cessation of airflow accompanied by respiratory effort

**Central Apnea** - Cessation of airflow and void of respiratory effort

**Mixed Apnea** - Cessation of airflow that has both obstructive and central apneic features

**Arousal** - 1 - 3 seconds of wake EEG

**Awakening** - 5 minutes of wake EEG

**O₂ nadir** - Lowest oxyhemoglobin saturation level recorded during PSG.
Arousal index (AI) - Number of respiratory arousals per hour of sleep

Oxygen saturation - Also referred to as oxyhemoglobin saturation, refers to the amount (percentage) of oxygen saturation in the blood read by an oximetry

Positive Airway Pressure (PAP) – PAP is the use of an automated airflow apparatus utilized for treatment of SRBDs in order to pressurize and splint the airway, preventing constriction and collapse of the upper airway. Most commonly, the use of Continuous positive airway pressure (CPAP) is used at a prescribed pressure setting by a sleep medicine physician.
Chapter 2

Review of the Literature

The following chapter will review the literature on OSA regarding the epidemiology and etiology of OSA, and further describes the effect OSA, depression, and the severity of each has on neurocognition and academic achievement. Although, OSA has been associated with many deficits in learning and memory functioning, for the purposes of the current study, the literature review focuses on frontal mediated tasks of executive functioning and working memory, attention & vigilance, fine-motor speed and coordination, perception and visuo-spatial skills, and language skills. Due to the significant paucity of pediatric literature in some areas, adult literature will be referenced. Due to the variations in classification of SRBDs in the literature, the term OSA will be used to refer to all forms of SRBD with the exception of PS, or where it would otherwise not be representative of the respiratory condition being described. Similarly the term depression will be used to describe measures that have assessed a clinically meaningful presence of symptoms or what the study researchers have defined as depression. The term depressive symptoms will refer to subclinical presence of depressive symptomology but will maintain reference to some presence of depressive symptoms. In order to reduce redundancy, outcomes will be discussed in the context of their studies together rather than according to the area of neurocognition affected. A summary of overall findings across studies will be provided at the end of each section.

Epidemiology and Etiology of SRBDs and OSA

SRBDs characterize a continuum of upper respiratory disease that varies in respiratory event severity as well as the associated neurobehavioral and psychophysiological manifestations and range from primary snoring (PS), to upper airway resistance syndrome (UARS), to OSA. The mildest form of SRBD on the continuum is PS. Currently, there is no universally accepted
definition of PS, however, the “gold standard” for assessment of PS may refer to the perception and categorization of harsh snorting sounds caused from respiratory vibrations during sleep (Strollo, & Sanderes, 1993) which are not accompanied with apneas, hypopneas, hypercarbia, or hypoxic events (PPS, 2002). The International Classification of Sleep Disorders: Diagnostic and Coding Manual further defines “snoring” (ICSD 786.09) as a “respiratory sound generated in the upper airway during sleep that typically occurs during inspiration but may also occur in expiration, without episodes of apnea or hypoventilation” (AASM, 2005). Estimates of the prevalence of PS are the highest on the continuum with prevalence rates ranging from 3 to 12% (Ferreira et al., 2000; Owen, Canter, & Robinson, 1995). Although the majority of children with PS have mild symptoms, and many outgrow the condition, there is also evidence that untreated mild SRBDs can have significant long term outcomes, including an increase in OSA severity and associated symptoms with age or weight gain (AASM, 2005). Despite being described as “benign” (AAP, 2002), many researchers have found significant neurobehavioral deficits in academic performance and neurocognition as well as alterations in sleep parameters compared to controls without PS (Gozal, 2001; Gozal, & Pope, 2001; O’Brien et al., 2004), further highlighting the possible significance of even the most modest forms of SRBDs in youth.

The second level of the SRBD that has been described on the continuum is UARS (Guilleminault et al., 1982). Although UARS is observed in the absence of apneas, hypopneas, or hypoxemia, increasingly negative intrathoracic pressures during inspiration leads to arousals, sleep fragmentation, and significant neurobehavioral deficits similar to OSA. There is also clinical evidence to suggest that UARS responds to OSA treatments in a similar manner. Due to the recent defining of UARS, and inclusion of respiratory-event related arousals (RERA) as a parameter used to obtain respiratory disturbance index (RDI) for diagnosing OSA, prevalence
rates of childhood UARS are assumed to be higher than those for OSA but lower than PS. Researchers have further suggested that due to the inclusion of RERA for defining OSA based on a clinical RDI, that many children with UARS could be categorized as having OSA (Lumeng, & Chervin, 2008).

Defined as “a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation during sleep and normal sleep patterns” (ATS, 1996, p.866), OSA is the most severe form of SRBD. While snoring is regularly recognized as a defining feature of OSA, not all patients with OSA snore, and as a result the gold standard for assessing the presence of OSA is through nocturnal PSG (AAP, 2002). Diagnosis of OSA through PSG is conducted by utilizing respiratory metrics such as the apnea hypopnea index (AHI) or respiratory disturbance index (RDI), that assess apneas, hypopneas, and other RERAs during sleep as an average number of respiratory events per hour of sleep. It is also well documented that OSA leads to a reduction in blood oxygen saturation levels and may result in hypercarbia. Other respiratory disorders such as obstructive hypoventilation (OH) may arise due to severe obesity and result in more hypercarbia compared to OSA. While OSA is the most prominent form of apneic syndrome, central sleep apneas occur when there is a collapse of the respiratory airway without respiratory effort. Mixed obstructive/central apneas also occur when a lack of respiratory effort subsequently results in a collapse of the upper respiratory airway and causes an obstructive event. Each of these types of obstructions have been associated with alterations in typical sleep and neurobehavioral deficits and are all included under the umbrella definition of OSA.

Prevalence of OSA in the general population has been observed to be age graded, with lower prevalence rates observed in children and adolescents (.7 – 3%) (Ali, Pitson, & Stradling,
1993; Rosen, et al., 2003), with higher rates observed in adults (2 – 4%; Young et al., 1993) and older adults (20-70%; Ancoli-Israel et al., 1991; Punjabi, 2008). There is also evidence that OSA may be more prevalent in African American children (Rosen, et al, 2003) while rates comparable to Caucasian youth have been observed in Thai (Anuntaseree, Rookkapan, Kuasirikul, & Thongsuksai, 2001) and American Hispanic youth (Goodwin et al., 2003a). However, it is important to note that Hispanic children have been found to display more neurobehavioral symptoms as a result of OSA (Goodwin, et al., 2003b).

Developmentally, premature birth (Rosen et al., 2003) and adenotonsillar hypertrophy have regularly been associated with increased risk of having OSA. In fact, adenotonsillar hypertrophy has often been cited as the primary cause of OSA in children (Greene, & Carroll 1997; Owens, 1998). Until recently it was thought that gender related prevalence was not observed until adulthood, however, recent evidence has highlighted the possibility that OSA may be more common in males as young as 2 to 28 weeks old (Kato et al., 2000) and this trend may remain stable throughout school-aged years (Li, et al., 2010) and adolescence and young adulthood (Delasnerie-Laupretre, Patois, Valtax, Kauffman, & Alperovitch, 1993; Lumeng, & Chervin, 2008). Moreover, there does not appear to be a significant change in prevalence of OSA with increasing age until adulthood. Living in a low socioeconomic status (SES) neighborhood has also been highlighted as a significant risk factor for developing OSA after controlling for ethnicity, obesity, and premature birth (Spilsbury et al., 2006).

By and large, the most ubiquitous cause of OSA in children is due to adenotonsillar hypertrophy (ATH), with the peak prevalence of ATH mirroring the highest prevalence rates of OSA during early childhood to occur between the ages of three and six years old. Neuromuscular diseases and craniofacial abnormalities have also been associated with high rates
of OSA, with these features being more common with OSA during infancy (Gislason & Benediktsdottir, 1995). In the majority of the adult and pediatric literature, being overweight or obese has also largely been determined to be a strong predictor for being diagnosed with OSA (Redline et al., 1999), although there is some evidence that increased body mass index (BMI) and obesity may not be a significant risk factor in children until they have reached the age of eight years old (Stepanski, Zayyad, Nigro, Lopata, & Basner, 1999). In addition, the increase of BMI may also make patients resistant to the frontline treatment of adenotonsillectomy or the palliative PAP therapies. Still, with the significant rise in body mass index (BMI) and obesity rates in the United States, the likelihood of OSA prevalence increasing in the coming years is highly plausible.

In adults, OSA is typically defined as having an AHI of five events or more per hour. However, the definition for defining OSA in children has observed a paradigm shift in recent years, defining mild OSA as experiencing one or greater obstructive apneic events per hour which is outside of normal values (Uliel, Tauman, Greenfeld, & Sivan, 2004), or a combination of apnea and hypopneas averaging more than 1.5 events per hour (Marcus et al., 1992; Perfect et al., 2012; Uliel et al., 2004; Verhulst et al., 2007; Witmans, Keens, Davidson, Ward, & Marcus, 2003). Some have utilized an obstructive specific index (O-AHI) for clinical criteria cutoff (Salloum et al., 2010; Perfect et al., 2012). This criterion has been proposed based on research evidence demonstrating morbidity at even mild levels in children compared to adults who may not appear to demonstrate significant problems with such conservative criteria. Some of this difference may be due to increased sensitivity to small vessel oxygen desaturation in cortical and medial temporal structures due to the timing of neural development. Children also have higher cardiorespiratory output during wakefulness (Salameh et al., 2008) and during nocturnal sleep
(Archbold, Johnson, Goodwin, Rosen, & Quan, 2010; Carskadon et al., 1978), which has been hypothesized to increase youth’s sensitivity to hypoxemia compared to adults. Overall, definition of OSA in pediatric literature has largely utilized adult criteria or varying severity of AHI or RDI above the 1.5 event threshold that may underestimate pediatric population prevalence rates.

**Snoring and Neurocognition**

Independently, OSA of all severities has been found to be associated with neurocognitive deficits, particularly those tasks that require attention, inhibition, and frontal lobe mediated execution of planning, organization, and working memory. Investigating the impact PS and OSA has on neurocognitive domains of intelligence, attention, and memory, Blunden et al. (2000) investigated a small sample of children with PS or OSA and gender and age matched controls. All children who were free from major comorbidities underwent a single in-lab PSG within 8 weeks after undergoing neuropsychological assessment. Analysis between the PS/OSA and control group revealed significantly reduced global, verbal, and performance IQs compared to controls. In addition, memory, selective attention, and vigilance were all found to be significantly lower in the PS/OSA group. It should be noted that although some of the participants had mild OSA, the average RDI of the PS/OSA group remained less than 1, while the RDI of the control group was 0.0, with no participants showing evidence of respiratory events during sleep.

Another study conducted by Blunden et al. (2005) further compared a group of children with a history of PS, to a group of children with behavioral sleep problems (BSP), those with both PS and BSPs, and a group of children who had neither problem on measures of neurocognition. Neuropsychological testing was conducted on 19 children under the age of 16
with parents reporting on BSPs, social and behavioral functioning, and frequency of snoring. Results for the neuropsychological outcomes showed that children with PS and BSPs as well as those who only had PS performed significantly poorer than BSP only and the control groups on all measures of IQ and attention. Memory, however, was observed to be most affected in those who had both PS and PS and BSPs. Behavior problems were also significantly higher in all groups compared to controls, with those with BSPs to demonstrate worse parental ratings. Although this study did not utilize overnight PSG for obtaining objective sleep measures, the study is notable due to the divergent cognitive impact BSPs and PS may have on cognition, particularly due to the common occurrence of BSPs in children with PS and OSA. Moreover, even though the authors used parent report for defining respiratory problems, the findings that attention was impacted is consistent with other research in PS and OSA. O’ Brien, Mervis, Holbrook, Bruner, Smith, et al., (2004) also looked at children with PS compared to healthy controls and found that those with PS performed significantly worse in domains of attention and executive functioning, planning, visual attention, phonological processing, nonverbal abilities, as well as overall intelligence compared to healthy controls.

Another study investigated the impact PS has on sleep architecture and cognition in children between the ages of 5 and 7. Including children without major comorbidities and excluding those with ADHD, the team looked at children with PS compared to a control group. Typical performance in both groups were in the average range, however, significantly lower performance was observed in children with PS in the domains of overall language and visual spatial abilities, as well as phonological processing and visual attention. Small effect sizes were observed with the exception of measures of phonological processing and visual spatial processing which approached moderate effect size.
Although some studies have not found any significant differences in mild disordered breathing (Beebe et. al, 2004; Calhoun et al., 2009), the above mentioned studies suggest that even the mildest form of SRBD (PS) could lead to mild neurocognitive dysfunction in school-aged children. Despite this, it should be noted that studies have largely ranged in their definitions for primary snoring and methods used for assessing the mild SRBD. Few conclusions can currently be made on the literature investigating PS on neurocognition, but it remains notable that even the mildest form of respiratory dysfunction during sleep may have an impact on neurocognitive functioning.

**OSA and Neurocognition**

Emancipator et al. (2006) investigated 164 children with confirmed presence of OSA assessed via in-home cardiorespiratory monitoring and compared them to those without OSA to assess differences on tests of achievement, attention, and cognition in children between the ages of 8 and 11. Compared to children without OSA, those with OSA demonstrated significantly poorer performance on nearly all tasks assessed, including those assessing language comprehension, planning, organizational, reaction time, and picture vocabulary knowledge. When covariates of age, sex, and birth weight were considered these findings remained with the exception of reaction time ($p > .05$). When more adjustments were made that included additionally correcting for caregiver marital status, caregiver education, and median income, vocabulary knowledge, planning and organization, and language comprehension still differed in the OSA group. In addition, the study found that the cognitive deficits observed in children with OSA were more severe in those who were born preterm compared to those with longer gestational periods, highlighting the need to assess for early child development when considering the impact OSA may have on cognition.
Kurnatowski et al. (2006) examined 117 youth between the ages of 6 and 13 who were currently suffering from adenotonsillar hypertrophy and underwent PSG to examine presence of OSA and were compared to those without OSA symptoms. Children with OSA were split into younger (6-9) and older groups (10-13) for comparisons to same aged controls. Compared to healthy controls, the younger children with OSA demonstrated significantly poorer performance on all tasks including those of verbal learning and memory, verbal comprehension and attention, a visuo-motor integration task, as well as a planning and visual construction task of executive functioning. The older youth demonstrated similar findings with the exception that there were no significant differences between older youth with OSA on tasks of visual construction and planning compared to controls, suggesting that younger children may be more susceptible to the impact of OSA on cognition.

Others have looked at obese participants with and without OSA, and assessed them via PSG and a neurocognitive battery. Comparing obese participants with OSA vs. average weight children with OSA, it was found that those with obesity and OSA performed worse on measures of verbal learning and memory, vocabulary, as well as general memory. Looking at the group as a whole, severity of OSA was also significantly related to neurocognitive impairment in memory and learning. (Rhodes, et al., 1995).

Due to the significant literature highlighting executive control and behavioral deficits in OSA, ADHD and associated neurobehavioral deficits have also been highlighted as a common occurrence in OSA. Huang et al. (2004) investigated a prospective cohort of 102 children between the ages of 6 and 12 who had been referred to a clinic for ADHD and behavioral disorders and compared them to 27 healthy age and gender-matched controls. In order to assess ADHD, initial screening included utilizing the DSM IV diagnostic criteria following a structured
interview and children were excluded if they had other major comorbidities. Following screening, a neuropsychological battery was administered to 102 eligible participants who had not been taking stimulant medications for at least a week prior to testing. All children (ADHD and controls) underwent the same rigorous screening and assessment procedures to reduce confounding neurological or psychological comorbidities.

Analyses from the study highlighted that from the sample of children with ADHD who participated in the PSG, 57% of the children met criteria for OSA (AHI > 1), while more than 37% had mild OSA (1 < AHI < 5) and approximately 19% of the children had an AHI > 5. No central apneas were found in any children, and PLMs were found in 10% of the ADHD sample. Analysis of neuropsychological performance in attention found that compared to those with ADHD only, those with ADHD and OSA performed worse on response time, however, no additional cognitive differences were found. Lastly, the researchers conducted exploratory data analysis on relations between affective-behavioral variables from the CBCL (anxious/depressed, withdrawal, hyperactivity, aggression, etc.) and found no relations to severities of the children’s AHI, PLMI, mean SaO$_2$, %REM sleep or TST. The authors also reported that severity of OSA was not related to severity or type of ADHD or cognitive outcomes as others have found.

Studies of preschool children (Montgomery-Downs, Crabtree, & Gozal, 2005; Montgomery-Downs, Jones, Molfese, & Gozal, 2003) have also investigated neurocognitive and academic outcomes in children with OSA. Montgomery-Downs et al. (2003) assessed parental reports of OSA and sociodemographic information in relation to academic performance from African American and Caucasian children between the ages of 3 and 6. Parental report of academic problems was associated with those who were at risk for OSA compared to those that did not report upper airway morbidity. In addition, children with symptoms of OSA were more
likely to rank below average in school and have more symptoms of ADHD. Montgomery-Downs et al., (2005) further looked at changes in sleep architecture and cognition in 19 preschool children with OSA before and after adenotonsillectomy and compared them to age and gender matched controls. Following surgery, improvements in cognition occurred for the OSA group in overall cognitive functioning. While OSA free participants performed significantly better on intellectual measures at baseline, there was no longer significantly lower performance exhibited by the OSA group following surgery. Deficits were, however, still noted in verbal fluency in the OSA group at baseline and the follow-up compared to the controls.

Owens et al. (2000) conducted a small study in 18 children with mild to moderate OSA who underwent PSG, cognitive testing, and were assessed pre and post adenotonsillectomy. Results indicated significant improvements after surgery on behavior on the CBCL, improvements in overall quality of life, as well as significant improvements on a test of vigilance. Another small-scale study found similar improvements in the same sustained attention paradigm, finding significant improvements in vigilance following surgical removal of the adenoids and tonsils (Avior et al., 2004).

Friedman et al. (2003) looked at the impact adenotonsillectomy has on neurocognitive functioning in 39 children (ages 5-9) with OSA compared to healthy controls. Testing was conducted prior to surgery and 6-10 months after surgery. Children with OSA scored lower than healthy controls on the tests of mental processing prior to surgery. At follow up, children with OSA had significant improvements in both daytime behavioral functioning as well as improved scores on tests of perceptual reasoning and induction, sequential organization, and fluid reasoning subtests and showed improvements on the sequential, simultaneous, and overall mental processing scales. All of the improvements on these scales demonstrated medium to
large effect sizes ($d = .64$ to $d = .83$) respectively. When comparing the control group to the OSA group at follow up, there were no longer any observed differences between groups. These results appear to suggest that with treatment for OSA, children may be able to reverse deficits in the domains of visual spatial perception and reasoning, visuomotor integration, short-term memory, executive functioning, analysis, and overall processing skills previously imposed by chronic symptoms of OSA.

Although all severities of OSA have generally been found to result in some deficits, not all studies have shown that increasing OSA severity leads to more significant deficits. However, there is notable research suggesting increasing severities of OSA to result in more cognitive morbidity. Lewin et al. (2002) looked at a group of children between the ages of 4 and 12 with OSA and investigated those with mild OSA (RDI .5 to 10.0, and 10% desaturation) and moderate to severe OSA (RDI greater than 10) compared to a healthy control group on measures of neurocognition and behavior. Results indicated that children with OSA demonstrated more behavior problems compared to the controls and that children diagnosed with moderate to severe OSA had significantly lower scored on a measure of processing speed, simple attention, and vigilance. There was also evidence that OSA severity was inversely related to measures of verbal abilities. Overall, these findings appear to suggest that clinical cutoff scores regarding classifying OSA severity may also be useful for determining the potential cognitive morbidity that presents in children with OSA. A study utilizing the Tucson Children’s Assessment of Sleep Apnea (TuCASA) cohort also found that compared to children (ages 6-12) with mild OSA symptoms, those with moderate to severe OSA (RDI > 5) symptoms displayed significantly worse learning and delayed recall on a 16 word task of encoding and memory (Kaemingk et al., 2003).
In order to assess the extent to which severity of OSA impacts executive functioning in school aged children, Beebe et al. (2004) investigated a sample of children who were divided into three groups based on objective respiratory measures of AHI obtained via overnight PSG; simple snoring group (AHI < 1), mild OSA (AHI 1-5), and moderate to severe OSA (AHI > 5). The sample included 49 children (ages 6 – 12, \( N = 17 \) African American), the majority who had been referred for snoring problems to a pediatric sleep clinic, and a control group matched for age and gender from similar geographic areas. All children were free from major comorbidities but children with ADHD were included if they agreed to discontinue stimulant medications prior to PSG and cognitive testing. All children underwent PSG and neuropsychological testing with the exception of the control group, which was deemed unnecessary to undergo PSG due to the extreme unlikelihood of OSA being observed in the absence of parental observances of snoring or respiratory disturbances during sleep. During neuropsychological evaluation, children’s parents and teachers also completed behavioral questionnaires.

Analyses were conducted in this study looking at group differences for increasing level of severity of AHI (controls, simple snorers, mild OSA, moderate to severe OSA). Investigation of neuropsychological variables was conducted while controlling for parental education and ethnicity due to controls having higher Caucasian participants and higher parental reported education. Results from evaluation of neuropsychological performance across all measures found significantly lower performance on verbal fluency, with the controls performing better than all groups with respiratory difficulties. Negligible differences were found between each group with respiratory problems. Due to the small sample size, exploratory trend analysis on group relation to neuropsychological performance identified significant relations between severity of AHI to processing speed, visual attention, executive functioning, and attentional
commission errors, with increasing severity related to reduction in performance. No differences were found in intellectual abilities after correcting for parental education and ethnicity (Beebe et al., 2004).

Beebe et al. (2003) conducted a meta-analysis of 25 case-controlled and norm-referenced findings in the neurobehavioral outcomes in children with OSA. Studies utilizing norm-referenced comparisons found that OSA actually demonstrated superior performance in overall intelligence ($d = -.67$) and verbal abilities ($d = -.59$) compared to normative values. However, OSA youth demonstrated long term verbal memory and executive functioning deficits from a small to moderate effect ($d = .52$). Small and nonsignificant findings were found when comparisons were made in domains of short-term verbal memory, short and long term visual spatial memory, and motor functioning. Comparisons between control referenced findings and those with OSA demonstrated nonsignificant effects for intelligence, verbal abilities, or short or long-term verbal memory. Significant moderate deficits were found between case-controls and those with OSA in the domains of visual abilities ($d = .68$), short ($d = .56$) and long-term visual memory ($d = .55$), and large effects were found for motor skills ($d = 1.21$) and vigilance ($d = 1.40$). Consistent with the norm referenced studies significant deficits were found for executive functioning ($d = .73$).

Overall, the findings from the meta-analysis and the literature on neurocognition in children with OSA suggest a pattern of deficits that are consistent with frontal lobe dysfunction. In particular, it appears these deficits are pronounced in the domains of executive functioning, working memory, vigilance and selective attention, as well as motor skills. Overall intellectual and verbal abilities appear to be preserved and have been found to fall well within the average range compared to same-aged peers.
OSA and Academic Performance

Guilleminault et al. (1981) conducted one of the earliest studies to describe marked academic difficulties in children with OSA was conducted by. The researchers examined 25 prepubertal children referred to a pediatric sleep disorders clinic for a variety of sleep complaints and a control group of equal proportions. All children underwent PSG to assess sleep architecture, MSLT to assess objective sleepiness, and a serial addition test between MSLT trials in order to assess changes between a baseline and follow up study of sleep and behavioral functioning for various participants at 3, 6, and 12 months. All referred children demonstrated significant PS but were void of conclusive OSA. In describing the sample of children, the researchers noted that 48% of the children displayed hyperactivity, and 40% of the patients had current learning problems or there had been suspicion of a learning disability. In addition, the authors found that all children over the age of seven had also been placed in special education programs due to significant learning problems. At the 3 month follow-up, the researchers found that school teachers and parents reported significant improvements in behavior and that school performance had been improved. In addition, at 6 months follow-up it was found that all children previously taking stimulant medications no longer required them. Interestingly, after a 12 month duration post-surgery all children who had previously been in special education programs no longer needed the services with the exception of two participants. Following surgery, participants who underwent MSLT and the serial addition test demonstrated improvements in objective sleepiness and increased the number of serial addition problems solved by approximately 35%, indicating improved sleepiness and functional alertness compared to baseline. Overall the study highlighted that even subclinical respiratory difficulties appear to
lead to compromised academic status and treatment of even mild PS may improve daytime functioning.

Further highlighting the higher base rates of OSA in children with learning problems, another study looked at non-referred patients with reported behavioral, developmental, and academic performance problems and looked at sleep difficulties in these children. The researchers used a case control design and identified 31 children with academic problems or ADHD and compared them to randomly selected controls stratified for age and parental education. Compared to the problem free controls, those with reported learning problems were rated as having significantly more snoring and respiratory problems during sleep (Weissbluth, Davis, Poncher, & Reiff, 1983), further confirming the presence of learning difficulties in children with OSA.

More recently, Gozal (1998) looked at 1st grade children who were ranked in the lowest 10th percentile compared to classmates. Screening for OSA included detailed parental reports and overnight recordings of oximetry and CO\textsubscript{2} output. In order to assess academic performance, school grades were also obtained for the entire school year prior and after the study. From the sample, children were identified as having varying sleep related breathing disorders and were split into groups based on desire to pursue treatment and the specified sleep related breathing disorder. Analysis in academic performance was assessed on children who underwent adenotonsillectomy and those who did not undergo treatment for their SRBD. Following the year after treatment school grades were compared between groups to assess improvements following surgery. These comparisons found that compared to children who did not undergo treatment, those who underwent adenotonsillectomy demonstrated a significant improvement in grades during the second grade. Results from this study appear to suggest that treatment of SRBDs may
lead to improvement in academic or behavioral functioning that result in an improvement in school classroom performance.

Gozal and Pope (2002) also investigated if experiencing upper airway difficulties during childhood was associated with later academic difficulties as adolescents. Specifically, the researchers sent questionnaires home to parents of 13 to 14 year old adolescents who were attending a large public school system to report on early childhood nocturnal breathing problems. Adolescents were chosen from the top and bottom quartiles of the class standing in the respective cohort, and were then matched on metrics of SES, age, gender, race, and school. Adolescents were excluded if they currently reported having snoring difficulties in order to assess the extent to which early childhood problems impacted later academic functioning. Analyses from the study revealed that children in the lowest quartile group had significantly higher rates of snoring and more severe snoring as children compared to the highest performing quartile group. There were no significant differences between groups on current snoring problems. The authors suggested that there may be irreversible effects from early childhood SRBDs that may lead to the marked underachievement during early adolescence.

Urschitz et al. (2003) conducted a cross-sectional study on the prevalence of SRBDs and the association they have with academic performance in 3rd grade children attending randomly selected public schools in Germany. Parents reported on questionnaires regarding sleep related breathing problems and children also underwent nocturnal home pulse oximetry. From a sample of more than 1000 children, the researchers examined relations between snoring, hypoxia, and academic performance. Analysis from those who had been reported to snore “frequently” or “always” revealed that increasing snoring frequency was associated with significantly poorer performance in the areas of mathematics, science, and spelling, both prior and after controlling
for covariates of teacher reporting style and class membership. There were no associations between frequency of snoring and reported performance in reading or handwriting. Children who experienced hypoxia, defined as having at least one desaturation event from pulse oximetry, demonstrated increased risk of doing poorly in all academic domains compared to those without desaturations ($p = .053$). Multivariate analysis controlling for confounds of age, gender, parental education, and class membership showed an increased risk for poor performance in mathematics was also revealed, but was no longer significant when frequency of snoring was accounted for. Although this study found that hypoxia and high frequency snoring may lead to reduced academic performance, not all children with OSA are chronic snorers, thus it remains unknown how many children across groups had OSA.

Beebe et al. (2010) looked at 163 youth aged 10-16.9 years old who were assessed on parental and teacher reported behavior, neurocognition, school grades, and in-lab nocturnal PSG. Groups were divided into 4 categories based on AHI and parental reported snoring; No OSA, Snorers, Mild OSA, and Moderate-Severe OSA. Comparisons between groups showed that those with PS had higher parental reported rates of hyperactivity, anxiety, and depression compared to those without OSA. No significant findings were found between groups on any measure of neurocognition, however, increasing severity of OSA was found to accompany lower parent and self-reported grades. After controlling for numerous covariates, the largest effect found was for self-reported grades. To further delineate the relations between behavioral symptoms, OSA, and school performance, secondary analysis was conducted to assess mediating variables associated with school grades. After adjusting for covariates, reported grades were found to be associated with parent and teacher reported attention problems, hyperactivity problems, and anxiety problems. Although they were not found to be mediators for academic
performance, reported study skills, leadership, social skills, and neurocognitive areas of intelligence, attention, and memory were associated with reported grades.

In order to further assess the extent that OSA impacts neurobehavioral and academic functioning overtime, Perfect et al. (2013) investigated 263 children studied prospectively via in-home nocturnal PSG and neurobehavioral assessment at two time points approximately 5 years apart between childhood and adolescence. Examining parental reported learning problems and grades for varying classification of OSA illness, the sample was split into four groups; never had OSA, remitted OSA, new incident OSA, and persistent OSA. Results from the study highlighted that having persistent OSA across the two time periods associated with significantly greater odds of having more problems in the areas of hyperactivity, aggression, and conduct problems. Those with persistent OSA also had increased odds of having learning problems and were also more likely to report grades that were C’s or less. Both groups that demonstrated OSA at follow-up also had higher rates of clinically differentiated scores for reports of academic functioning. Overall, this study appears to suggest that academic and behavioral problems may not only arise from the initial onset of OSA, but any presence of OSA overtime as well as longer duration of having OSA may contribute to more severe neurobehavioral morbidity. Nonetheless, the study did not consider the impact of SDB severity on long-term outcomes.

Consistent with the above mentioned studies, numerous researchers have also linked OSA to significant behavioral symptoms of inattention, hyperactivity, conduct problems, and academic problems (Ali, Pitson, & Stradling, 1993; Chervin et al., 2002; Chervin, Dillon, Archbold, & Ruzicka, 2003; Guilleminault et al., 1981; Kaemingk et al., 2003; O’Brien et al., 2004) that may further compromise children’s performance in academic settings. Altogether, the results from these studies appear to suggest that higher rates of learning and academic problems
may occur in youth with OSA and that these problems may translate into reduced academic performance measured by grades compared to those who never had respiratory difficulties.

**Epidemiology and Etiology of Depression**

In order to understand the nature of the neurobehavioral sequelae of depression within children with OSA, it is important to understand how depressive symptomology manifests during childhood. Characterized by fatigue, psychomotor retardation, diminished concentration, anhedonia, and feelings of worthlessness (DSM-V, 2013), symptoms of a major depressive disorder often appear during childhood and early adolescence. Epidemiological studies of childhood depressive disorders provide varying estimates of prevalence rates depending on criteria for classifying depressive disorders in childhood, however, there appears to be strong evidence that prevalence of depressive disorders increase from childhood through early to late adolescence. In fact, less than 1% of preschool children have been found to demonstrate symptoms of MDD (Kashani, & Carlson, 1987), whereas prepubertal children and adolescents range from as low as .03 to 2.5% (Costello, et al., 1996; Fleming, & Offord, 1990; Keenan et al., 2004). Rates of depression increase significantly for adolescents, with estimates ranging from .4 to 6.4% with a significantly higher proportion females experiencing depression during adolescents (Fleming, & Offord, 1990; Hoffman, Baldwin, & Cerbone, 2003). Moreover, lifetime prevalence for having had a depressive disorder has been reported to be 14% for males and 28% for females (Hanish, & Gurra, 2002; Lewinsohn, Hops, Roberts, Seeley,, & Andrews, 1993).

Ethnic difference have also been noted in prevalence, including higher rates in African Americans (Leech, Larkby, Day, & Day, 2006), Native Americans (Armstrong, 1993), and Hispanic children (Twenge, & Nolen-Hoeksema, 2002), however, differences in prevalence may
be reduced when controlling for socioeconomic status (SES) (Doi, Roberts, Takeuchi, & Suzuki, 2001). Evidence has also suggested that Mexican Americans in particular may be at higher risk for depressive symptoms and Asian Americans are less at-risk compared to African American and Caucasian youth (Chen, Roberts, & Aday, 1998; Roberts, & Chen, 1995).

Conceptualization of depression in youth is conducted through various etiological models. First, depression has been found to be largely biological, with children of depressed parents to be more at-risk for developing depression, particularly for recurrent depressive episodes (Klein, Lewinsohn, Rohde, Seeley, & Durbin, 2002) and for developing depression into adolescence (Wallace, Schneider, & McGuffin, 2002). Specifically, it has been highlighted that biological mechanisms such as dysfunction of the serotonergic neurotransmitter system (Birmaher et al., 1997) and hypoactivation of the prefrontal cortex (Davidson et al., 2002) may be responsible for the manifestation of depression in youth. Further biological risk may be exacerbated from the parenting style at home (Kessler et al., 2001) or from medical comorbidities. In addition to the biological etiology of depression, several interpersonal, contextual, and social-cognitive influences also contribute to depression. Particularly notable is the contribution that family and peer relationship stress (Hankin, & Abramson, 2001), low SES, parental unemployment and low levels of education, child-parent attachment issues, and chronic daily stressors (Garber & Horowitz, 2002; Rudolph, Hammen, & Daley, 2006) have been found to contribute to depression in youth. Lastly, Beck (1967) highlighted through an informational processing theory that depression may result from idiosyncratic processing of self. In particular, youth may commonly have irrational beliefs, dysfunctional attitudes, and endorse statements of low self-worth that contribute to depression (Hankin & Abramson, 2001).
Although less than 3% of school-aged children experience depression, many children still experience subclinical depressive symptoms that can be classified according to taxonomy of three distinct approaches (Compas, Ey, & Grant, 1993). The most common approach for detecting the presence of depressive symptoms is through the subjective report of mood. In particular, this approach may include verbal acknowledgement of depressive symptoms or a brief checklist that specifies symptoms being experienced. A second approach is a focus on the symptoms as part of a diagnosis of a mood disorder. This approach often classifies a diagnosis of depression according to DSM criteria that utilize a combination of quantitative and qualitative indicators in order to assess the presence of a depressive disorder via structured clinical interview. Although this approach provides a category for the depressive symptoms to fall into based on useful quantitative symptoms, it has been suggested that depression in youth may be best conceptualized under a continuum rather than a distinct diagnostic entity (Hankin, Fraley, Lahey, & Waldman, 2005). Accordingly, the third approach commonly used is to assess depressive symptoms according to empirically derived clusters, which in youth, may be best factored into an anxious-depressed syndrome classification (Achenbach, 1990; Achenbach, Connors, Quay, Verhulst, & Howell, 1989) due to significant overlap of internalizing symptoms between syndromes. Using the empirically derived approach, the most common method employed for assessing depressive symptoms is through the use of multi-informant reports of youth’s behavior and mood, such as the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001).

**Depression and Neurocognition**

Depressive symptoms have been linked to significant neurobehavioral morbidity including alterations in neurocognition, academic performance, and sleep architecture. Although
the majority of the research has focused on the neurocognitive sequelae of depression in adults, a growing body of research has been developing over the last 30 years in adolescents and prepubertal youth. Similar to adults, much of the findings have linked depression to deficits in performance on tasks largely mediated by the prefrontal cortex and medial temporal structures.

Livingston et al. (1996) investigated the neurocognitive functioning in a small sample of 17 depressed youth aged 9 to 14 and found that depressed children performed significantly lower on a measure of freedom from distractibility, auditory processing, and tactual performance. A pair of early studies also investigated how the number of depressive symptoms relates to measures of neurocognitive performance. Kaslow et al. (1984) found that the number of depressive symptoms endorsed on a self-report measure was negatively associated with performance on visuospatial problem solving, processing speed, simple attention, and working memory in youth. McGee et al., (1986) further highlighted these findings in older school-aged children, and found that depressive symptoms were inversely related to performance in mathematical reasoning, working memory, and visuospatial problem solving that requires visuomotor integration speed. Although these and other findings (Lundy et al., 2010) have suggested promising evidence that severity of depressive symptoms may be related to increased neurocognitive morbidity, other researchers have failed to find such relations in inpatients with a MDD (Weiner & Pfeffer, 1986).

Although the presence of depressive symptoms in school-aged children can take many forms, there has been limited investigation of the impact varying severities, diagnoses, time of onset, or duration of the disorder may have on neurocognitive outcomes. Despite this, one study attempted to assess the extent to which first episode MDD impacts neurocognitive functioning in adolescents. Kyte, Goodyer, and Sahakian (2005) examined adolescents who had obtained a
recent diagnosis for a first time MDD episode and compared them to youth without history of depression. Depression diagnoses were made based on a validated structured interview and self-report was used to assess current depressive symptomology. Utilizing the Cambridge Neuropsychological Test Automated Battery (CANTAB) and an intelligence test, the researchers compared neuropsychological performance between the controls and those with first episode MDD. Results from the study indicated that there were no significant differences in those with first episode MDD and controls for intelligence or attention, however, those with MDD demonstrated more errors for targeting “happy” vs. “sad” cues presented during an inhibition task but did not demonstrate difficulty in shifting attentional set based on new rules, suggesting a negative bias for emotional processing. Those with MDD were also more impulsive on a task of decision making compared to controls.

Another study assessed a small sample ($N = 10$) of children with a MDD compared to healthy children of equal age between the ages of 10 and 12. Investigating distractibility from auditory stimuli while watching videos void of sound, the researchers investigated children’s event related potentials upon presentation of novel and repeated sounds during the task. Comparisons between groups found that compared to healthy controls, the depressed group demonstrated shorter latency for discriminating the variation in sounds. Children with depression also demonstrated quicker attentional switching at an involuntary level to stimulus changes. Overall, the investigators concluded that depressed children demonstrate an increased sensitivity to sensory information and subsequently have increased attentional distractibility as a result of increased cognitive and attentional load in depression (Lepisto et al., 2004).

More recently, Wilkinson and Goodyer (2006) looked at a sample of both medicated and nonmedicated depressed youth compared to healthy controls on measures of selective attention,
vigilance, and the ability to switch attentional sets. On selective attention tasks assessed through paradigms requiring pairing of identical shapes from an array of similar shapes, the researchers found that there were no significant differences in accuracy between groups, although the depressed youth not on medication had slower reaction time compared to controls. On measures of attentional switching and vigilance, depressed youth who were not on medication were slower and made more errors on attentional switching compared to controls. Additionally, depressed youth who were taking medication also performed significantly worse than healthy controls for accuracy for attentional switching.

Cataldo et al. (2005) also looked at vigilance and inhibition in youth with depression vs. healthy controls. Investigating youth between the ages of 9 and 17, depressed youth demonstrated more inattentive errors and slower reaction times compared to the healthy controls, but did not demonstrate differences in response inhibition. It should be noted however, that compared to non-depressed controls, the depressed adolescents displayed a larger discrepancy between time taken to complete a color naming task compared to a word-color inhibition task suggesting difficulty for inhibition of responses.

Still, others have not found significant differences between healthy controls compared to depressed youth in measures of inhibition, vigilance, or selective attention (Gunther et al., 2004). Similarly, another recent study investigating attention and executive functioning in youth with MDD looked at youth participants between the age of 8 and 17 with MDD vs. healthy controls who were all free from medications for at least 2 weeks prior to evaluation found no significant differences between the groups on measures of set shifting, verbal fluency, abstraction, executive perseverations, or distractibility (Favre et al., 2009).
In addition to the observed deficits in the domain of attention and inhibition in those with depression, working memory and executive functioning has also been an area of interest in children with depression. Using the CANTAB to assess the neurocognitive impact of depression, multiple researchers have found that short term spatial and visual memory tests from this battery are sensitive for detecting neurocognitive deficits (Mathews, Coghill, & Rhodes, 2008; Porter et al., 2003). Specifically, Porter et al. (2003) conducted a study investigating 44 adults who had not been taking medication and who had been diagnosed with depression. Comparing this group of depressed adults to a nondepressed control group, the researchers found that those who were in the depressed group performed significantly worse on tasks of spatial pattern recognition as well as spatial working memory.

Mathews, Coghill, and Rhodes (2008) investigated neurocognitive deficits in a group of depressed adolescent females free from medication and compared them to a healthy control group. Results from the study found that the adolescent females who were depressed made significantly more errors and used poorer strategy on spatial working memory compared to the controls. In addition, the depressed group also performed significantly lower for pattern recognition and visual recognition. Lastly, depressed females also made more errors on a paired associate word learning task, requiring encoding and retrieval of learned words.

McClure, Rogeness, and Thompson (1997) examined neurocognitive correlates with depression in adolescent females who were free from major psychiatric comorbidities. Using a comprehensive neuropsychological battery the researchers looked at adolescent females based on their current depressive symptoms rated from parental and self-reports, as well as a clinical interview. From this assessment, a depressed and nondepressed group compared on neuropsychological measures, revealed no significant differences in academic achievement,
executive functioning, or memory. Significant findings were observed in intelligence, and subtests involving visual spatial and verbal skills, there was also significantly lower performance observed in a task of visual perception of line segments. It should be noted that consistent with other studies, the nondepressed control group demonstrated high average intelligence and the depressed group still had average range intelligence.

Due to the common finding that anxiety and depressive symptoms generally accompany each other in school-aged children, other researchers have investigated how symptoms of anxiety may contribute to neurocognitive morbidity among those with depressive symptoms. One such study conducted by Emerson, Mullet, and Harrison (2005) looked at 38 boys aged 9 to 11 who were free from major comorbidities or learning difficulties and looked at both depression and anxiety compared to neurocognitive performance. Groups were made into an anxious/depressed group, and a non-anxious/non-depressed group based on state-trait anxiety and depressive symptoms. Results from the neuropsychological comparisons found no significant differences for simple visual attention and sequencing, however, the anxious/depressed group took significantly longer to complete the a test of rapid visual scanning and attentional switching. In addition, those in the anxious/depressed group made more errors compared to their non-anxious/non-depressed peers. Another significant difference between the groups appeared in the domain of concept formation, which the non-anxious/non-depressed group performed significantly better.

Ladouceur, Dahl, and Williamson (2005) examined mechanisms of underlying cognitive emotional processing using distracting emotional stimuli during an n-back working memory task with affective prompts. Using a sample of 75 youth between the ages of 8 and 16 the researchers identified groups who had an anxiety disorder, depressive disorder, comorbid anxiety and
depression, as well as a low risk control group from the sample. Results from the study highlighted that those with a MDD or comorbid anxiety and depressive disorders displayed longer reaction times on the n-back test when negative emotional prompts were given while the control group took longer to respond on positive prompts compared to the other groups. The findings from this study appear to suggest that higher order cognitive processes in particular may be disrupted when emotional contrasts are tied to the cognitive task in those with depression or comorbid anxiety and depression. Overall, these results may suggest that the allocation of attentional resources may be compromised in youth with depressive disorders and anxiety.

Others have focused on assessing the domains of attention and memory in youth with depression and anxiety. Gunther et al. (2004) found few attentional differences between youth with anxiety compared to those with depression, but found significantly poorer memory in those with depression. Others have further corroborated the findings that depression in male children may also be implicated in poorer rehearsal and short-term memory recall as well as delayed free-recall series (Osborn, & Meador, 1990). Horan et al. (1997) also looked at a group of depressed adolescents compared to those with a comorbid conduct disorder, conduct disorder only, same aged norms, and adult based norms from the memory test. Results indicated that adolescents with depression performed below norms on all primary outcome measures but did not differ from the other groups. Compared to adult norms, male adolescents were not significantly different; however, female adolescents demonstrated lower performance across all measures of the memory and learning. These findings suggest that gender selective impairment may be present in adolescent females in the domains of encoding and memory. Children with depressive symptoms compared to matched controls also have demonstrated worse memory and meta-
memory performance, which may further be exacerbated by the severity of the depressive symptoms observed (Lauer et al., 1994).

Lundy et al. (2010) investigated neurocognition in children between the ages of 6 and 11 with no major comorbidities. The authors made comparisons between children who demonstrated clinical depressive symptoms on measures of Anxious/Depressed and/or the Withdrawn clinical scales of the CBCL compared to those who were without clinical symptoms. Comparing those who met clinical depressive symptoms on the Anxious/Depressed scale demonstrated significantly lower performance for overall intelligence, and nonverbal intellectual measures on an abbreviated intelligence test and also demonstrated reduced visuospatial skills, language and vocabulary, attention, processing speed, executive functioning, and psychomotor speed compared to those without clinical symptoms. Compared to those without clinically withdrawn symptoms, children with clinical symptoms demonstrated poorer performance for overall intelligence, language skills, processing speed, attention, executive functioning, and psychomotor speed. In addition, those with clinically withdrawn symptoms demonstrated poorer performance on memory and verbal intelligence. Overall correlations were also made with the full sample and found similar findings, with increasing depressive symptoms being related to lower performance in all indices of intelligence, and specific abilities in vocabulary knowledge, attention and processing speed, executive function abilities, and psychomotor speed.

Compared to adult studies, there have been many fewer investigations into the neurocognitive impact depressive symptoms has on adolescents and even fewer for investigations into school children. In addition, the method’s employed for the evaluation of depressive symptoms in the studies has been variable and limited studies have ascertained how the length of having depressive symptoms or how repeated or initial episodes may impact overall
functioning. Despite this, there appears to be growing evidence that depressive symptoms in youth has been associated with decreased performance in fluid reasoning, attention and concentration, processing speed, and frontal mediated tasks of executive functioning and working memory. In addition, when symptoms of anxiety accompany depressive symptoms, preliminary evidence suggests that there may be increased difficulties in areas of attention and executive control for efficient mental flexibility.

**Depression and Academics**

Although it is largely known that children with depression often experience marked underachievement in school, and may consequently qualify for special educational services under the category of ED, there remains limited research investigating the presence of underachievement as a result of depression. However, a few studies have attempted to address the relation between depression and academic underachievement. One early study investigating academic achievement in children with depression was conducted by Vincenzi (1987). Investigating two diverse groups of children that included 139 students in the 6th grade, Vincenzi examined the relation between depression and reading achievement in a group of low-income children and those who were from a more middle class background. Using the self-report measure to assess depressive symptoms, scores were split into three categories based on number of symptoms endorsed; no depression, mild depression, and moderate to severe depression. Reading achievement was measured using previous years standardized test scores, current teacher reports, and current GPA for 6th grade in the areas of math reading, science, and social studies. Comparisons between schools in low vs. middle class schools demonstrated significantly higher rates of depression in the low-income school. Comparisons between achievement in those with depression demonstrated no significant differences on standardized
scores or single subject GPA. However, having higher depression significantly related to lower reading achievement, lower overall reading level, and lower overall GPA. A significant positive relation was also observed between income of the school and reading achievement. Overall, these findings appear to suggest that the presence of subclinical depressive symptoms may be more pronounced in those from a low SES school, and that severity of depressive symptoms may increase risk for underachievement in school.

Colbert, Newman, Ney, and Young (1982) examined inpatient children referred for a wide range of psychological and behavioral pathologies, and the impact depression may have on academics and cognition. Using DSM-III criteria, the researchers found that 54% of the sample met criteria for a DD. Investigation of previous year school records, administration of academic and cognitive tests, and review of psychiatric unit behavioral forms was conducted. Results from the study highlighted that 71% of the depressed children found that children with depression were underachieving by at least a year or greater for grade level in one or more academic domains compared to their intellectual abilities. Although more than 50% of the parents and teachers reportedly believed the marked underachievement was due to a learning disability, little more than 7% of the sample actually demonstrated a significant discrepancy indicative of a learning disability in the study.

Lefkowitz and Tesiny (1985) investigated correlates of peer rated depression in relation to academic records and estimated intelligence scores derived from a child draw-a-person task. Findings from the peer rated depression and correlates with reading achievement demonstrated severe depression in both girls and boys was consistently associated with an inverse relation to reading achievement. Similarly, estimates of intelligence were found to be inversely related to
depression severity for boys and girls, with the exception of boys who scored in the highest quartile of depressive symptoms.

Hodges and Plow (1990) examined the academic achievement and intellectual abilities of 76 clinically recruited school-aged children with varying pathologies, but were free from traumatic brain injuries, developmental disorders, or severe intellectual impairment. Children were assessed using DSM-III criteria and a validated structured interview schedule to assess for anxiety disorders and depression. Children who met criteria for a conduct, anxiety, or depressive disorder were included in the study and compared on measures of academic achievement and intelligence. Results from the analyses between the groups found that in comparison to the other groups, children with depression did not suffer from compromised cognition but did demonstrate reduced academic achievement in the areas of mathematics and knowledge clusters.

Another study conducted by Rapport et al. (2001) investigated neurocognition, psychometric educational achievement, and SAT scores in 325 youth who were also assessed for Internalizing Symptoms, Withdrawal, and Anxious/Depressed symptoms on the CBCL. Analyses evaluated the extent that classroom performance and cognitive functioning mediate internalizing and intelligence on later scholastic functioning. Primary results from the study found that differences in intelligence were associated with variation in classroom performance and neurocognitive functioning, and that classroom performance and cognitive functioning each made unique contributions to scholastic aptitude above and beyond intelligence alone. Lastly, the authors also found that Anxious/Depressed and Withdrawn symptoms each contributed to prediction of classroom performance and neurocognitive performance above and beyond intelligence. Although the researchers found that Withdrawn symptoms may contribute more to scholastic aptitude than Anxious/Depressed features, the authors argued that the increased
contribution of Anxious/Depressed symptoms to both cognitive and academic performance may ultimately predict later difficulties in those who have symptoms of internalized anxiety.

Using a large epidemiological sample of children who had volunteered to undergo PSG as part of the TuCASA cohort, Lundy et al. (2010) also investigated the impact having depressive symptoms on academic achievement in children between the ages of 6 and 11. Using the CBCL to assess Anxious/Depressed symptoms, it was found that children who had clinically significant Anxious/Depressed symptoms displayed significantly lower academic achievement in the areas of math skills and spelling skills. Children who had clinically significant Withdrawn symptoms demonstrated significantly lower performance in basic math skills. Converse to this team’s findings that increasing depressive symptoms were inversely related to numerous measures of neurocognition, no linear relation was found for measures of academic achievement.

In summary, there is currently a significant paucity of literature on the impact depressive symptoms has on academic functioning in school-aged children. The studies cited above appear to suggest that children with depression may exhibit lower academic achievement for math, spelling, academic knowledge, and may have further difficulties in long term scholastic aptitude. Despite the lack of literature, test developers have continued to be aware of the impact depression may have on academic functioning and have cited small to moderate effect sizes for reduced academic achievement on standardized achievement tests (Woodcock, McGrew, & Mather, 2001, 2007).

**Prevalence of OSA and Comorbid Depression**

Although limited information is available regarding the rate of comorbidity of OSA and depression in children, prevalence of this comorbidity has recently been described in adults. One study looked at a nationally representative sample of more than 9,700 adults over the age of 18
who were asked to report frequency of sleep related breathing problems and prior diagnosis of OSA as part of the National Health and Nutrition Survey in the United States. Patients were asked to complete the nine item patient health questionnaire (PHQ) in order to assess likely clinically significant depressive symptoms. Amongst the sample, 6% of men reported a diagnosis of OSA, whereas just over 3% of women reported a diagnosis of OSA. Analysis of self-reported OSA found a significant association between OSA with probable major depression based on the PHQ with higher odds of major depression observed in women than men. The researchers did not find an association of between self-reported snoring and depression (Wheaton et al., 2012).

Another population-based survey of nearly 19,000 adults from several European countries conducted phone interviews to assess OSA and depressive symptoms. From this sample, 857 adults were identified as having OSA, whereas 17% of these individuals were highlighted as having a clinically significant depressive mood based on a questionnaire that assessed questions consistent with the Diagnostic and Statistical Manual Fourth Edition (DSM – IV TR, 2000). In contrast to this, only 4.3% of the sample that was void of OSA and sleep related breathing problems were identified as having a clinical depressive mood disorder, highlighting the marked comorbidity of OSA and depressive symptoms (Ohayon, 2003).

Vandeputte and Weerd (2003) also investigated prevalence of sleep disorders and depressive symptoms in 917 patients between the ages of 14 and 84 ($M = 49$) referred for a suspected sleep disorders. Patients were subjected to two consecutive 24-hr in-home PSG recordings and depressive symptoms were assessed via the Beck Depression Inventory (Beck, Ward, & Mendelson, 1961). From the study, 167 patients had OSA and 51 participants had PS. From the OSA patients, 41% of the patients met criteria for mild depression on the BDI (10 or
greater items), and 1.6% of the patients had severe depressive symptoms. Compared to other sleep disorder referrals, those with OSA had the second highest rate of depressive symptoms, second only to psychophysiological insomnia which had more than 60% of the patients with depressive symptoms. Interestingly, the researchers also found that 31% of patients with PS also had mild depressive symptoms, and 2.8% had severe depressive symptoms present. Although these patients were referred for possible sleep disorders depression was not their referring complaint. Despite this, 123 patients had previously been using antidepressant medications prior to undergoing sleep disorder evaluation, further highlighting the importance of assessing depressive symptoms in those referred for clinical sleep disorders.

Although prevalence rates of comorbid OSA and depression have recently been established in adults, less is known regarding the prevalence of this comorbidity in children or the nature of the relationship between the two. Notable to this, is the significant overlap of symptoms between depression and OSA, including; irritability, anhedonia, alterations in appetite, changes in sleep patterns, restless sleep, poor concentration, psychomotor retardation, and somatic complaints and social withdrawal in children (DSM IV TR, 2000; DSM V, 2013). A significant gap exists in that no current study to date has attempted to investigate the prevalence of OSA and depression in school-aged children, and in particular, no study has attempted to investigate the complex neurobehavioral impact this comorbidity may have in children.

In summary, the current literature appears to provide significant evidence that OSA and depression each contribute to significant neurocognitive deficits in the domains of executive functioning, working memory, attention, and motor speed and coordination. In addition, both depression and OSA have been associated with compromised performance in academic functioning. Provided the sensitive developmental time frame school-aged children are in for
cortical development and the significant long term effects that may result from compromised cognition and academic status during childhood, it appears imperative to investigate the impact OSA and comorbid depressive symptoms may have in children. In addition, due to the numerous medical comorbidities that accompany OSA and depression (hypertension, obesity, diabetes) which may further exacerbate neurobehavioral morbidity or disturb sleep architecture, examination of the relationship having OSA and depression has on neurocognition and academic functioning in school-aged children is warranted. Provided the extensive literature surrounding possible confounding factors in understanding the mechanisms of the complex relationship between OSA, depression, and neurobehavioral/sleep outcomes, a proposed theoretical model outlines possible relations in the literature (Appendix A). The present study is an initial step in validating the model and targets a small portion of the model that includes the investigation of depression in children with OSA.
Chapter 3

Method

The following chapter describes the methodology employed in the current study. This chapter highlights a description of the study participants, procedures, instruments, and procedures of data analysis.

Participants

The sample of participants in the current study included total enrollment of 72 participants, with 26 participants declining participation or being unable to participate in the study after initial enrollment, and 46 participants initiating data collection procedures as part of the study. From the 46 participants who initiated the study, 38 participants received neuropsychological evaluation and overnight PSG, 4 participants only received neuropsychological testing, and 4 participants only received overnight PSG and subsequently were not included in data analysis. One participant was not assessed via PSG due to intellectual impairment. As a result, a total of $N = 38$ participants who completed neuropsychological testing and overnight PSG were included in the current study.

Children included in analysis were recruited from a clinical sleep lab ($N = 9$), flyers and advertisements posted around the community and from a televised informational segment ($N = 13$), and from Tucson Unified School District (TUSD; $N = 15$) via the use of a psychometrically validated OSA screening questionnaire (Appendix B). One participant was recruited from an unknown source. A total of 3523 questionnaires were sent to children stratified for ethnicity in grades pre-K through 7th grade and 243 questionnaires (7%) were returned.

All children included in the current study were void of having a previously treated SRBD, did not have a formal diagnosed sleep disorder or major medical or psychological
comorbidity (ADHD, MDD, dysthymia, trisomy 21, diabetes, rheumatoid arthritis, etc.), and had not previously used PAP therapy at the start of the study. One child was diagnosed with Attention Deficit Hyperactivity Disorder following completion of all baseline data collection procedures, but was included in analysis due to having no formal diagnosis at the time of initial evaluation. All children were fluent in English, and accepted willingness to complete the entire study protocol whether they were initially randomized into the placebo or the treatment group for the larger study.

An a priori power analysis was initially conducted to assess the number of participants needed to obtain significant findings based on $p < .05$ using G*Power version 3.1.2 (Buchner, Erdfelder, Faul, & Lang, 2009). Based on a medium effect size of .25 for a multivariate analysis, 75 participants would have been needed in order to obtain power at .80. Approximately 60 school-aged children between the ages of 6.0 and 11.9 were projected to complete all procedures of participation, which was to yield an estimated power of .70. Due to reduced participant enrollment as a result of restrictions from the primary recruitment source (TUSD; PSQ), the current study was not able to recruit sufficient participants in order to obtain optimum power for analyses. Despite this, the current study was conducted in its underpowered form due to restrictive participant recruitment procedures of the study and the use of objective gold standard assessment procedures. Compromised power based on $N = 38$ yielded a power estimate .52.

Based on prior research and to investigate the impact that clinically significant depressive symptoms has on neurocognition and academic outcomes, the groups were first divided into two groups based on presence of depressive symptoms using clinical cut-offs on the CBCL (Anxious/Depressed or Withdrawn/Depressed $T \geq 63; N = 15$) and children were differentiated on OSA severity into 3 groups with an RDI $< 1.5$ (Primary Snorers; $N = 10$), an RDI $\geq 1.5 \leq 5$
(Mild OSA), and those with RDI > 5 (Moderate-Severe OSA). However, due to continuing controversy and variable discriminability between neurobehavioral outcomes based on RDI cut-offs, analyses were also conducted using an alternative grouping of those with OSA (RDI ≥ 1.5) against those with typical range RDI’s but who were referred for snoring (RDI < 1.5). Altogether primary analysis included a 3x2 group design (PS, PS Depressed, Mild OSA, Mild OSA Depressed, Moderate Severe OSA, Moderate Severe OSA Depressed) and alternative analysis included a 2x2 grouping (PS, PS Depressed, OSA, OSA Depressed).

**Sample Characteristics**

Participants in the current sample were 8.84 (1.44) years of age, 39.47% female ($N = 15$), and 60.53% male ($N = 23$). Ethnic makeup of the sample reflected a diverse group of 28.95% Caucasian ($N = 11$), 50% Hispanic ($N = 19$), 10.53% Mixed Race ($N = 4$), 2.63% African American ($N = 1$), and 7.89% Native American ($N = 3$). There were $N = 28$ (73.68%) participants that met criteria for clinically indicated OSA and $N = 10$ participants that did not meet criteria for OSA. Average RDI was 4.79 ($SD = 6.71$) and affective symptoms were 58.57 ($SD = 9.56$) for Anxious/Depressed and 58.87 ($SD = 8.88$) for Withdrawn/Depressed. Primary language spoken at home were 71% English, 8% Spanish, 13% Spanish/English, and 8% were unknown. Median family income was $56,000 and parental education level was on average 13.09 ($SD = 3.36$) years. Average BMI percentile was 73.54% ($SD = 27.09$). There was a total of 44.74% ($N = 17$) of the participants who were overweight, with 12 (31.6%) of these participants’ BMI percentile within the obese range. Participants who were not included in analysis and who only completed PSG ($N = 4$) and only completed neuropsychological functioning ($N = 4$) did not differ on demographic characteristics ($p > .05$). A table of sample demographic characteristics is provided in Table 1.
Table 1.

**Participant Characteristics**

<table>
<thead>
<tr>
<th>Characteristic (N = 38)</th>
<th>Mean</th>
<th>S.D.</th>
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<tr>
<td>Age (Years)</td>
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<td>Full Scale Intelligence (IQ) a</td>
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<td>13.97</td>
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<td>RDI</td>
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<td>O₂ Nadir</td>
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<td>BMI %ile</td>
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<td>Depressed/Withdrawn</td>
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<td>8.88</td>
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<tr>
<td>Parental Education (Years)</td>
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</tr>
<tr>
<td>Family Income</td>
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<td>Median = $56,000</td>
</tr>
</tbody>
</table>

*Note: Descriptive statistics are provided for all participants included in analysis. aScores presented from standard scores (M = 100, SD = 15)*

**Instruments**

**Screening Instrument**

Pediatric Sleep Questionnaire (PSQ) Sleep Related Breathing Disorder Index (SRBD-I) (Appendix B): The SRBD-I of the PSQ contains 22 items that ask about snoring frequency, intensity of snoring, parentally observed apneas, difficult breathing, daytime sleepiness, as well as inattentive and hyperactive behaviors and OSA related problems including being overweight or having enuresis. These symptoms have been shown to be correlated with individuals who have a diagnosis of OSA in children. Responses are given as follows; "yes" = 1, "no" = 0, and "don't know.” Other subscales within the SRBD scale includes a 4-item snoring scale, 4-item breathing scale, 4-item level of sleepiness scale, a 4-item snoring scale, 6-items asking about inattention/hyperactivity that are tied to DSM-IV TR criteria, and 4 supplemental items.

Psychometric validation of the scale was conducted on 102 children and adolescents age 2 to 18 who had had previously confirmed SRBDs in Michigan. Reliability ranges from moderate to good over the span of approximately a month (Snoring = .92, Sleepiness = .66, Behavior = .83, SRBD-I = .75) and internal consistency for scales range from .77 for sleepiness, .86 for snoring,
.83 for behavior, and overall the SRBD-I is .88. The measure has demonstrated good sensitivity (.81 - .85) and specificity (.87) for detecting PSG documented OSA when an overall SRBD-I score yields an average of .33 for all items, indicating that at least 8 items must be endorsed as “yes” (Chervin, Hedger, Dillon, & Pituch, 2000). From the mentioned study, the measure was able to accurately identify OSA in 85% of participants who had an AHI of 5 or more respiratory events per hour of sleep. For the current study, the PSQ was used to screen for presence of OSA participants from TUSD for participant recruitment.

**Measure of Depressive Symptoms**

Child Behavior Checklist 6-18 Parent Report (M = 50, SD = 10): The Child Behavior Checklist (CBCL/6-18), Achenbach, & Rescorla 2001) is an updated version of the original CBCL/4-18 - 118-item questionnaire (Achenbach, 1991) that assesses parental report of their child’s engagement in various life and social activities, school performance, and behavior across numerous domains in the past six months of the child’s life. The measure further assesses the parental report of the child’s competency in the areas of general activities, social, and school contexts, as well as areas of general maladaptive behavior, demographic information, and parental reported school performance. The CBCL has established eight empirically-based syndrome scales that aim to assess current clinical symptoms that include the following: Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule – Breaking Behavior, and Aggressive Behavior. From these clinical scales, three overall problem clusters are composed into Internalizing Problems, Externalizing Problems, and Total Problems. The CBCL/6-18 further assesses problems that are consistent with the DSM-IV diagnoses that include; Affective Problems, Anxiety Problems, Somatic Problems, Attention Deficit/Hyperactivity Problems, Oppositional Defiant Problems,
and Conduct Problems. The measure also includes additional scales based on the original 118-item questionnaire that includes a 2007 addition of the Obsessive-Compulsive Problems, Post-traumatic Stress Problems, and Sluggish Cognitive Tempo scales (Achenbach, & Rescorla, 2007).

Reliability of the CBCL/6-18 has demonstrated to be high to very high overtime using test-retest reliability with Pearson product-moment coefficients ranging from .82 to .93 for Competence scales, .82 to .92 for Empirical clinical scales, and .80 to .93 for DSM-IV oriented scales. Internal consistency based on Cronbach’s Alpha range from .63 to .79 for Competence, .78 to .97 for Empirical scales, and .72 to .91 for DSM-IV oriented scales. The CBCL/6-18 has also established content and criterion-related validity, and has demonstrated a significant ability to discriminate between clinical and nonclinical population populations using discriminant analysis procedures based on combined clinical and borderline criteria p > .01 and correctly classifying 80 to 88% based on clinical scores.

The current study utilized the empirically derived scales of Anxious/Depressed and Withdrawn/Depressed in order to assess presence of depressive symptoms. Specific reliability coefficients include test-retest reliability of .82 and alpha of .84 for Anxious/Depressed, and .89 test-retest reliability and .80 alpha for Withdrawn/Depressed measures. Concurrent validity of these measures correlated with other measures including Anxious/Depressed and Withdrawn/Depressed scale with the DSM-IV Checklist (.51 and .49) (Hudziak, 1998). Correlations between the Anxious/Depressed scale and the Behavior Assessment Scale for Children (BASC; Reynolds & Kamphaus, 1992) correlated with the BASC Anxiety scale for father raters (.70) and mother raters (.54) and with the BASC Depression scale (.52 and .60).
The Withdrawn/Depressed scale correlated with BASC Withdrawal (.65 and .58) and with Depression (.66 and .38).

Data analysis for symptom scales were analyzed using raw scores when analyzed as continuous variables as instructed in the manual due to bottom score truncation of standardized T-scores to the mean of T = 50 of the CBCL clinical scales. All CBCL’s were scored using the Assessment Data Manager (ADM) computer software version 9.1 (University of Vermont Department of Psychiatry, Burlington, Vermont, USA), and were double entered for verified accuracy of scoring by the neuropsychometrist. All scores were based on gender and age-based norms. Parental report of academic performance and academic problems were also utilized for the current study from the CBCL-School Competence items as dependent outcome measures. The clinical symptom scales of Anxious/Depressed and Withdrawn/Depressed were used as primary independent variables in the current study. Presence of depressive symptoms was set based on a clinical cut score of $T \geq 63$ due to the high level of discriminability based on these cut scores (Achenbach, & Rescorla, 2001). Although previous studies have utilized cut score of $T \geq 60$ (Lundy et al., 2010) for discriminating between depressed vs. nondepressed groups, the current study utilized the more stringent cut score in order to most accurately discriminate between those with and without clinical depressive symptoms.

**Neuropsychological Instruments**

Kaufman Brief Intelligence Test Second Edition (KBIT-2; Index Scores M = 100, SD = 15, Subscales M = 10, SD = 3): The KBIT-2 (Kaufman, & Kaufman, 2004) is a brief intellectual measure designed for assessing children and adults (ages 4 to 90). The KBIT-2 is derived from the original KBIT (Kaufman & Kaufman, 1990) and was renormed based on the March, 2001 Current Population Survey stratified for sex, race/ethnicity, geographic region, and education
level from each age group (23 age groups with equal males/females). Scores for the KBIT – 2 includes an overall Composite IQ, Verbal Index (VI), and Nonverbal Index (NVI). Subscales within the VI measures crystallized skills in the areas of general information and receptive vocabulary with the Verbal Knowledge subtest, and comprehension, vocabulary knowledge, and verbal reasoning through the Riddles subtest. Fluid abilities are measured with the Matrices subtest that assesses visuospatial reasoning. The KBIT – 2 has been hypothesized to be more culturally sensitive to those from Spanish speaking backgrounds due to items on the verbal subtests by allowing answers given in Spanish to be counted as correct.

Overall, internal consistency of the measure is considered high via Cronbach’s alpha coefficients that range from .89 to .96 for all age ranges assessed on the measure. Verbal (.91) and Nonverbal (.88) alphas are also viewed to be good. Test-retest reliability coefficients at approximately 30 days for the Verbal index range between .86 and .96 ($M = .91$), and ages 4 through 18 have been shown to be .90. Nonverbal reliability range between .78 and .93 ($M = .88$), ages 4 through 18 ($M = .86$). Reliability of composite IQ scores range between .89 and .96 ($M = .93$); ages 4 to 6 (.90), ages 7 to 9 (.92), 10 to 18 years (.93). Average increase in scores is observed to be approximately 4 points for both verbal and nonverbal composites at retest. Differences between scores based on gender were null, however, typical changes with age were noted with the highest performance for the fluid abilities measured by Matrices to peak during young adulthood and gradually decline with age. In contrast, crystallized abilities were found to be relatively stable throughout adulthood. Assessment of clinical populations further revealed varying intellectual performance for intellectually gifted (115), traumatic brain injury (73.4), dementia (74.1), LD (88), ADHD (90.5), speech and language difficulties (85.3), and mental retardation (61.1).
Concurrent validity between the KBIT-2 and the Wechsler Abbreviated Scale of Intelligence WASI (Wechsler, 1999) have been analyzed for verbal (.80-.86), nonverbal (.62 to .80), and overall IQ (.81 to .90). Correlations between the KBIT-2 composite IQ and the Wechsler Intelligence Scale for Children Fourth Edition (WISC-IV; Wechsler, 2003) were .82 for the Verbal Comprehension Index, .62 for Perceptual Reasoning Index, .48 for Working Memory Index, .12 Processing Speed Index, and .77 for the Full Scale Intelligence Quotient. For the current study, overall composite IQ was entered as a covariate between group comparisons.

Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition, Ltd 2006; Subtests M = 0.0, SD = 1.0): The CANTAB is a computerized neuropsychological test battery that was originally designed in order to assess dementia in older adults. The primary domains of neurocognitive functioning assessed by the battery are in the areas of induction, visual memory, executive functioning, attention, semantic and verbal memory, decision-making and response control, and social cognition. The comprehensive battery includes 23 tests of which 21 are nonverbal regarding general test presentation as well as participant responding (Cambridge Cognition Ltd 2006a). Due to the nonverbal nature of the majority of the tests and findings demonstrating no differences between English speakers and English language learners (Luciana & Nelson, 2002) the tests are largely viewed as culturally sensitive and valid across a range of linguistic ability (Roque, Teixeira, Zachi, & Ventura, 2011). Scoring of the CANTAB subtests are automatic, with computer based analysis of time and responding strategies. CANTAB eclipse version 3.2.19 was utilized for the current study.

To date, few psychometric studies have been conducted on the CANTAB, however, an adult study of the reliability of the CANTAB demonstrated modest to good reliability for healthy adult participants (N = 100, mean age = 44.1 years) that range from .40 to .87 (Cambridge Cognition, Ltd 2006).
Cognition Ltd, 2006b). Limited reliability data are available for children, however, Luciana (2003) reported high internal consistency coefficients (.73 – .95) in a sample of children 4 to 12 years old. Construct validity for the CANTAB measures of executive functioning has converged for diverse research studies in both clinical and nonclinical samples of children based neuropsychological and neuroanatomical findings (intensive care patients, Elison, Shears, Nadel, Sahakian, & Garralda, 2008; high functioning autism and ADHD, Goldberg et al., 2005; bipolar disorder, Dickstein, et al., 2004; stimulant drug medications, DeVito et al., 2009). Specific reliability coefficients for the tests to be utilized in the current study include Stockings of Cambridge (SOC) (.69 initial thinking time, .64 subsequent thinking time, minimum moves .60), Spatial Span (SSP) (.60), and Short Term Working Memory (SWM) (.70 between number errors, .63 strategy) (Cambridge Cognition Ltd, 2006b). Reliability for the Motor Screening Test (MOT), Choice Reaction Time (CRT), and Stop Signal Test (SST) have not been reported, in part due to the addition of the SST as a newer test to the battery. Of particular interest in the current study is that MOT, SOC, and SWM tests have been found to be sensitive to executive dysfunction as a result of depression and mood disorders in adults and adolescent females (Cambridge Cognition Ltd, 2006c; Mathewes, Coghill, & Rhodes, 2008). CANTAB comparisons are generated based on two normative studies investigating CANTAB performance on individuals aged 4 through 80+ (Robins et al., 1997; Robins et al., 1998) and samples in Minnesota and Brazil (De Luca et al., 2003; Luciana & Nelson, 2002; Roque et al., 2011). It should be noted that the normative sample from Minnesota (Luciana & Nelson, 2002) were collected without assessing measures of sleep problems or affective disturbances of anxiety or depression (M. Luciana, Personal Communication, May 8, 2013). In the current study, the following measures were utilized as primary dependent variables.
Motor Screening Test (MST): The MST is administered at the beginning of the CANTAB battery. The MST serves as a simple introduction to the touch screen method of responding on the CANTAB, screens for visual, movement, and overall comprehension difficulties, and serves as a measure of simple reaction time and pointing accuracy. Participants are instructed to touch flashing crosses that vary in spatial placement on the computer screen as quickly as possible. The outcome primary measure derived from the test measures speed of response.

Stockings of Cambridge (SOC): The SOC test is a spatial planning test derived from the original Tower of Hanoi Test (Simon, 1975) which provides a measure of frontal lobe mediated executive functioning in the area of planning. The test includes the participant being shown two displays of colored balls that appear to be stacked and held in suspended stockings on the top of the computer screen. After being provided a display on the top of the screen, the participant is required to copy the pattern shown by moving one ball at a time to the lower display to replicate the above image. Three primary outcome measures on the SOC test assess number of correct trials, response latency, and number of errors.

Spatial Working Memory (SWM): The SWM test is a test of visuospatial working memory. The first part of the test includes participants being shown colored squares on the computer screen, and the goal of the test is to find a blue token by touching each of the boxes (search and elimination). After finding each of the tokens, the participant is instructed to place each token on the right side of the screen until 8 tokens have been found and placed correctly. Variation in the color schemes of the boxes change on each trial to reduce rigid search strategies. The self-ordered search employed in the test further allows for heuristic strategy analysis. Primary outcomes measured search errors, strategizing, and perseverations.
Spatial Span (SSP): The SSP test assesses overall visuospatial working memory manipulation and capacity and is comparable to the Corsi Block task (Milner, 1971). The test assesses working memory capacity through looking at displays of white squares which change colors in a variable sequence. Following presentation the participant is required to touch each box that changed color in the same order as they originally changed. A reversal mode can also be administered that requires the participant to touch the boxes in reverse order. Outcome measures for the current study include span length, errors, and perseverations.

Choice Reaction Time (CRT): The CRT test is a 2-choice variation of the simple reaction time test (SRT), with the exception that simple stimulus are replaced with two possible stimuli and two response choices. This addition increases the complexity of the task and introduces response uncertainty. Specifically, the test displays arrow stimuli on either the right or left side of the testing screen and the participant must press the left arrow if the presentation is on the left side and press the right arrow if the stimuli are on the right side. The overall constructs assessed with the test are simple perception, alertness, and motor speed. Primary outcomes on this measure include omission errors and commission errors.

Stop Signal Test (SST): The SST is similar to classic stop signal response inhibition tests, which uses variation staircase functions to generate a metric of stop signal reaction time. The underlying construct measured on the test is the ability to inhibit prepotent response. The test is broken down into two parts. First the participant is introduced to the press pad and instructed to press the left arrow when they see a left arrow on the screen and to press the right arrow when they see a right arrow. Following 16 trials, the participant completes another set of trials that includes an auditory beep signal to indicate that the child should not press the button.
but should wait for the next signal to be presented. Measures from the SST were outcome metrics including errors and response times.

**Grooved Pegboard Test (GPT):** The GPT (Mathews, & Klove, 1964) is a complex test of manual precision that assists in measuring motor impairment in those ages 6 to 85 years old. Specifically, the GPT measures psychomotor speed, fine motor control, and rapid visual-motor coordination. The test has also been proposed to be an adequate measure of brain lateralization (Mitrushina, Boone, Razani, & D’Elia, 2005). The GPT consists of the standard 10.1mm x 10.1 mm Lafayette grooved pegboard (Lafayette instruments # 32025) which is a metal board with a matrix of 25 (5 x 5) randomly positioned slots. The test requires the patient to place 25 pegs that measure 3 mm in diameter and have a round and square edge into each of the holes in the matrix board. The patient is instructed to place all 25 pegs into the board as quickly as possible, first with the dominant then nondominant hand. Although methods for administering the GPT to children often only requires 10 pegs to be placed, the current study will employ suggested methods (Roselli, Ardila, Bateman, & Guzman, 2001; Strauss, Sherman, & Spren, 2006), and will be required to place all 25 pegs into the board. Two scores will be derived from this measure, including overall time taken to complete the task with dominant and nondominant hands.

Reliability of the GPT has been reported to be .69 to .76 for the dominant hand and between .68 and .78 for the nondominant hand over the course of a 6 month period in adults (Lezak, Howieson, & Loring, 2004), however, limited data is available for children. Few differences have been observed between genders or race, however, age has been a significant predictor of performance with performance improving during childhood into adolescence (Roselli, et al., 2001). In fact, between 30 to 34% of the variance between test scores may be
accounted for by age (Heaton, et al., 2004). The GPT has been found to be sensitive to depression, with lower performance being produced in adults with depression (Hinkin et al., 1992). The most up to date normative values available for school aged children were derived from a sample of 268 Spanish-speaking children form Bogata, Columbia, from which none were severely impaired intellectually. Scores derived from the current study were converted to $z$ scores based on the normative sample (Roselli, et al., 2001).

**Academic Instruments**

Woodcock Johnson III Tests of Achievement (WJ-III ACH; $M = 100$, $SD = 15$): The WJ-III ACH (Woodcock, McGrew, & Mather, 2001, 2007) has been derived and expanded from the WJ Tests of Achievement and the WJ-R (Woodcock & Johnson, 1977, 1989) to include seven additional tests and eight clusters (22 tests total) that measure academic achievement in five areas: reading, mathematics, written language, knowledge, and oral language. The test is based off of the Cattell-Horn-Carroll theory of cognitive abilities. Each of the five core areas includes tests that assess competence in basic skills, fluency, and application of academic skills. The Woodcock-Johnson III Normative Update (WJ-III NU; Woodcock et al. 2001, 2007) was published in 2007 and includes an updated normative sample for the test based on the 2005 United States census data. The updated standardization sample was based off of a representative sample of the United States that included 8,818 individuals between the ages of 24 months and 95+ years of age from more than 100 diverse United States sites. Stratification was made based on sex, race, Hispanic origin, occupational status, and 13 SES variables.

Reliability for the WJ-III ACH NU has been found to be moderate to superior. Individual subtest reliability coefficients based on Pearson coefficients have found subtest reliability to range from .69 to .96 and overall achievement cluster reliabilities range from .93 to .99 for retest
at approximately a year. Inter-rater reliability coefficients range from .71 to .99 for scores that require examiners to score subjective responses. Specific reliability coefficients for children aged 6 to 12 for the tests administered in the current study include have found to be the following: LW-ID (.84 - .92), RF (.59 - .78), AP (.85 - .92), SP (.75 - .91), UD (.83), and BA (.93 - .94). Validity for the use of the WJ-ACH III for the assessment of academic skills has been extensively established. Specifically, the test has good face and construct validity, and has been concurrently validated with cognitive and alternative academic achievement tests. Notably the WJ-III ACH has also demonstrated that compared to the norming sample, clinical samples of youth under the age of 19 with depression demonstrate lower scores in basic math ($d = .33$), basic reading ($d = .46$), and basic writing ($d = .46$).

One deviation was made to the administration of the Understanding Directions (UD) subtest from the standardization protocol, in that the standardization of the instrument utilizes an auditory compact disc that reads the instructions to the participant. The UD subtest for the current study was read aloud at an even pace by the neuropsychometric examiner. Normative comparisons were made based on age and grade comparisons to standardized scores (SS) for each test and index. All scores were computed utilizing the WJ-III NU Compuscore program version 3.0 (Shrank & Woodcock, 2007).

Letter-Word Identification (LW-ID): The LW-ID subtest is a measure of basic reading and decoding skills. The test requires the participant to identify and read words from a list.

Reading Fluency (RF): The RF test is a measure of reading and processing speed and basic reading comprehension. Task demands for the RF test includes reading and comprehending simple sentences and answering whether or not the statement is true or false within a 3-minute time limit.
Understanding Directions (UD): The UD subtest is a measure of listening ability and language development. During the test, participants are asked to follow directions instructed from an audio compact disc; however, for the current study the trained examiner read the directions. Specifically, the examiner reads instructions that increase in linguistic complexity and the child is asked to point to the specified pictures on a page with cartoon images.

Spelling (SP): SP requires the child to spell increasingly difficult words presented in an auditory manner from the examiner. It is a basic measure of the ability to spell dictated words.

Applied Problems (AP): AP requires the participant to identify pertinent mathematical information, comprehend presented problems, and perform increasingly complex mathematical information. The child is allowed to utilize paper and a writing utensil in order to execute the problems. The test is a measure of mathematical reasoning and the ability to analyze and solve mathematical problems.

Brief Achievement (BA): The BA measure is an approximated average of overall achievement level based on the average scores obtained from the LW-ID, AP, and SP subtests. The measure is an estimate of overall academic proficiency.

Parental Reported Academic Performance: As alluded to above, parental reported academic performance were obtained via parental report from the CBCL (Failing, Below Average, Average, Above Average). Specifically, academic performance was reported and coded to reflect scores comparable to a grade point average, with scores coded as the following; Failing (1), Below Average (2), Average (3), Above Average (4).

Nocturnal PSG

Overnight PSG has long been viewed as the “gold standard” for assessing sleep quantity, quality, and determining sleep architecture and measuring sleep parameters. In brief, PSG is a
physiological and objective measure of recording sleep that involves continuous, non-invasive recordings of the following: electroencephalogram (EEG), electro-oculogram (EOG), electrocardiogram (ECG), electromyelogram (EMG), and respiratory monitoring. Another primary use of PSG is to divide sleep into four stages based on defining EEG characteristics and the patterns of psychophysiological measurements (Iber et al., 2007) according to visual assessment and analysis of the psychophysiological measures by a RPSGT. Although PSG parameters in children have been found to demonstrate moderate to strong reliability (Wise, et al., 2011), reliability is contingent upon consistent visual scoring of polysomnograms.

The AASM proposed revised scoring parameters for visual polysomnogram interpretation in 2007 (Iber, et al., 2007). Partially facilitated by the findings and suggestions by Scholle and Schafer (1999) and the new AASM criteria, Novelli, Ferri, and Bruni (2010) compared quantitative sleep parameters obtained from both scoring methods and found scoring between the two methods to produce higher N1, reduced N3 and REM, and overall low consistency between scoring minutes of N1 vs. S1, N2 vs. S2, and in the number of sleep stage shifts per hour when comparing the new AASM guidelines to previous methods with the Scholle and Shafer suggestions for pediatrics. Despite this, Grigg-Damberger and a team of sleep medicine experts (2007), reviewed the reliability of visual and automatic scoring of pediatric polysomnograms and concluded visual scoring is more accurate than automatic scoring and reliability can be obtained at a high level (87 – 88%).

Further regarding psychometrics, an executive summary from a task force of pediatric sleep experts completed a comprehensive review of pediatric sleep literature in order to assess the reliability and validity of PSG for assessing sleep related respiratory problems in childhood. From the review of 243 manuscripts, it was found that PSG recordings for assessing SRBDs in
children have strong face and content validity. Moderate to strong convergent validity was found when comparing PSG respiratory recordings to valid alternative measures. Test-retest reliability is moderate to strong for assessing SRBDs in those with obesity, craniofacial abnormalities, metabolic syndromes, neurological problems, genetic disorders, and other neurodevelopmental disorders. Good predictive validity is also present for predicting perioperative difficulties and persistence of a SRBD following adenotonsillectomy when PSGs are conducted before the specified operations (Wise et al., 2011).

Methods employed for the current study required placement of electrodes according to standard criteria (Jasper, 1958). Specifically, the EEG electrodes were positioned according to the 10-20 system of measurement with two central (C3, C4) and one occipital (O2) location and are placed superior to the contralateral mastoids. Electromyogram (EMG) recordings were measured from chin-placed electrodes, and electrodes for right and left electro-oculogram (EOG) are also attached lateral to the right outer canthus and left outer canthus. An appropriate sized nasal cannula was used to measure airflow from the nose. Respiratory effort was measured from thoracic and abdominal placements via plethysmography with bands placed around the chest and abdomen. Oxyhemoglobin saturation was measured from either the left or right index finger by a pulse oximeter. A discrete microphone recording sensor was placed lateral to the trachea on the throat in order to record auditory snoring. Periodic limb movements (PLM) were measured by EMG electrodes placed on each of the anterior tibialis of each leg. ECG measures were taken from the chest according to the standard modified lead II configuration.

All signals were amplified, recorded and digitized by the Grass Technologies Twin® recording system and displayed and stored on a desktop computer. The sampling rate for the EEG, EMG, PLM, and ECG data was sampled at 200 Hz. The sampling rate for the snoring
sensor was 100 Hz, nasal airflow and respiratory effort was 10Hz, and oximetry was recorded at 1Hz. All digitized data was acquired, stored, and maintained at wide bandwidth amplitude. Prior to each recording session, a standard 50 microvolt, 10 Hz calibration signal was recorded for five minutes. The monitor display available to the sleep technician shows 30 seconds of data (1 epoch) at a time on a high-resolution 21-inch color monitor, on a continuing basis during recording. In-lab recordings were used to score all sleep and wake epochs then each were reviewed by a RPSGT.

Definitions for the present study include defining PLMs as four or greater movements of 0.5 to 5 seconds duration separated by no less than 4 and not greater than 90 seconds (Atlas Task Force of the American Sleep Disorders Association, 1993). Mild OSA was defined as having an RDI of ≥ 1.5 events per hour and > 5 events per hour. Moderate to severe OSA is defined as having an RDI of ≥ 5 events per hour. Children without an RDI ≥ 1.5 were defined as primary snorers (PS) due to all participants being referred for suspicion of sleep apnea and presence of snoring.

Sociodemographic Questionnaire

Sociodemographic Report Questionnaire (SRQ; Appendix C): The SRQ was created for the current study in order to assess rater relationship status to the child, race/ethnicity of the child, self-reported income for both parents, and marital status of each of the parents. The SRQ was used to describe the sample utilized to assess for potential confounds and covariates.

Procedures

Data for the current study was collected at baseline as part of an ongoing double-blind, cross-over randomized control trial investigating PAP therapy compared to sham therapy (Placebo PAP) to determine the effects of PAP on neurobehavioral outcomes and sleep
architecture. The project is part of the sleep apnea treatment study (SleepCATS) lead by primary investigator Kristen H. Archbold, RN, Ph.D. and co-investigators James Goodwin, Ph.D. and Stuart Quan M.D. The project is funded by the National Institute of Health; grant number R01 HL - 102151. All child participants and parents, primary researchers, research associates, and each clinical neuropsychometrist were blinded to the treatment status of each participant.

Treatment randomization was originally based off of stratification for BMI, ethnicity, and gender, and was conducted by the study’s project coordinator. Treatment blinding was maintained until the end of the entire 6-month study protocol, when the participants were notified of their treatment status. The age group for the current study was set due to large developmental differences between children’s sleep architecture between the ages of 5 and 6 as well as executive functioning and attentional network differences observed after the age of 12 into adolescence (Diamond, 2002; Montgomery-Downs, O’Brien, Gulliver, & Gozal, 2006; Welsh, 2002).

Recruitment

Following IRB approval, recruitment was initiated in June 2011 and continues to be ongoing. Children were recruited from a clinical pediatric sleep lab, from flyers (Appendix D), advertisements posted locally around the community, and from information provided as part of an informational television interview. Beginning October, 2011, recruitment also included sending a SRBD questionnaire to a diverse and largely Hispanic urban school district in the Southwest United States. In-clinic participants were asked if they would like to participate in the study through sleep lab personnel approaching willing parents and children at the local pediatric sleep clinic. Recruitment flyers were placed in community-based settings (hospitals, university buildings, community recreation centers, dentist offices, coffee shops, etc.) and asked those
interested in participating to call the SleepCATS project coordinator to see if they meet criteria for the primary study.

Recruitment from the school district was initiated following approval of the University of Arizona’s IRB office and the Office of Accountability and Research at the public school district in October, 2011. Following approval, principals from stratified schools based on grade (pre – K through 7th) and ethnicity were contacted and asked to participate in recruitment for the study. If approved by the principal, an introduction letter and consent form (Appendix E) accompanied a demographic and health questionnaire (Appendix B) in a premade packet to parents of each student in the school. The questionnaire includes four demographic questions, three health specific questions to assess for exclusion status for the study, and also included a psychometrically validated 22-item SRBD questionnaire (PSQ; Chervin et al., 2000). If the parent reported clinically significant SRBD problems, did not endorse exclusionary criteria, and left their contact information indicating interest in participating in the study, then the parent was contacted by study personnel for enrollment in the study.

**Anthropometric Assessment**

Participants who volunteered to enroll in the study were explained study protocol and completed informed consent procedures prior to undergoing neuropsychological testing at the University of Arizona College of Nursing or PSG study at the pediatric sleep clinic. Following consent, all participants had multiple anthropometric measures taken. Specifically, height measurements were taken utilizing a metric folding ruler while the child stood on a hard and flat surface. Weight measurements were taken using a portable electronic digital scale without additional clothing such as jackets or shoes worn by the child. Neck circumference was measured using an inelastic tape measure placed around the neck below the laryngeal
prominence and perpendicular to the elongated axis of the neck while the participant was sitting in the Frankfort horizontal plane position. Waist and hip measurements were taken around the abdomen and hips using standard measurement criteria while the participant was wearing light outerwear. All measurements were taken two times and only average measurements were used in analysis. Overweight and obesity status were determined based upon the height and weight of each child and converting them to nationalized BMI z-scores based on the Center for Disease Control metrics (CDC, 2013). Conversions from z-scores to percentiles were conducted by research staff, and obesity was defined as those participants that fall in the 95th or greater percentile for age and sex, and overweight was defined as those that fall in the 85th – 95th percentile.

Blood pressure measurements were taken by a neuropsychometrician who was trained in taking blood pressure measurements. All measurements were taken from the right arm using a portable mercury sphygmomanometer and appropriate cuff fitting for the size of the child’s arm. Initial cuff inflation pressure was determined by adding 30mmHg to the palpated systolic measurement and cuff deflation occurs at approximately 2mm per second. A second measurement was repeated following a 30 second latency period. Due to circadian effects on blood pressure, each blood pressure reading is taken at approximately the same time for each participant. Hypertension was defined as those participants that fell in the 90th percentile or greater for age and sex for either systolic or diastolic blood pressure, and hypotension was defined as those that fell in the 10th percentile or lower for systolic or diastolic blood pressure. All anthropometric measurements were taken by the neuropsychometrician received training from a registered nurse (P.I.; KHA) in the recording of each the above-specified measurements.
Neuropsychological Evaluation

Following anthropometric measurements, all participants underwent the same neuropsychological battery that was administered in a standardized order (KBIT-2, WJ III ACH, GPT, CANTAB). Assessment occurred between the hours of 8:00 and 12:00 ($M = 9:39$ and $12:04; SD = 1:32, 1:32$) and within a week prior to PSG study in order to minimize circadian rhythm and timing effects generated as a result of initiating PAP therapy on cognition. Average latency between neuropsychological evaluation and PSG was 1.52 days (Median = 2 days) and 4 participants obtained PSG and PAP titration prior to neuropsychological evaluation with unknown impact on neuropsychological outcomes. Each neuropsychological battery took approximately three hours in duration with a mean of 2 hours 34 minutes ($SD = 00:34$). Children were allowed breaks throughout testing to minimize testing fatigue. During the neuropsychological evaluation parents completed numerous sociodemographic, behavior, and sleep questionnaires in a separate room from the child who underwent evaluation. Parents also completed a school records release form to provide access to their child’s academic records. Due to limited completion of participants who completed school record releases, school records were not analyzed in the current study. All children were assessed by a clinically trained neuropsychometrist in a quiet and well-lit testing environment. Children were disqualified from the study if neuropsychological findings indicated overall intelligence scores two or more standard deviations below the norms ($N = 1$). Endorsement of critical items on psychometric questionnaires were also screened for immediate suicidal ideation, homicidal ideation, or intent to harm oneself or others. If significant threat was apparent, the protocol called for the primary investigator (KAH) to be informed and appropriate community based referrals to be made. No children were excluded for endorsement of imminent harm to self or others. All participants were
compensated for their time in the current study through providing all necessary PAP therapy equipment (i.e. PAP device, hoses, pillows, masks, etc.) and providing each participant $100 in gift cards for successful completion of the neuropsychological evaluation and two night in-lab PSGs. This compensation occurred at each time point for the overall study. All scoring of the neurobehavioral instruments and questionnaires administered in the present study were scored and interpreted by a doctoral student research associate in school psychology or a trained neuropsychometric technician.

**Nocturnal In-Lab PSG**

Full nocturnal in-lab PSG was conducted in the Tucson Medical Center (TMC) Pediatric Sleep Disorders Center on two sequential nights, which included an adaptation night. All children were required to have at least 4 hours of scorable sleep. Overnight PSG was conducted by a RPSGT with consultation from a licensed medical professional (Co-PI, S.Q.) who confirmed the diagnosis of OSA and made decisions regarding the qualification for research study participation. Primary sleep variables were computed for every patient utilizing a locally developed software program.

The PSG visit was initiated at approximately 18:00 on the nights of the study in order to provide participants with information regarding the procedure and to connect PSG equipment and electrodes. Parents were required to stay with the participant during all in-lab sleep nights, so a separate but nearby room and bed was provided for parental use in the sleep laboratory during the overnight stays.

During the first night, a registered polysomnographic technologist at the sleep laboratory performed pediatric PAP titration via industry specified guidelines and manually determined the appropriate pressure setting to acquire therapeutic threshold settings. In addition to titration, the
participants underwent two sequential nights in lab in order to reduce first-night artifact on PSG parameters, which has been shown to provide more valid measures of PSG recordings during the 2nd night PSG (Scholle et al., 2003). During sleep laboratory stays, lights out was aimed at approximately 20:00 – 22:00 ($M = 22:10$, $SD = 36:21$). On the second night, a PSG recording of the entire night of sleep was again conducted and subsequently scored and interpreted for use in analyses. Participants awoke at their own time or were awakened by 7:00 by sleep lab staff, if not awake.

**Data Analyses**

Data analyses employed in the current study first included a descriptive summary of sample characteristics. Prior to analysis normality of distribution of dependent variables were assessed for kurtosis, and via Q-Q plots and checked for outliers and need to conduct transformations to the data. Due to some skewed distribution and outlying data on the GPT, scores were truncated at three standard deviations below the mean, which resulted in altering 2 scores (1 mild OSA, 1 moderate–severe OSA). These scores were altered due to scores outside this cutoff occurring rarely in normative samples (Mitrushina et al., 2005). There were no other transformations found necessary for transformation. Three subjects had more severe OSA compared to the rest of the sample (RDI: 19.1, 20.1, 27.6), but were retained in analysis due to similarities between demographic characteristics between these participants and other children in the sample.

Due to the underpowered nature of the study (compromised power .52), primary data analyses were conducted utilizing multivariate analysis of variance (MANOVA) models. The use of MANOVA analysis was deemed most appropriate for the current study for multiple reasons. First the primary purpose of the study was to best determine the impact of clinically
meaningful depressive symptoms and OSA severity on neurocognition and academic performance, thus the use of categorical cut-scores were used in the MANOVA for clinical relevance. Secondly, the statistical power of moderation when analyzing variables in their continuous form will result in particularly low power (McClelland & Judd, 1993), so the MANOVA would optimize the opportunity for reducing type-2 error. Lastly, due to numerous variables being evaluated within the same subtest and construct, the use of MANOVA allowed for the testing of multiple neuropsychological and academic outcome measures without further inflating the risk of making type 1 error and accounting for associations between the dependent variable. Due to the current study utilizing a group of participants that were void of OSA and averaging RDI severity comparable to morbidity free normative values from large cohorts of children, normative comparisons were not deemed valuable in the current study. In addition, due to small cell size on normative values on the CANTAB, and having no knowledge of sleep or affective symptoms from the normative values (M. Luciana, Personal Communication, May 8, 2013), normative comparisons were not deemed to be of major value in the current study. Of additional note, the current study also utilized clinical depressive cut off scores as $T \geq 63$ due to better discrimination between clinical vs. nonclinical depressive groups over the commonly used $T \geq 60$. The use of this cutoff resulted in one participant with depressive symptoms $T \geq 60$ being included in the nondepressed group.

Prior to analysis, the group by covariate distribution was checked for potential confounds to the analysis including the use of Fisher Exact Tests, Chi Square, Kruskal Wallis H-Tests (Income, time between PSG and neuropsychological evaluation) and analysis of variance models (age, BMI, PLMs) to determine if groups significantly differed on potential confounding factors in the analysis. Normal distribution of variables was checked for significance via Shapiro-Wilk
tests.

The following questions and hypotheses were investigated:

1. Do children with mild or moderate/severe OSA (RDI 1.5 ≤ 5 vs. > 5) and mild vs. clinical depressive symptoms (CBCL-Anxious/Depressed or Withdrawn/Depressed T ≥ 63) experience reduced neurocognitive performance compared to children without sleep apnea (RDI < 1.5)?

2. Do children with mild or moderate/severe OSA (RDI 1.5 ≤ 5 vs. > 5) and mild vs. clinical depressive symptoms (CBCL-Anxious/Depressed or Withdrawn/Depressed T ≥ 63) experience reduced neurocognitive performance compared to children without sleep apnea?

3. Do children with mild or moderate/severe OSA (RDI 1.5 ≤ 5 vs. > 5) and mild vs. clinical depressive symptoms (CBCL-Anxious/Depressed or Withdrawn/Depressed T ≥ 63) experience reduced neurocognitive performance compared to children without sleep apnea?

   a. Hypothesis 1a: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures of working memory.

   b. Hypothesis 1b: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures of planning.

   c. Hypothesis 1c: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures of fine motor speed.
d. Hypothesis 1d: There will be a main effect on severity of OSA with those with Moderate-Severe OSA performing lower on measures of working memory compared to those without OSA.

e. Hypothesis 1e: There will be a main effect on severity of OSA with those with Moderate-Severe OSA performing lower on measures of attention/vigilance compared to those without OSA.

f. Hypothesis 1f: There will be an interaction between clinical depressive symptoms and OSA severity on tasks of working memory, with those who have Moderate Severe OSA and clinical depressive symptoms exhibiting lower performance than all other groups.

4. Do children with mild or moderate/severe OSA (RDI 1.5 ≤ 5 vs. > 5) and mild vs. clinical depressive symptoms (CBCL-Anxious/Depressed or Withdrawn/Depressed T ≥ 63) experience reduced academic achievement compared to those without sleep apnea?

a. Hypothesis 2a: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures Applied Problems.

b. Hypothesis 2b: There will be a main effect of the presence of clinical depressive symptoms, with those exhibiting clinical symptoms performing lower on measures Reading Fluency.

c. Hypothesis 2c: There will be an interaction effect between presence of clinical depressive symptoms and severity of OSA for Applied Problems, with those who have Moderate-Severe OSA and clinical depressive symptoms exhibiting lower performance than all other groups.
d. Hypothesis 2d: There will be no significant main effect or interaction effects between groups on measures of Letter Word Identification, Understanding Directions, Brief Achievement, or parent reported academic performance.

All hypotheses were investigated through the use of a one way multivariate analysis of variance (MANOVA) model using a 3x2 design (PS, PS Depression, Mild OSA, Mild OSA Depression, Moderate Severe OSA, Moderate Severe OSA Depression) and accounted for covariates that have been theoretically or empirically identified as potential confounds (MANCOVA). First, analyses were checked for violation of the assumption of homogeneity of variances have been violated between factors. In order to maximize power, covariates were only maintained in the analysis if it was significantly correlated with the dependent measures or differed between groups. Due to marked consistency in the presence of clinically measured depressive symptoms in the sample, separate analyses were not conducted for Anxious/Depressed and Withdrawn/Depressed symptoms in order to minimize redundancy and increased error in testing. In order to determine specific effects within the multivariate analysis, follow-up univariate analyses and post-hoc testing (Bonferroni corrections, Tukey post-hoc tests) were conducted when significant multivariate effects were found. The Tukey post-hoc test was chosen for its utility in determining significant difference with small sample sizes without inflating risk of type 2 error as could occur with the Scheffe test. Wilk’s Lambda tests were used for significance testing of multivariate analyses and eta squared was used to measure effect size. Independent sample t-tests were used to determine differences between two groups (sex, clinical depressive symptoms) on demographic grouping factors, and zero order Pearson correlations were used to determine relations between continuous variables while Spearman rank-order correlations were used to determine relations between ranked data. Chi Square and Fisher Exact
tests were used to determine significant proportions of characteristics between groups. All data analysis were conducted using the Statistical Package for the Social Sciences for windows version 20.0 (SPSS; IBM, Armonk, NY).
Chapter 4

Analysis and Results

This chapter will provide an overview of the participants and will present the analysis of the statistical methods employed in the present study. Analysis of hypotheses will be conducted and summarized.

Sample Comparisons

An independent samples t-test indicated that there were no significant difference in males vs. females for Anxious/Depressed, $t(37) = .79, p = .492$, or Withdrawn Depressed symptoms $t(37) = 1.32, p = .089)$. Pearson correlations also highlighted age was not significantly associated with Anxious/Depressed ($r = -.11, p = .518$) or Withdrawn/Depressed ($r = -.11, p = .522$) symptoms. Those with clinical Anxious/Depressed or Withdrawn/Depressed also did not have higher RDI’s compared to those without clinical symptoms $t(37) = .77, p = .45$.

Prior to primary analysis, groups that were determined based on the clinically derived scores were compared on demographic, sleep, and neuropsychological characteristics. Analysis of variance (ANOVA) indicated no differences across groups in age, mother’s educational level, father’s educational level, or start or end times for neuropsychological testing ($p > .05$). Chi Square and Fisher Exact tests also did not identify significant differences between groups on proportions of ethnicity, sex, or primary language spoken at home between groups ($p > .05$). As expected, the clinically depressed groups all had significantly higher depressive symptoms for Anxious Depressed and Withdrawn Depressed symptoms $p < .001$ (Table 2). Specifically, all clinically depressed groups had significantly more depressive symptoms compared to nondepressed groups, but differences between OSA severity were not significant. Although no differences between confounding factors between groups were found, correlations between
demographic and neuropsychological characteristics identified significant associations with age and measures of attention/vigilance, family education and working memory, and family education on academic achievement and parent reported academic performance. As a result, these were entered as covariates in MANCOVA analysis along with overall intellectual abilities (IQ). Correlation matrix of descriptive and confounding variables and associations with pertinent neuropsychological test performance is displayed in Table 3.

Group differences between health characteristics and PSG measures also were not significantly different between groups on Fisher Exact Tests for proportions of overweight and obese participants or for participants with tonsils removed ($p > .05$). ANOVA analysis also did not identify significant differences between groups on BMI percentile, PLM index, mean oxygen saturation, or oxygen saturation nadir measurements ($p > .05$). Consistent with the groupings made on depressive symptoms, ANOVA was significant ($p < .001$) for RDI between OSA severity groupings (Table 3). Nondepressed groups were not significantly different from each other ($p > .05$).

**Group Comparisons**

Primary analysis for the study utilized multivariate analysis with univariate results provided for in depth analysis of the findings. MANCOVA analysis was conducted on several sets of primary dependent variables that were grouped based on a conceptual basis within consistent constructs. Although intelligence was not deemed a primary outcome variable in this study, it was used as a covariate throughout each analysis and was first assessed across groups (Table 5). Overall intelligence scores were $98.71 (SD = 13.97)$ for the entire group. To test the first hypothesis, a MANCOVA was conducted between groups with Verbal and Nonverbal intelligence as dependent measures and family income and education entered as covariates due to
Table 2.

Demographic and Neuropsychological Characteristics

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>PS (N = 5)</th>
<th>PS + D (N = 5)</th>
<th>Mild OSA (N = 13)</th>
<th>Mild OSA+D (N = 5)</th>
<th>M-S OSA (N = 5)</th>
<th>M-S OSA + D (N = 5)</th>
<th>P-Value</th>
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<td>Female</td>
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<td></td>
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<td></td>
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</tr>
<tr>
<td>Male</td>
<td>20 (1)</td>
<td>60 (3)</td>
<td>76.92 (10)</td>
<td>60 (2)</td>
<td>40 (2)</td>
<td>80 (4)</td>
<td>.587(^a)</td>
</tr>
<tr>
<td>Female</td>
<td>80 (4)(^a)</td>
<td>40 (2)</td>
<td>23.08 (3)</td>
<td>40 (2)</td>
<td>60 (3)(^a)</td>
<td>20 (1)</td>
<td></td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>White/nonHispanic</td>
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<td>20 (1)</td>
<td>30.77 (4)</td>
<td>20 (1)</td>
<td>60 (3)</td>
<td>20 (1)</td>
</tr>
<tr>
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<td>60 (3)</td>
<td>46.15 (6)</td>
<td>40 (2)</td>
<td>20 (1)</td>
<td>80 (4)</td>
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</tr>
<tr>
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</tr>
<tr>
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<tr>
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<td>20 (1)</td>
<td>20 (1)</td>
<td></td>
<td></td>
<td>.386(^b)</td>
</tr>
<tr>
<td>Primary Language</td>
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<td>60 (3)</td>
<td>80 (4)</td>
<td>76.92 (10)</td>
<td>40 (2)</td>
<td>100 (5)</td>
<td>60 (3)</td>
</tr>
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<td>Spanish</td>
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<td>7.89 (1)</td>
<td>20 (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>English/Spanish</td>
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<td>20 (1)</td>
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<td>20 (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>Neuropsychological Characteristics</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time Start</td>
<td>9:06(1:05)</td>
<td>9:01(1:22)</td>
<td>9:40(1:21)</td>
<td>9:36(0:32)</td>
<td>11:21(2:51)</td>
<td>9:12(0:34)</td>
<td>.152(^c)</td>
</tr>
<tr>
<td>Time End</td>
<td>11:18(1:24)</td>
<td>11:18(0:57)</td>
<td>12:12(1:28)</td>
<td>11:55(0:38)</td>
<td>13:47(2:35)</td>
<td>11:41(0:14)</td>
<td>.093(^c)</td>
</tr>
<tr>
<td>Anxious/Depressed</td>
<td>53.40(2.60)</td>
<td>68.50(5.18)</td>
<td>51.92(2.49)</td>
<td>74.00(6.16)</td>
<td>50.20(4.5)</td>
<td>64.00(5.43)</td>
<td>&lt;.001(^d)</td>
</tr>
<tr>
<td>Dep/Withdrawn</td>
<td>54.00(2.83)</td>
<td>66.40(5.89)</td>
<td>53.54(4.48)</td>
<td>67.20(8.41)</td>
<td>51.00(1.41)</td>
<td>69.60(7.27)</td>
<td>&lt;.001(^d)</td>
</tr>
<tr>
<td>Family Income</td>
<td>51,800</td>
<td>45,000</td>
<td>54,000</td>
<td>56,000</td>
<td>68,000</td>
<td>48,000</td>
<td>.517(^c)</td>
</tr>
<tr>
<td>Mother Education</td>
<td>13.00(2.58)</td>
<td>13.00(2.54)</td>
<td>14.61(4.89)</td>
<td>15.00(1.87)</td>
<td>13.25(1.89)</td>
<td>13.50(1.00)</td>
<td>.874(^d)</td>
</tr>
<tr>
<td>Father Education</td>
<td>11.25(1.50)</td>
<td>12.00(0.00)</td>
<td>11.61(4.59)</td>
<td>13.40(2.61)</td>
<td>13.50(2.38)</td>
<td>12.00(2.00)</td>
<td>.848(^d)</td>
</tr>
</tbody>
</table>

Note: \(^1\)Values presented as percent % of sample (N). \(^\ast\)There were only 3 left handed participants between the groups. \(^\ast\)indicates left handed participants (N =1). 
P-Values presented from data analysis: \(^a\)Chi Square, \(^b\)Fisher Exact Tests, \(^c\)Kruskal Wallis H Tests, \(^d\)one way analysis of variance (ANOVA). Primary Snoring (PS), Moderate Severe OSA (M-S), clinical depressive symptoms (+ D), Time Start indicates time neuropsychological testing began and Time End indicates time testing was completed. Parent income represented as median self-reported income, education presented in years.
their significant relations to these measures. Multivariate analysis revealed no significant main
effects for depressive symptoms, $\lambda = .99$, $F(2,31) = .18$, $p = .840$, $\eta^2 = .01$, OSA severity $\lambda = .88,$
$F(2,62) = 1.05$, $p = .390$, $\eta^2 = .06$, or any interaction effects $\lambda = .154$, $F(2,62) = 1.54$, $p = .201$, $\eta^2$
$= .09$. Separate univariate ANCOVA was conducted on overall IQ due to the Verbal and
Nonverbal measures cumulating into this score. This ANCOVA analysis was also nonsignificant
across groups when controlling for family income and educational level for OSA severity,
$F(5,32) = 1.72$, $p = .195$, $\eta^2 = .09$, depressive symptoms $F(5,32) = .17$, $p = .682$, $\eta^2 = .01$, or any
interaction effects $F(5,32) = .82$, $p = .450$, $\eta^2 = .05$.

**OSA Severity and Depressive Symptoms on Working Memory**

The first primary analysis investigated the first two hypotheses proposing there would be
a significant main effect for depressive symptoms and an interaction effect for the combination
of clinical depressive symptoms and severity of OSA. Although working memory and planning
are theoretically associated with executive functioning and frontal lobe dysfunction, tasks of
working memory and planning were evaluated in separate MANOVAs in order to optimize
power and reduce error of the multivariate analysis with small sample size.

The first MANCOVA analysis of working memory was conducted on the Spatial Span
test (SSP) with the outcome measures of longest span length, total errors, and error usage as
dependent variables while controlling for covariates of family educational level and intelligence.
Results from the MANCOVA revealed overall significant main effects for OSA severity, $\lambda =$
.58, $F(6,46) = 2.42$, $p = .041$, $\eta^2 = .24$, but no main effects for depressive symptoms, $\lambda = .07$,$F(3,32) = .07$, $p = .976$, $\eta^2 = .01$, or interactions of OSA and depression, $\lambda = .78$, $F(6,46) =$
.825, $p = .593$, $\eta^2 = .09$. Follow-up ANOVA’s revealed that specific group differences
Table 3.

*Health and PSG Characteristics Between Groups*

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>BMI</td>
<td>78.95(20.77)</td>
<td>72.18(32.41)</td>
<td>80.58(21.43)</td>
<td>53.96(30.88)</td>
<td>51.94(33.20)</td>
<td>93.42(6.84)</td>
<td>.076a</td>
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<td>Overweight</td>
<td>20 (1)</td>
<td>40 (4)</td>
<td>7.69 (1)</td>
<td>20 (1)</td>
<td>60 (3)</td>
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<td>.289a</td>
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<tr>
<td>Obese</td>
<td>20 (1)</td>
<td>20 (1)</td>
<td>46.15 (6)</td>
<td>20(1)</td>
<td>60 (3)</td>
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<td>.225a</td>
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<tr>
<td>Tonsils</td>
<td>23.08 (3)</td>
<td>61.54 (8)</td>
<td>80 (4)</td>
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<td>20 (1)</td>
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<td>.554a</td>
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<tr>
<td></td>
<td>60 (3)</td>
<td>80 (4)</td>
<td>61.54 (8)</td>
<td>80 (4)</td>
<td>20 (1)</td>
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</tr>
</tbody>
</table>

**PSG Measure**

| RDI                   | .16(.18)  | .52(.38)      | 2.71(1.33)        | 2.94(1.18)         | 12.02(8.83)   | 13.81(5.69)        | <.001b  |
| PLM Index             | 1.17(7.2) | 1.01(.98)     | 3.92(6.09)        | 1.84(3.4)          | 1.84(3.2)     | 0.00(0.0)          | .665b   |
| Mean O₂               | 97.90(.62) | 97.70(.42)   | 96.60(1.50)       | 97.18(1.18)        | 97.54(.38)    | 97.30(1.49)        | .456b   |
| Nadir O₂              | 90.63(3.25) | 91.68(1.89)  | 87.57(4.17)       | 92.66(3.31)        | 87.30(5.39)   | 83.93(8.89)        | 1.08b   |

Note: Values presented from data analysis: *Fisher Exact Tests, one way analysis of variance (ANOVA). Primary Snoring (PS), Moderate Severe OSA (M-S), clinical depressive symptoms (+ D), Values presented as percentile rank (SD), Values presented as percent % of sample (N), Values presented as mean (SD). Overweight participants were classified as having BMI percentiles of 85+, Obese was defined as having a BMI percentile rank of 95+. PSG measures include respiratory disturbance index (RDI), periodic limb movement index (PLM Index), Mean O₂ indicates average blood oxygen saturation recorded via oximetry during overnight PSG, Nadir O₂ is minimum oxygen saturation recording observed during PSG study.
Table 4.

Correlation Matrix of Descriptive and Neuropsychological Variables

<table>
<thead>
<tr>
<th>Measure</th>
<th>Age</th>
<th>Inc$^1$</th>
<th>Ed-M</th>
<th>Ed-F</th>
<th>A/D</th>
<th>D/W</th>
<th>BMI</th>
<th>RDI</th>
<th>PLMi</th>
<th>M-O$_2$</th>
<th>Min O$_2$</th>
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<tbody>
<tr>
<td>Inc$^1$</td>
<td>.15</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ed-M</td>
<td>-.18</td>
<td>.68**</td>
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<td></td>
</tr>
<tr>
<td>Ed-F</td>
<td>-.19</td>
<td>.43*</td>
<td>.55*</td>
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<td></td>
</tr>
<tr>
<td>A/D</td>
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<td>-.08</td>
<td>.07</td>
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<tr>
<td>D/W</td>
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<td>-.24</td>
<td>.02</td>
<td>-.07</td>
<td>.73**</td>
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<td>.02</td>
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<td>.08</td>
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<td>PLM-I</td>
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<td>.31</td>
<td>-.11</td>
<td>.04</td>
<td>-.31</td>
<td>-.21</td>
<td>-.19</td>
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<tr>
<td>M-O$_2$</td>
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<td>.51*</td>
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<td>.22</td>
<td>.24</td>
<td>.13</td>
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<tr>
<td>SWMWithin</td>
<td>-.18</td>
<td>.26</td>
<td>.41*</td>
<td>.27</td>
<td>.21</td>
<td>.59*</td>
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<td>.51*</td>
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<td>.31</td>
<td>.31</td>
<td>.59*</td>
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<td>.27</td>
<td>.31</td>
<td>.20</td>
<td>.18</td>
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<td>.19</td>
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<tr>
<td>SSPUse</td>
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<td>.29</td>
<td>.12</td>
<td>-.49*</td>
<td>-.14</td>
<td>-.24</td>
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<td>SST Go</td>
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<td>-.16</td>
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<td>-.14</td>
<td>.14</td>
<td>-.14</td>
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<tr>
<td>SSt Last</td>
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<td>-.16</td>
<td>.12</td>
<td>.26</td>
<td>.05</td>
<td>-.56*</td>
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<td>.22</td>
<td>-.21</td>
<td>-.14</td>
<td>.08</td>
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<tr>
<td>MOT Lat.</td>
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<td>.27</td>
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<td>.13</td>
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<tr>
<td>MOT Error</td>
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<td>.29</td>
<td>.24</td>
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<td>-.24</td>
<td>-.19</td>
<td>-.11</td>
<td>.08</td>
<td>.16</td>
</tr>
</tbody>
</table>

Note: $^*$ significant at $p < .01$, $^{**}$ significant at $p < .05$. $^1$ Tests include p-values from Pearson zero-order correlations, $^2$ Indicate tests include p-values form Spearman rank-order correlations. Income (self-reported family income), Ed-M (maternal education), Ed-F (father education), A/D (Anxious Depressed symptoms), D/W (Depressed Withdrawn), M-O$_2$ (mean oxygen saturation), Min O$_2$ (minimum oxygen saturation), Stockings of Cambridge (SOC), SOCThink (initial thinking time), SOCMove (number of moves), SOCSubThink (subsequent thinking time), Spatial Span Test (SSP), SSPSpan (length of memory span), SSPError (number of errors), SSPUse (error usage), Short Term Working Memory (SWM), SWMBetween (between errors), SWMDouble (double errors), SWMStrategy (strategy score), SWMError (total errors), SWMWithin (within trial errors), Choice Reaction Time (CRT), CRT Lat. (response latency), CRT S.D. (latency standard deviation), SST Go (response time on go trials), SST Last (response time last half), Motor Screening Test (MOT), MOT Lat. (response latency), MOT Error (number of errors).
### Table 5.

**Intelligence Scores Between Groups Based on RDI and Depressive Symptoms**

<table>
<thead>
<tr>
<th>Measure</th>
<th>PS (N = 5)</th>
<th>PS + D (N = 5)</th>
<th>Mild OSA (N = 13)</th>
<th>Mild OSA + D (N = 5)</th>
<th>M-S OSA (N = 5)</th>
<th>M-S OSA + D (N = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal IQ&lt;sup&gt;a,1&lt;/sup&gt;</td>
<td>87.40(15.69)</td>
<td>98.40(14.74)</td>
<td>98.92(14.13)</td>
<td>103.00(15.05)</td>
<td>107.00(92.40)</td>
<td>92.40(7.16)</td>
</tr>
<tr>
<td>Riddles&lt;sup&gt;2&lt;/sup&gt;</td>
<td>7.60(1.30)</td>
<td>8.69(2.91)</td>
<td>9.15(3.02)</td>
<td>10.20(3.11)</td>
<td>10.00(1.58)</td>
<td>7.80(2.39)</td>
</tr>
<tr>
<td>Verbal Knowledge&lt;sup&gt;2&lt;/sup&gt;</td>
<td>8.00(2.65)</td>
<td>10.20(3.11)</td>
<td>9.85(1.95)</td>
<td>10.20(3.27)</td>
<td>11.80(1.92)</td>
<td>9.60(1.14)</td>
</tr>
<tr>
<td>Nonverbal IQ&lt;sup&gt;a,1&lt;/sup&gt;</td>
<td>90.60(17.59)</td>
<td>97.60(10.97)</td>
<td>105.38(15.86)</td>
<td>102.00(23.31)</td>
<td>92.20(11.10)</td>
<td>98.40(14.35)</td>
</tr>
<tr>
<td>Composite IQ&lt;sup&gt;b,1&lt;/sup&gt;</td>
<td>87.40(17.88)</td>
<td>97.80(12.68)</td>
<td>102.77(11.29)</td>
<td>103.00(21.85)</td>
<td>99.80(7.29)</td>
<td>98.60(14.78)</td>
</tr>
</tbody>
</table>

Note: Scores presented from KBIT-2 test of cognitive abilities. <sup>a</sup>No significant multivariate (MANCOVA) main or interaction effects were found between groups.<br><sup>b</sup>No significant univariate (ANCOVA) main or interaction effects found between groups. Primary Snoring (PS), M-S OSA (Moderate-Severe OSA), clinical depressive symptoms (+ D). <sup>1</sup>Values presented are standard scores M = 100, SD = 15. <sup>2</sup>Values presented as scaled scores M = 10, SD = 3.
Figure 1.

Means of Total Error Usage on SSP Task Between Groups

![Graph showing means of total error usage on SSP task between groups.](image)

Note: SSP (Spatial Span Test), Tukey HSD Post-Hoc test of one way ANOVA identified Moderate-Severe (MS) OSA subjects performed significantly lower than those in Mild OSA group after Bonferroni Corrections $F(2,35) = 5.122$, $p = .011$, $\eta^2 = .234$

appeared to be due to group differences on the measure of total error usage during the task, even after making Bonferroni corrections for multiple testing. Tukey HSD test of one way ANOVA identified Moderate-Severe (MS) OSA subjects displayed significantly more errors on the SSP task than the Mild OSA group after Bonferroni Correction, $F(2,35) = 5.122$, $p = .011$, $\eta^2 = .234$ (Figure 1).

Multivariate analysis for the Spatial Working Memory test (SWM) was conducted on dependent variables of between trial errors, double trial errors, total errors, within trial errors, and overall strategizing scores with overall intelligence and family education entered as covariates. Results from the MANCOVA demonstrated no significant main effects on OSA severity, $\lambda = .84$, $F(6,46) = .41$, $p = .748$, $\eta^2 = .11$, depressive symptoms, $\lambda = .89$, $F(6,46) =$
.53 p = .932, \( \eta^2 = .09 \), or interaction effects between OSA severity and depressive symptoms, \( \lambda = .707, F(6,46) = .83, p = .081, \eta^2 = .16 \), on SWM tasks.

**OSA Severity and Depressive Symptoms on Executive Functioning (Planning)**

Hypothesis three proposed there would be a main effect for depressive symptoms on measures of planning. A MANCOVA with the dependent variables of initial planning time, subsequent planning time, number of moves, and problems solved in minimum number of moves were entered as dependent variables and intelligence was entered as a covariate. Results from the MANCOVA highlighted no significant main effects on OSA severity, \( \lambda = .73, F(10,30) = .50, p = .875, \eta^2 = .14 \), depressive symptoms, \( \lambda = .94, F(5,30) = .94, p = .484, \eta^2 = .14 \), or interaction effects between OSA severity and depressive symptoms, \( \lambda = .89, F(10,30) = .56, p = .529, \eta^2 = .13 \). Table of executive functioning and working memory is presented in Table 6.

**Severity and Depressive Symptoms on Attention/Vigilance**

Analysis of hypothesis four, suggesting there would be a main effect on OSA severity on measures of attention was conducted using the dependent measures of response latency on correct items (Latency) and variability of response latency (SD Latency) on the Choice Reaction Time (CRT) test and response latency on go-trials and during the last-half of the Stop Signal Test (SST). Due to no normative value being available on this measure and finding age significantly associated with the outcome measures, age and intellectual functioning were entered as covariates while comparisons were made on raw scores. Results from the MANCOVA indicated no significant for main effects on OSA severity, \( \lambda = .81, F(8,46) = .65, p = .744, \eta^2 = .09 \), depressive symptoms, \( \lambda = .96, F(4,23) = .27, p = .612, \eta^2 = .14 \), or interaction effects between
Table 6.

Executive Functioning and Working Memory Scores

<table>
<thead>
<tr>
<th></th>
<th>PS (N = 5)</th>
<th>PS + D (N = 5)</th>
<th>Mild OSA (N = 13)</th>
<th>Mild OSA+D (N = 5)</th>
<th>M-S OSA (N = 5)</th>
<th>M-S OSA + D (N = 5)</th>
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<tbody>
<tr>
<td>SOCa</td>
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<td></td>
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<td></td>
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</tr>
<tr>
<td>Initial Thinking</td>
<td>.80(.46)</td>
<td>1.01(.19)</td>
<td>.83(.31)</td>
<td>1.08(.11)</td>
<td>.85(.43)</td>
<td>1.04(.09)</td>
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<tr>
<td>Moves</td>
<td>.05(.22)</td>
<td>-.41(.78)</td>
<td>-.47(1.16)</td>
<td>-.47(1.16)</td>
<td>-.76(.14)</td>
<td>-.96(1.12)</td>
</tr>
<tr>
<td>Sub-Thinking</td>
<td>.49(.67)</td>
<td>.54(.28)</td>
<td>.45(.61)</td>
<td>.64(.48)</td>
<td>.66(.14)</td>
<td>.69(.34)</td>
</tr>
<tr>
<td>Problem Solved</td>
<td>-.45(.69)</td>
<td>-1.04(.44)</td>
<td>-.69(.67)</td>
<td>-.96(.48)</td>
<td>-1.04(.76)</td>
<td>-1.04(.44)</td>
</tr>
<tr>
<td>SWMb</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Btw Errors</td>
<td>-.55(.59)</td>
<td>-.47(.44)</td>
<td>-.21(.83)</td>
<td>-.41(1.15)</td>
<td>-.75(.72)</td>
<td>-.51(.46)</td>
</tr>
<tr>
<td>Double Errors</td>
<td>.43(.13)</td>
<td>.44(.23)</td>
<td>.46(.17)</td>
<td>.23(.40)</td>
<td>.21(.31)</td>
<td>.39(.12)</td>
</tr>
<tr>
<td>Strategy</td>
<td>-.55(1.39)</td>
<td>-.85(.49)</td>
<td>-.28(1.13)</td>
<td>-.55(.83)</td>
<td>-.71(.82)</td>
<td>-.92(.61)</td>
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<tr>
<td>Total Errors</td>
<td>-.49(.56)</td>
<td>-.44(.42)</td>
<td>-.15(.81)</td>
<td>-.35(1.10)</td>
<td>-.68(.71)</td>
<td>-.46(.44)</td>
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<tr>
<td>Within Errors</td>
<td>.52(.15)</td>
<td>.44(.19)</td>
<td>.37(.29)</td>
<td>.37(.29)</td>
<td>.35(.27)</td>
<td>.44(.17)</td>
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<tr>
<td>Span Length</td>
<td>-.56(.62)</td>
<td>-.42(.67)</td>
<td>-.21(1.23)</td>
<td>.13(1.43)</td>
<td>.03(.66)</td>
<td>-.49(1.19)</td>
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<tr>
<td>Total Error</td>
<td>.19(.87)</td>
<td>-.34(.67)</td>
<td>-.02(.99)</td>
<td>-.58(1.65)</td>
<td>-.34(1.00)</td>
<td>.19(1.13)</td>
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<tr>
<td>Total Error Use</td>
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<td>-.04(1.27)</td>
<td>1.14(.49)</td>
<td>.65(.54)</td>
<td>-.56(1.64)</td>
<td>.31(.49)</td>
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</tbody>
</table>

Note: Scores presented from CANTAB: Stockings of Cambridge (SOC). aNo significant multivariate main or interaction effects were found between groups. Short-Term Working Memory (SWM). bNo significant univariate main or interaction effects found between groups. Spatial Span (SSP). cSignificant multivariate main effect for OSA severity $\lambda = .58, F(6,46) = 2.42, p = .041, \eta^2 = .24$, no significant main effect for depressive symptoms or interaction effects. Primary Snoring (PS) M-S OSA (Moderate-Severe OSA), clinical depressive symptoms (+ D)
Table 7.

Mean Scores on Measures of Attention and Vigilance

<table>
<thead>
<tr>
<th>Attention/Vigilance</th>
<th>PS (N = 5)</th>
<th>PS + D (N = 5)</th>
<th>Mild OSA (N = 13)</th>
<th>Mild OSA+D (N = 5)</th>
<th>M-S OSA (N = 5)</th>
<th>M-S OSA + D (N = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT^a Latency</td>
<td>561.41(62.56)</td>
<td>545.83(124.35)</td>
<td>548.96(153.94)</td>
<td>642.89(269.06)</td>
<td>717.49(324.71)</td>
<td>653.41(197.51)</td>
</tr>
<tr>
<td>S.D. Latency</td>
<td>219.44(84.97)</td>
<td>204.31(88.72)</td>
<td>218.31(115.09)</td>
<td>213.67(110.78)</td>
<td>240.00(133.46)</td>
<td>246.88(131.36)</td>
</tr>
<tr>
<td>SST^a Go Trials</td>
<td>696.30(184.31)</td>
<td>735.60(263.93)</td>
<td>752.09(422.56)</td>
<td>760.92(197.21)</td>
<td>753.63(279.62)</td>
<td>634.25(161.65)</td>
</tr>
<tr>
<td>Last-Half</td>
<td>315.15(62.87)</td>
<td>339.32(74.36)</td>
<td>321.76(276.71)</td>
<td>313.06(145.33)</td>
<td>319.46(141.53)</td>
<td>316.42(86.18)</td>
</tr>
</tbody>
</table>

Note: Scores presented from CANTAB: Choice Reaction Time Test (CRT), Stop Signal Test (SST) in Milliseconds; mean (SD). S.D. Latency measures standard deviation variability of mean latency to response. Moderate-Severe OSA (M-S), with clinical depressive symptoms (+ D). ^a No significant multivariate main or interaction effects were found between groups (p > .05). M-S OSA (Moderate-Severe OSA), clinical depressive symptoms (+ D)
Table 8.

**Motor Functioning Scores**

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>MOT&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency</td>
<td>.18(.78)</td>
<td>.27(.96)</td>
<td>.40(.69)</td>
<td>.16(.23)</td>
<td>.08(.64)</td>
<td>.08(.93)</td>
</tr>
<tr>
<td>Errors</td>
<td>.89(.27)</td>
<td>-.97(.13)</td>
<td>-.64(.22)</td>
<td>-.79(.18)</td>
<td>-.78(.18)</td>
<td>.59(.24)</td>
</tr>
<tr>
<td>GPT&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominant</td>
<td>-.101(1.1)</td>
<td>-.149(1.40)</td>
<td>-.53(1.50)</td>
<td>-.84(1.86)</td>
<td>-.69(1.18)</td>
<td>-.87(1.80)</td>
</tr>
<tr>
<td>Nondominant</td>
<td>-.105(.98)</td>
<td>-.77(.87)</td>
<td>-.16(1.40)</td>
<td>-.32(1.85)</td>
<td>-.17(1.17)</td>
<td>.46(1.06)</td>
</tr>
</tbody>
</table>

Note: Scores presented from CANTAB Motor Screening Test (MOT) and Grooved Pegboard Test (GPT). *No significant multivariate main or interaction effects were found between groups, *No significant multivariate main or interaction effects found between groups (p > .05). PS (Primary Snoring). M-S OSA (Moderate-Severe OSA), clinical depressive symptoms (+ D)

OSA severity and depressive symptoms, $\lambda = .73, F(8,46) = .87, p = .546, \eta^2 = .11$, on tasks of vigilance. Mean scores between groups on attention are presented in Table 7.

**OSA Severity and Depressive Symptoms on Motor Functioning**

Hypothesis five proposed there would be a main effect on depressive symptom for performance on tasks of fine-motor speed and dexterity. The first MANCOVA investigated the impact depressive symptoms and OSA severity has on dominant and nondominant hand performance on the Grooved Pegboard Test. This analysis was not significant for main effects for OSA severity, $\lambda = .96, F(4,60) = .33, p = .854, \eta^2 = .02$, or depressive symptoms, $\lambda = .98, F(2,30) = .38, p = .689, \eta^2 = .03$. There were also no significant interactions found in this analysis, $\lambda = .32, F(4,60) = .32, p = .863, \eta^2 = .02$. Further investigation of fine motor speed and control on the Motor Screening Test (MOT) was also nonsignificant for main effects for OSA severity, $\lambda = .74, F(4,56) = 2.16, p = .076, \eta^2 = .14$, depressive symptoms, $\lambda = .99, F(2,30) = .05, p = .949, \eta^2 = .004$, or interactions between OSA severity and depressive
symptoms, $\lambda = .87$, $F(4,54) = 1.06$, $p = .386$, $\eta^2 = .07$, while controlling for intelligence. Group scores for performance on tasks of motor functioning are presented in Table 8.

**OSA Severity and Depressive Symptoms on Academic Functioning**

Lastly, the final hypotheses proposed there would be an overall main effect for depression on academic achievement with specific main effects for depression and interaction effects on the test of applied problems, and a significant main effect for depressive symptoms on reading fluency. The impact OSA severity and depressive symptoms has on academic achievement was evaluated using one MANCOVA and two ANCOVAs. Specifically, the multivariate analyses included the evaluation of academic skills for single word reading (Letter-Word Identification), processing speed and quickly reading passages for basic comprehension (Reading Fluency), spelling of words (Spelling), and use of conceptual mathematics skills (Applied Problems). Due to multiple subtests in the MANCOVA deriving the Brief Achievement outcome measure, and risking having too many dependent measures included in analysis with small sample size, a univariate ANCOVA was run to evaluate the impact that OSA and depression has on this abbreviated achievement metric independently. In addition, the Understanding Directions test was less appropriate for analysis within the specific academic skills due to relatively small loading of the test with the other tests of academic skills. As a result, the Understanding Directions subtest was analyzed independently due to the measure assessing a combination of listening comprehension and working memory abilities. As a result, univariate analysis was also conducted on this measure.

The MANCOVA analysis for academic achievement skills was conducted while controlling for parental education and overall intellectual abilities. Multivariate analysis from this investigation revealed no primary main effects for OSA severity, $\lambda = .72$, $F(8,52) = .14$, $p$
Running head: OSA and Depressive Symptoms on Neurocognition

= .355,  \( \eta^2 = .15 \), or depressive symptoms,  \( \lambda = .91 \),  \( F(4,38) = .65 \),  \( p = .657 \),  \( \eta^2 = .09 \); however, a significant interaction effect was found for OSA severity and depressive symptoms,  \( \lambda = .51 \),  \( F(8,50) = 2.00 \),  \( p = .04 \),  \( \eta^2 = .25 \). Univariate analyses were conducted to ascertain specific group differences which appeared to be due to group differences, which appeared to be due to an interaction of OSA severity and depressive symptoms on the Applied Problems task,  \( F(2,35) = 6.12 \),  \( p = .012 \),  \( \eta^2 = .24 \). Tukey post-hoc testing revealed the significant finding was due to those with moderate-severe OSA and depression performing significantly lower on Applied problems than those with mild OSA, mild OSA and depression, and those with moderate severe OSA without clinical depressive symptoms. Those with Mild OSA also exhibited significantly higher performance on this task compared to the primary snoring groups by almost one standard deviation. Mean’s plot of this finding is displayed in Figure 2.

Analysis utilizing ANCOVAs while controlling for intelligence and parental education found no significant main effects for OSA severity,  \( F(2, 36) = .67 \),  \( p = .523 \),  \( \eta^2 = .09 \), depressive symptoms,  \( F(1,36) = 1.15 \),  \( p = .293 \),  \( \eta^2 = .16 \), or interaction effects,  \( F(2,36) = .48 \),  \( p = .625 \),  \( \eta^2 = .07 \) on the task of Understanding Directions. Similarly, there were no significant main effects on OSA severity,  \( F(2,36) = .15 \),  \( p = .859 \),  \( \eta^2 = .01 \), depressive symptoms,  \( F(1,36) = 1.02 \),  \( p = .322 \),  \( \eta^2 = .04 \), or interaction effects for the Brief Achievement measure of academic performance,  \( F(1,36) = 1.51 \),  \( p = .241 \),  \( \eta^2 = .11 \).

Lastly, final multivariate analysis was conducted on parental report of academic achievement in the areas of Reading, Math, Social Studies, and Science. Analysis of scores from parental ratings revealed no significant multivariate effects for OSA severity,  \( \lambda = .87 \),  \( F(8,48) = \).
.51, \( p = .846 \), \( \eta^2 = .08 \), depressive symptoms, \( \lambda = .89 \), \( F(4,24) = .75, p = .566, \eta^2 = .11 \), or interaction effects between OSA severity and depressive symptoms, \( \lambda = .59 \), \( F(8,48) = 1.78, p = .107, \eta^2 = .23 \). A summary of academic achievement scores and parental report of academic performance is presented in Table 8.

**Neuropsychological Functioning in Snorers vs. OSA**

Secondary analysis was conducted in order to evaluate neurocognitive and academic functioning between groups using a 2x2 design in comparing those in the PS group with all participants that were part of the OSA group (combined OSA Mild and OSA Moderate-Severe). Secondary analysis appeared to be consistent with the primary null findings on neurocognitive and academic performance (\( p > .05 \)) with the exception of an additional significant multivariate main effect found for OSA severity on the MOT, \( \lambda = .77 \), \( F(2,30) = 4.42, p = .021, \eta^2 = .23 \). Univariate analysis revealed this effect was still significant after making Bonferroni corrections due to those with OSA making significantly more errors on the MOT task compared to those without OSA, \( F(1, 36) = 6.78, p = .014, \eta^2 = .18 \). Means of MOT errors is represented in Table 3. Despite this effect, multivariate analyses were no longer significant for RDI severity on the working memory SSP task \( \lambda = .93 \), \( F(3,30) = .62, p = .508, \eta^2 = .07 \), or for interaction effects on academic achievement on the WJ III ACH, \( \lambda = .59 \), \( F(8,52) = 1.91, p = .08, \eta^2 = .23 \). This largely appeared to be due to the primary significant findings occurring when comparisons across groups were made between mild OSA and moderate-severe OSA groupings. There were no additional significant findings when academic domains were analyzed independently in univariate analyses.
Means from Applied Problems (WJ III ACH)

Means plot of scores from the Applied Problems task from the WJ ACH III with significant interaction effects found with those with Moderate-Severe OSA and depressive symptoms performing significantly lower than those with mild OSA, mild OSA and depression, and those with moderate severe OSA without clinical depressive symptoms $F(2,35) = 6.120, p = .012, \eta^2 = .244$
Table 9.

**Academic Achievement Scores and Parent Reported Academic Performance**

<table>
<thead>
<tr>
<th>Academic Measures</th>
<th>PS</th>
<th>PS + D</th>
<th>Mild OSA</th>
<th>Mild OSA+D</th>
<th>Severe OSA</th>
<th>Severe OSA + D</th>
</tr>
</thead>
<tbody>
<tr>
<td>M(SD) (N = 5)</td>
<td></td>
<td>(N = 5)</td>
<td>(N = 13)</td>
<td>(N = 5)</td>
<td>(N = 5)</td>
<td>(N = 5)</td>
</tr>
<tr>
<td><strong>WJ ACH III</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letter-Word-ID</td>
<td>98.20(8.67)</td>
<td>100.20(9.99)</td>
<td>100.69(14.53)</td>
<td>96.40(27.86)</td>
<td>106.40(13.01)</td>
<td>105.20(9.01)</td>
</tr>
<tr>
<td>Reading Fluency</td>
<td>87.40(9.34)</td>
<td>98.00(12.88)</td>
<td>99.67(13.09)</td>
<td>92.20(25.33)</td>
<td>97.50(19.39)</td>
<td>94.80(8.89)</td>
</tr>
<tr>
<td>U-D</td>
<td>82.40(13.39)</td>
<td>85.20(10.49)</td>
<td>91.00(6.95)</td>
<td>83.20(29.98)</td>
<td>97.40(11.63)</td>
<td>85.60(11.97)</td>
</tr>
<tr>
<td>Spelling</td>
<td>88.00(10.63)</td>
<td>95.40(14.74)</td>
<td>94.38(10.46)</td>
<td>100.40(11.63)</td>
<td>98.20(17.02)</td>
<td>94.60(9.76)</td>
</tr>
<tr>
<td>Applied Problems</td>
<td>91.00(14.09)</td>
<td>98.20(5.02)</td>
<td>101.46(7.62)</td>
<td>111.60(13.79)</td>
<td>104.40(10.26)</td>
<td>87.40(7.79)</td>
</tr>
<tr>
<td>Brief Achievement</td>
<td>88.75(10.01)</td>
<td>103.33(6.66)</td>
<td>100.55(12.58)</td>
<td>107.20(10.35)</td>
<td>104.00(14.63)</td>
<td>96.50(11.62)</td>
</tr>
</tbody>
</table>

**Parent-Reported Academic Performance*  
Reported (1-4)**

<table>
<thead>
<tr>
<th></th>
<th>Reading</th>
<th>Social Studies</th>
<th>Math</th>
<th>Science</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.80(.44)</td>
<td>2.80(.44)</td>
<td>2.80(.84)</td>
<td>2.80(.44)</td>
</tr>
<tr>
<td></td>
<td>3.20(.84)</td>
<td>3.00(.82)</td>
<td>3.00(.82)</td>
<td>3.25(.50)</td>
</tr>
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<td>3.08(.49)</td>
<td>3.15(.38)</td>
<td>3.40(.55)</td>
<td>3.60(.55)</td>
</tr>
<tr>
<td></td>
<td>3.40(.89)</td>
<td>3.00(.71)</td>
<td>3.40(.55)</td>
<td>3.67(.58)</td>
</tr>
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<td>3.25(.50)</td>
<td>3.40(.55)</td>
<td>3.60(.55)</td>
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<tr>
<td></td>
<td>2.60(1.14)</td>
<td>3.20(.45)</td>
<td>2.40(.89)</td>
<td>3.00(.71)</td>
</tr>
</tbody>
</table>

Note: *Academic performance coded from parent reported academic performance on CBCL: Failing (1), Below Average (2), Average (3), Above Average (4).  
No significant multivariate main effect for OSA severity or depressive symptoms, significant multivariate interaction effect was found $\lambda = .509, F(8,50) = 2.001, p = .04, \eta^2 = .246$.  
*bNo significant univariate main or interaction effects found between groups for Understanding Directions.  
*cNo significant univariate main or interaction effects found between groups for overall Brief Achievement.  
U-D (Understanding Directions), M-S OSA (Moderate-Severe OSA), clinical depressive symptoms (+ D)
Chapter 5

Discussion

This final chapter will discuss the present study, and discuss relevant and divergent findings in comparison to the literature as well as discuss the hypotheses, conclusions, and implications from the current study. The chapter will also present limitations to the current study design and findings and will discuss future directions and implications for psychological and sleep medicine practitioners.

Purpose

The purpose of the present study was to investigate how OSA and comorbid depressive symptoms impact neurocognition and academic performance. Specifically, the study aimed to test the hypotheses that having clinically reported depressive symptoms and increasing OSA severity results in neurocognitive dysfunction in the areas of executive functioning, working memory, attention/vigilance, fine-motor speed, academic achievement, and parent reported academic performance.

OSA and Depressive Symptoms on Intelligence and Working Memory

Consistent with previous literature (Beebe et al., 2004; Kaemingk et al., 2003; Beebe, 2006), there were not significant differences between groups with regard to OSA severity on measures of overall intellectual abilities as a result of OSA severity or depressive symptoms. The next two hypotheses in the current study proposed there would be a significant main effect for depressive symptoms and an interaction effect for depressive symptoms and OSA severity on working memory performance. In order to investigate this, the current study utilized two separate MANCOVA’s while controlling for family education on two nonverbal tasks of working memory that require varying attentional and procedural demands. Investigation of the
SWM task, which requires more demands on visual attention and scanning, revealed there were no significant main effects or interactions on the dependent measures although the findings approached significance within this group. In contrast, findings from the SSP task which requires more sequential visual processing demands in working memory revealed an overall significant main effect for OSA severity in the multivariate analysis. Specifically, univariate analysis found that those with Moderate-Severe OSA subjects performed significantly lower than those in the Mild OSA group for making perseverative usage errors on this task. The difference did not exist between those with moderate-severe OSA and the PS group. These findings appear to suggest that those with moderate-severe OSA may exhibit increased inefficiency in maintaining and updating working memory during serial visual search tasks with high visual spatial demands.

In contrast to the hypotheses, there were no significant main effect or interaction findings for depressive symptoms on working memory. Although there were no significant differences observed between the PS and Moderate-Severe OSA groups, it is likely that the small sample size may have impacted the ability to discern differences between these two groups on this task, in fact, the average scores were most comparable to representative samples in the mild OSA group which had the largest cell sizes in the current study.

The findings from the current study found that compared to those with mild OSA, those with moderate-severe OSA displayed significantly more perseverative errors on a task of working memory but did not differ from PS subjects in this domain. The finding that higher severity OSA may lead to more working memory difficulties appear to be consistent with previous findings that children with moderate-severe OSA may have reduced working memory abilities (Beebe, 2003; Kaemingk et al., 2003). Although no significant effects were found for
working memory in the domain of sequential visual processing and visual spatial manipulation (SWM), this is not inconsistent with previous findings that have identified no significant differences between OSA and control groups on sequential verbal recall (Beebe et al., 2003) and short-term memory span (Blunden et al., 2000; Kaemingk et al., 2003). It is of note that the working memory tests employed in the current study have not been used to assess cognitive functioning in OSA and patients were not assessed on backwards trials of the working memory tasks, which may be more robust to neurocognitive difficulties due to larger demands placed on attention and manipulation of information in working memory. Still the finding that those with moderate-severe OSA displayed increased errors on the SSP task compared to those with mild OSA highlights that more severe OSA may lead to more inefficient use of working memory.

Based on the relatively small sample size of the current study, it may be inappropriate to fully accept the null findings in the current study, as large effect sizes would have been required in most cases in order to detect significant differences. Despite this, the findings from this study appear to corroborate previous findings that increasing OSA severity, particularly moderate-severe OSA severities, may lead to increased neurocognitive difficulties in the areas of working memory. In fact, the significant findings in the current study approached large effect size ($\eta^2 = .23$) for the number of perseverative errors made on the sequential immediate visual memory test employed in the study.

**OSA and Depressive Symptoms on Planning**

The next hypothesis proposed there would be a significant main effect for depression in the domain of visual planning, which was assessed on a Tower of London analogue test via the Stockings of Cambridge task. Investigation into performance differences on this task revealed no significant main effects for depression, OSA severity, or interaction effects between OSA
severity and depressive symptoms. It is of note that the current study utilized the SOC task as part of its assessment battery, which measures the higher order domain of executive functioning in the area of planning. Few executive functioning tests of planning assess this construct in children as young as 6 years of age (Strauss, Spreen, & Sherman, 2006), thus limited literature is available to ascertain the findings from the current study. Although multiple studies assessing executive functioning in the domains of set-shifting, lexical fluency, and mental flexibility in the verbal domain have found modest impairments with OSA (Beebe et al., 2010; Owens et al., 2000), and for constructional planning requiring visuomotor integration (Emancipator et al., 2006; Kurnatowski et al., 2006) other studies utilizing tests of nonverbal conceptualization and abstract reasoning have also failed to identify significant differences between groups in executive functioning in those with OSA (Beebe et al., 2004) and depression (Favre et al., 2009; Weiner & Pfeffer, 1986) consistent with the current study.

**OSA and Depressive Symptoms on Attention**

Based on the mounting literature highlighting difficulties in the area of attention in children with increasing severity of OSA, hypothesis four proposed there would be a significant main effect for OSA severity on measures of attention and vigilance. Analysis was conducted utilizing outcome measures (CRT, SST) from the CANTAB. Results from this analysis failed to identify any significant main effects or interactions for depression and OSA severity on attention when controlling for intelligence and age. Previous investigations have identified areas of attention/vigilance to be a particular area of deficit in those with OSA and evidence has suggested those with depressive symptoms may also exhibit increased difficulties on sustained attention tasks (Avior et al., 2004; Beebe et al., 2003; Emancipator et al., 2006; Owens et al., 2004). Results from the current study also did not identify significant differences between
groups on measures of attention and vigilance. Although a significant finding was not found between groups based on OSA severity, other researchers investigating differences between these groups have also failed to identify significant findings when small sample sizes have been investigated (Beebe et al., 2004). Still others have found modest significant differences even with small sample sizes (Archbold et al., 2004; Kennedy et al., 2004). The difference between this finding in the current study may be due to the nature of the outcome measures derived from the tests in the current study. Specifically, the CRT and SST task predominantly assessed simple and sustained response time and variability in vigilance throughout the task without assessment of omission (inattention) or commission (impulsivity) errors. Previous studies utilizing different vigilance tasks (Archbold et al., 2004; Beebe et al., 2004; Kennedy et al., 2004) have found significant findings between controls and mild and more severe forms of OSA despite small sample sizes. In fact, the effect size in many studies have typically been large (Beebe, 2003).

**OSA and Depressive Symptoms on Motor Control**

Hypothesis five proposed that there would be a significant main effect for depression on measures of fine-motor speed and coordination. Analysis of this effect was investigated on the CANTAB MOT task and the GPT. Results from these analyses failed to find any significant main effects or interaction effects for OSA severity or presence of depressive symptoms. When secondary analysis was conducted comparing those with PS to those with OSA without distinguishing severity, multivariate findings were significant for the MOT task, with univariate analysis identifying significantly more errors made by children who had OSA compared to those with primary snoring. Although no significant differences were observed between mild OSA and moderate-severe OSA in the analysis, this finding may suggest that even modest levels of OSA may lead to difficulties in basic motor control or simple attentional skills as assessed on the
MOT task. This findings was observed in the current study by those with OSA making significantly more errors compare to those in the primary snoring group, with a large effects size observed between the groups ($\eta^2 = .23$).

Although tests of fine-motor speed have demonstrated sensitivity to depressive symptoms in adult literature (Hinkle et al., 1992) and large effect sizes have been observed in those with OSA compared to controls (Beebe, 2003), the current study failed to identify significant findings between groups when the sample was split into PS, mild OSA, and moderate-severe OSA groupings. However, when groups were made based on presence of clinical OSA vs. PS groups, it was found that those with OSA made significantly more errors on a task of simple visual attention and motor control compared to those without OSA. It is likely that this finding may be due to the simple attention demands rather than motor control problems due to the lack of significant differences observed between these groups on the more complex GPT task.

**OSA and Depressive Symptoms on Academic Achievement**

The final hypotheses proposed that there would be a significant main effect for depression and an interaction effect between depression and OSA on academic achievement. Specifically, it was expected that those with depressive symptoms alone and those with both depressive symptoms and more severe OSA would perform worse on a task of conceptual math knowledge and application (Applied Problems). Further, individuals with depression were expected to have lower scores on a measure of processing speed and brief reading. Results from this analysis revealed an overall multivariate interaction effect for OSA severity and depressive symptoms but failed to identify any primary main effects on OSA severity or depressive symptoms. Univariate analysis revealed those with moderate-severe OSA and depressive symptoms displayed significantly lower performance on the Applied Problems task compared to
those with Mild OSA, Mild OSA with depression, and moderate-severe OSA without depressive symptoms with a large effect size ($\eta^2 = .24$) observed in these group differences. In contrast to normative values of children with depression performing almost a half standard deviation lower than the overall normative sample on the test employed in the current study (Woodcock, McGrew, & Mather, 2007), there were no significant differences between depressed and nondepressed groups. In fact, children in the PS and mild OSA group who had depression exhibited slightly higher performance on conceptual math skills when they had PS and mild OSA, but exhibited significantly lower performance only when they had moderate-severe OSA and clinical depressive symptoms. Altogether, this finding appears to suggest that those with moderate-severe OSA and depression may experience increased difficulties in executing conceptual math skills but only when significant OSA is present. It remains unknown the extent that possible daytime sleepiness and motivation may have played in performing this task. However, depression has been linked to increased daytime sleepiness and reduced motivation, working memory, and processing speed that may yield more difficulties in execution of conceptual math problems.

Lastly, in the domain of academic achievement and parent report of academic performance, it was hypothesized there would be a significant main effect for depressive symptoms on tasks of conceptual math skills and reading fluency with an interaction effect also observed on the Applied Problems task. Results from the current study found that although there were no significant differences observed in parental reported academic performance across depressed and OSA severity groups; however, children with moderate-severe OSA and depression performing the lowest on the Applied Problems task. Across groups they displayed significantly lower performance on this task compared to those with mild-OSA, Mild-OSA
Depressed, and Severe OSA without Depression. The finding that depression and OSA may independently impact performance in mathematics has also been supported in youth (Lundy et al., 2010; Vincenzi, 1987) and may have consequences for later academic difficulties (Gozal & Pope, 2002; Perfect et al., 2013).

Although there were limited significant findings in the current study, results from the current study were consistent with previous studies employing similar groups and clinical criteria for defining OSA. Specifically, Beebe et al. (2003) found that there were no significant differences between any primary multivariate outcome of neurocognitive functioning (working memory, executive functioning, attention, intelligence) between groups of simple snorers, Mild OSA, or Moderate-Severe OSA, although findings in their study were found between OSA groups and those who had not undergone PSG but were assumed to be free from a SRBD from questionnaire responses. Several other studies have reported no significant differences in neurocognitive outcomes for PS and Mild OSA groups (Beebe et al., 2010; Calhoun et al., 2009) and Moderate-Severe OSA (Beebe et al., 2004; Beebe et al., 2010). The main contribution of the current study is the consideration that depressive symptoms may interact with increasing severities of OSA to result in increased neurobehavioral difficulties.

In summary, the current study highlighted significant differences in children with higher severity of OSA compared to other groups in visual spatial working memory and visual motor control with children also displaying significantly lower performance in mathematical reasoning and application when depression and moderate-severe OSA was present. Although these deficits span multiple domains of functioning, it is most likely that children’s visual motor control performance and visual spatial working memory is a direct impact from having OSA and may have been further exacerbated by potential attention difficulties as previous studies have
suggested. Moreover, due to the high demands of working memory, attention, and visual motor integration in the application and use of novel and learned mathematical concepts, the deficiency in math observed in children with moderate severe OSA with depressive symptoms appears to highlight an ability-achievement consistency with difficulties also arising in visuomotor and working memory in these children. Overall, limited studies have investigated academic achievement and underlying neurocognitive processes that may impact academic math performance in children with OSA and depression and more research in this area appears to be warranted.

Although the ability to fully deduce the underlying reason for the findings in the current study are unknown, the research investigating the neurophysiological sequelae in those with OSA have suggested that patients experience alterations in functioning and mass reduction in prefrontal cortical structures responsible for complex reasoning and attentional orientation (Cross et al., 2008). In addition to the neurophysiological implications, motivation and behavioral manifestations may also occur in the context of depression that may manifest in further neurobehavioral difficulties. Preliminary research has also found that adults with OSA and comorbid depressive symptoms may experience increased alterations in brain structures and these alterations have also been associated with the degree of neurocognitive dysfunction (Macey et al., 2012).

Limitations

In review, the current study is the first of its kind to report findings from the possible effects depression and comorbid OSA may have on neurocognition and academic performance. Without question, the current study is valuable provided it is the first of its kind to investigate and identify significant differences in children with OSA and comorbid depressive symptoms,
however, the significance of the study as a whole is largely attenuated by the limitations imposed due to small sample size and potential referral bias based on suspicion of having OSA symptoms. It is also notable that from the larger study, nearly half of the participants chose not to begin data collection procedures as part of the study after being enrolled in the overarching study. In addition several participants ($N = 8$) did not undergo both PSG and neuropsychological evaluation and as a result, were not able to be included in analysis. It is possible that those who chose not to undergo neuropsychological assessment or PSG were different from the sample in neurocognition, academic performance, or RDI. In addition to the underpowered nature of the study, there was also lack of a pure control group and the study may have failed to identify differences between those with no concerns of a SRBD and mild to moderate forms of SRBDs. Despite this, the PS group in the current study’s average RDI did not significantly deviate from same-aged normative samples with no suspicion of a SRBD (Marcus, 2001).

Regarding outcome measures, although some literature has found significant differences in those with depression compared to controls on the CANTAB (Kyte, Goodyer, & Sahakian, 2005; Matthews, Coghill, & Rhodes, 2008; Porter et al., 2003), there has been extremely limited published studies utilizing the CANTAB in the evaluation of neurocognitive functioning in children with varying severities of sleep apnea and the sensitivity of this test in assessing nuanced neurocognitive sequelae in these children has not been established. The current study is also valuable as it provided the first known investigation to utilize the CANTAB for the assessment of neurocognitive dysfunction in a diverse sample of school-aged children with OSA and identified multiple areas of significant dysfunction even in its underpowered form. The current study highlighted a high proportion of school-aged children referred for possible OSA with depressive symptoms in each category of the OSA spectrum (PS = 50%, Mild OSA = 28%,...
Moderate-Severe OSA = 50%), with mean depressive symptoms nearly one standard deviation higher than normative values. This significant presence of depressive symptoms in children referred for OSA screening appears to be consistent with the high rates of affective illness that has been recently highlighted in adults with OSA and sleep disorders (Ohayon, 2003; Picchietti & Winkelman, 2005; Vaudeputte & Weerd, 2003; Wheaton et al., 2012).

Although the current study utilized gold-standard instruments in the assessment of sleep apnea and overnight PSG, the study also utilized a general measure of social and emotional functioning (CBCL) that assesses a wide range of behaviors that were not specific to depression. Specifically, despite the CBCL demonstrating adequate to good discriminability for determining clinical threshold symptoms of depression and anxiety, the inclusion of a psychodiagnostic interview and self-report measures of affective anxious and depressed symptoms may have provided a better overall measure of depression and would have provided more specificity and sensitivity to the nature of the disorder and symptoms. Despite this, many measures of self-reported affective functioning do not span the entire age range of the current sample (6-12), thus the CBCL allowed for the entire sample to be evaluated using consistent parental report of behaviors across the full sample. Regardless, using a more specific measure of depressive symptoms, utilizing self and parent report measures, and conducting formal diagnostic consideration via a structured clinical interview, may have provided valuable information in better identifying the nature of the samples depressive symptoms and disorders.

The current study did not find significant group differences across multiple confounding variables, however, several variables were not utilized within the current sample that may have an impact on neurocognitive functioning. First, OSA is associated with numerous neurodevelopmental circumstances that are associated with executive functioning, attention, and
academic difficulties. Although some developmental information was reported for the current sample, it remains unknown how many children may have been born prematurely or had other respiratory or developmental conditions that may have been associated with neurobehavioral sequelae and OSA. Furthermore, although children were excluded from the study if they had major comorbidities that may have impacted their neurobehavioral functioning based on parent report, the study did not involve the review of medical records which may have helped further ascertain the participant’s specific medical and psychological status.

Considerations regarding the overlap of OSA and depressive related symptoms may also be considered as limitations in this study. Specifically, the current study did not partition out potential symptoms of sleepiness that were included in the clinical depressive symptoms on the CBCL. Indeed, OSA and depressive symptoms are inextricably tied due to the overlap of sleep disturbance present in both disorders. Despite this overlap of symptoms, sleepiness symptoms were deemed best categorized as depressive symptoms due to few symptoms of daytime somnolence observed in school-aged children (Gozal, Wang, & Pope, 2001). Furthermore, adult literature has suggested that daytime sleepiness may be best accounted for by depressive symptoms rather than OSA related morbidity (Bardwell, Ancoli-Israel, & Dimsdale, 2003). Moreover, although the current study employed the use of the validated PSQ that includes a brief measure of parent reported sleepiness, due to this measure being added after the initial study began, sleepiness was not included in between-group analysis due to missing data at the beginning of the study. Despite this, previous research suggests that school-aged children do not typically display significant daytime sleepiness, thus this may not be a significant factor unless significant obesity is present (Beebe et al., 2007; Gozal et al., 2001). The current study also did not report sleep time from the night before the study, typical sleep time on weekdays and
weekends, or circadian rhythm preference that may have impact neurocognitive performance.

Lastly, it is also notable that in order to optimize sample size in the current study, those children who had initiated PAP therapy (N = 4) were included in analysis despite unknown impact on neurocognitive performance, as it remains unknown the impact one or multiple nights/hours of CPAP therapy may have on children’s neurocognitive functioning and mood. It also remains unknown the age of onset or how long those participants who had health related morbidities (overweight, obese, depressive symptoms, RDI) had been affected by the condition, which may be of relevance in consideration of neurocognitive dysfunction.

As a sample, the participants in the current study were ethnically diverse and generally representative of the region the study was conducted, however, the participants were also from well-educated homes and family income was higher than average. This higher level of education may have impacted scores in the current study and future investigations with more socioeconomically and scholastically diverse homes may show varying results from the current study provided the association of socioeconomic status and parental educational achievement on neuropsychological and school performance. Participants in the current sample also exhibited relatively higher BMI percentiles compared to the average population and much of the current sample was overweight or obese (44%).

Future Directions

Despite the increasingly large literature base that has investigated OSA associated morbidities in children during the last 30 years, little research has explored the complex interaction between OSA and comorbid depression on neurocognitive functioning. Although it remains relatively unknown the nature of the interaction between OSA and depression and how the comorbid disorders may impact neuropsychological functioning, both conditions
independently have been associated with neurocognitive difficulties. The current study is the first step in attempting to identify how depressive symptoms in children with OSA impacts neurocognition and academic functioning. Although the current study compared those with PS to mild and moderate severe OSA and secondary analysis compared those with PS to those with any clinical form of OSA (PS vs. Combined Mild OSA and Moderate-Severe OSA), researchers may find further value in determining if neurobehavioral functioning differs in children with moderate-severe OSA compared to those with more mild forms. This may be of particular importance provided previous findings that children with milder SRBDs (RDI < 5) compared to those with at least moderate OSA (RDI > 5) may experience increased attention and behavioral difficulties (Chervin, 2001), reduced learning and memory abilities (Kaemingk et al., 2003; Rhodes, 1995), and reduced verbal reasoning skills (Rhodes, 1995). Still, more research will be needed in order to understand how varying levels of OSA interact with sequelae associated with depressive symptoms.

Consistent with the potential neurocognitive sequelae associated with OSA and depression, evidence in adults has also highlighted additional alterations observed in neurophysiological functioning in adults with OSA and comorbid depression (Cross et al., 2008). Consistent with this, future research should attempt to further understand the impact that having both OSA and depression may have on neuroanatomical substrates in school-aged children. The benefits from learning how having both disorders impacts physiology and neurobehavioral functioning may allow for better interventions for addressing the disorders and allow for an understanding into the causal mechanisms between both disorders and related symptomology. Indeed the few studies conducted in this area have found that those who had OSA may experience academic difficulties later on, but no indication of how the presence of depressive
symptoms in combination with OSA impacts children’s academic performance and functioning inside the classroom has been investigated. The use of additional assessment instruments and methods such as in-vivo observations could provide significant information in the overall functioning of these children across settings (home, school, community). Few studies to date have obtained school records, state standardized achievement scores, or teacher/school based questionnaires for determining level of functioning in these children, which may also be of significant value in future studies.

Although sleep parameters and sleep architecture were assessed during the full overnight PSG, sleep architecture was not included as part of this study. Future research should focus on determining how having depressive symptoms and OSA impacts sleep architecture. Moreover, future studies may be inclined to investigate if alterations in sleep architecture and psychophysiological measurements during sleep serve as predictors of neurocognitive morbidity. There is some evidence to suggest that sleep parameters are related to specific areas of neurocognitive performance, albeit small and diffuse (O’Brien et al., 2004), however, adults with mental illness and depression have been identified as having significantly different patterns of sleep architecture and sporadic findings in alterations in sleep architecture have also been described in children and adolescents with depression (Benca, 2000; Puig-Antich et al., 1982; Puig-Antich 1983). Future investigations may be inclined to investigate if alterations in sleep architecture serve as mediators for neurocognitive dysfunction, particularly if alterations in REM are observed due to increased apneic events occurring during REM states in children.

Despite limited research investigating OSA and depression, treatment studies in adults using CPAP has highlighted that despite improvement in OSA, depressive symptoms may still remain after treatment (Habukawa et al., 2010). Future studies will also be extremely valuable in
determining how different intervention methods (CPAP, adenotonsillectomy, psychotherapy, behavioral consultation) may help reduce symptoms of OSA and depression and improve neurobehavioral functioning and mood. This may be of particular importance provided that OSA and depression often manifest during childhood and may have a long term course into adolescence and adulthood.

As eluded to above, depression and OSA are both associated with neurocognitive morbidity and a host of additional symptomology that may accompany further neurobehavioral difficulties. Specifically, higher rates of OSA and depression are observed in patients with high waist/hip ratios, short or variable time spent in bed, and those who are overweight and obese and this higher adiposity has been associated with higher blood pressure, hypertension, and insulin resistance that could further exacerbate the neurocognitive impact of OSA and depression (Adams, Szilagyi, Gebhardt, & Lande, 2010; Lande, Kaczorowski, Auinger, Schwartz, & Weitzman, 2003; Lassek & Gallin, 2003 Stress, 2003). Daytime sleepiness has also been associated with both disorders and is included in the criteria for diagnosing adult OSA and is also utilized in diagnosing major depressive disorder in children (DSM V, 2013). As a result of these symptoms, further studies should attempt to identify how these comorbid symptoms may also impact the neurobehavioral development and sequelae in children with OSA and depression while including early developmental difficulties such as premature birth and low birth weight that have also been associated with OSA and later executive functioning and attention difficulties.

As the research in pediatric sleep medicine continues to increase, better definitions and use of techniques to identify depressive disorders and SRBDs may also help to better understand the complex symptomology in patients with OSA and depression. In the future the use of
prospective cohorts looking at OSA and depressive symptoms over time using adequately powered sample sizes should help provide insight into causal mechanisms and effective treatments for the two disorders. Clinical investigations would also benefit from further study into predictors of responders and nonresponders to treatment for depression and OSA. Despite lack of differences between males and females with regard to clinical depression in the current study, future investigations should also consider if higher rates of depression is present in females with OSA and if particular genders and ethnicity exhibit increased neurobehavioral morbidity when both conditions are present. This may be particularly important in adolescent's who exhibit increased depressive symptoms and may have higher rates of depressed females compared to males. Investigations in children and adolescents may be of particular importance due to the fact many of these problems (major depression, obesity) begin course during youth.

**Implications for Practitioners and School Psychologists**

In summary of the findings from the current study and the literature, it appears that clinicians who work with children with depression and sleep disorders should maintain awareness of high rates of comorbid depressive symptoms among children with OSA in clinical settings. Although psychologists should not diagnose OSA based on reports or report measures, psychologists should consider screening for OSA when depression is present. In addition, practitioners who work with clinical sleep populations should strongly consider screening for depressive symptoms in the presence of diagnosed OSA. Clinicians should be inclined to familiarize themselves with clinical sleep evaluation tools such as the SRBDi utilized from the PSQ in the current study in order to screen for OSA and make appropriate referrals to sleep specialist if deemed appropriate.

Compared to the high rates of comorbid OSA and ADHD symptoms that have been
established in the literature for several years (Vandeputte & Weerd, 2003; Wheaton et al., 2012), fewer studies have highlighted the prevalence of depression in OSA in children. Children with ADHD often exhibit difficulties with concentration, motor restlessness, atypical behaviors, and deficiencies in attention and executive functioning that are similar to sequelae exhibited in children with depression. Clinician psychologists and physicians should familiarize themselves in methods for assessing ADHD and depressive symptoms in order to facilitate accurate diagnosis and appropriate interventions. Provided the high rates of medications prescribed to children with attention difficulties and depression, accurate diagnostic assessment appears to be of the highest importance in order to optimize outcomes and mismanagement of symptoms. Children who are misdiagnosed with one of these disorders may receive ineffective medication management which could result in further exacerbation of behavioral and affective symptoms and increasingly disrupted sleep. Due to significant changes to circadian rhythm throughout development and into youth (Ohayon et al., 2004), considerations should be made for assessing and treating circadian rhythm difficulties as these may further exacerbate neurobehavioral difficulties experienced due to OSA and depression. As a result, diagnostic consideration of multiple conditions and differential diagnosis is highly warranted for practitioners in clinical settings.

As the field of pediatric sleep medicine continues to expand its research into exploring the complex relationship between OSA and comorbid affective symptoms, psychologists should consider how psychological interventions such as brief behavioral consultations, cognitive behavioral therapy, interpersonal psychotherapy, or cognitive remediation may be able to benefit patients who are suffering from OSA and depression. In particular, interventions that focus on enhancing sleep hygiene, adherence to medical and sleep intervention devices such as CPAP
therapy, and direct psychological interventions aimed at improving adaptive coping skills and addressing cognitive distortions all appear to be of potential benefit in this population. In addition, practitioners working with children should consider the use of behavioral family therapy and parent training interventions for increasing structure and sleep hygiene that may enhance overall outcomes in children. Overall, psychological practitioners and physicians working with individuals with depressive symptoms and sleep disorders should consider the possibility of treating OSA in conjunction with depression when symptoms of both disorders are present. Based on the current study, school psychologists may also be particularly interested in the neurocognitive sequelae associated with OSA and comorbid depressive symptoms as the participants in the OSA and depressed group displayed conceptual mathematics performance that was almost one standard deviation below the norms despite having generally average intellectual abilities. This finding may suggest that particular consideration of OSA and depressive symptoms should be considered when evaluations are being conducted for specific learning disabilities in mathematics. Although currently it is not feasible for psychologists to treat sleep apnea in children directly, it may be possible to reduce their symptoms of anxiety and depression that may be corresponding to the neurobehavioral deficits observed in patients suffering from OSA and comorbid depressive symptoms, thus psychological interventions should be further explored and implemented for addressing these difficulties in clinical practice.
Appendix A

Sorensen Model of Neurobehavioral Deficits in OSA & Depression

Risk Factors: Adenotonsillar Hypertrophy, Craniofacial Abnormalities, Neuromuscular Diseases (hypotonia), Premature Birth, Nasal inflammation/Inflammatory diseases, asthma, allergies/chronic sinusitis, African American, Male, Low SES, High BMI, environmental inhalants

Possible Risk Factors: APOE Genes, Serotonin Dysregulation, overexpression of tumor necrosis factor alpha (TNF-α), other genetic polymorphisms
Appendix B
Demographic and Health Questionnaire

What Grade is your child in?________________________
Child’s age________________________
Child’s gender________________________
Child’s ethnicity (please describe)________________________

Health Questions (please circle yes/no)
Has your child ever had his/her tonsils removed? Yes No
Has your child ever had his/her adenoids removed? Yes No
Has your child ever used a PAP device (CPAP, APAP, etc.)? Yes No

Please answer the questions on the following pages regarding the behavior of your child during sleep and wakefulness. The questions apply to how your child acts in general, not necessarily during the past few days since these may not have been typical if your child has not been well. If you are not sure how to answer any question, please feel free to ask your husband or wife, child, or physician for help. You should circle the correct response or print your answers neatly in the space provided. A “Y” means “yes,” “N” means “no,” and “DK” means “don’t know.” When you see the word “usually” it means “more than half the time” or “on more than half the nights.”

<table>
<thead>
<tr>
<th>While sleeping does your child…</th>
<th>Y</th>
<th>N</th>
<th>DK</th>
</tr>
</thead>
<tbody>
<tr>
<td>…snore more than half the time?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>…always snore?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>…snore loudly?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>…have “heavy” or loud breathing?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>…have trouble breathing or struggle to breathe?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Have you ever…

<table>
<thead>
<tr>
<th>…seen your child stop breathing during the night?</th>
<th>Y</th>
<th>N</th>
<th>DK</th>
</tr>
</thead>
</table>

Does your child…
<table>
<thead>
<tr>
<th>Question</th>
<th>Y</th>
<th>N</th>
<th>DK</th>
</tr>
</thead>
<tbody>
<tr>
<td>...tend to breathe through the mouth during the day?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...have a dry mouth on waking up in the morning?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does your child...</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...wake up feeling unrefreshed in the morning?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...have a problem with sleepiness during the day?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...occasionally wet the bed?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has a teacher or other supervisor commented that your child appears sleepy during the day?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it hard to wake your child up in the morning?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does your child wake up with headaches in the morning?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did your child stop growing at a normal rate at any time since birth?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is your child overweight?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>This child often...</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...does not seem to listen when spoken to directly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...has difficulty organizing task and activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...is easily distracted by extraneous stimuli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...fidgets with hands or feet or squirms in seat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...is ‘on the go’ or often acts as if ‘driven by a motor’</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...interrupts or intrudes on others (e.g., butts into conversations or games)</td>
<td></td>
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Appendix C

Parent Socio-Demographic Report Questionnaire

1. What is your relationship to the child?
   - Mother
   - Father
   - Step-Mother
   - Step-Father
   - Other (please describe)_________________

2. What best describes your child’s racial/ethnic background?
   - White/Caucasian
   - Black/African American
   - Hispanic/Latino
   - Asian/Asian American
   - Native American /American Indian
   - Multiracial (please specify)______________
   - Other (please specify)_________________

3. How many years of education has the child’s mother received? __________

4. Mother’s current occupation (if outside home)? __________

5. What best describes her work? (Check all that apply)
   - Day Shift
   - Evening Shift
   - Night Shift (Graveyard)
   - Changing Shifts
   - Full-time
   - Part-time
   - One-Job
   - Multiple Jobs
   - Other (please describe)_________________

6. What is mother’s estimated annual income? __________
Appendix C continued

7. Mother’s marital status
   - Married
   - Separated
   - Widowed
   - Single
   - Divorced
     (if divorced) Child custody with?

8. How many years of education has the child’s father received? ________

9. Father’s current occupation (if outside home)? ________________

10. What best describes his work? (Check all that apply)
    - Day Shift
    - Evening Shift
    - Night Shift (Graveyard)
    - Changing Shifts
    - Full-time
    - Part-time
    - One-Job
    - Multiple Jobs
    - Other (please describe)_________________

11. What is father’s estimated annual income? ________________

12. Father’s marital status
    - Married
    - Separated
    - Widowed
    - Single
    - Divorced
      (if divorced) Child custody with?______________
Appendix D

Recruitment Flyer

Does your child snore?
Are you interested in participating in a sleep research study at the University of Arizona?

We are looking for children who snore to participate in a study of treatment for obstructive sleep apnea.

IS MY CHILD ELIGIBLE?

- Between the ages of 6-11
- Has never had treatment for a sleep disorder before
- Does not have any chronic illnesses
- Understands English

WHAT IS INVOLVED?
Study Requirements:
6 overnight sleep visits to a sleep lab over a period of 6 months
3 daytime visits to complete questionnaires and behavioral tests
Nightly use of a treatment for sleep apnea

Participants will be compensated for their time and will be given all necessary treatment supplies.
Appendix E

PARENT PERMISSION FORM

Dear Parent/Guardian,

My name is Kristen Hedger-Archbold; I am a researcher from the University of Arizona College of Nursing. I have a research project with children who have breathing problems during sleep and am trying to understand how these problems may affect children’s sleep, behavior, and thinking patterns.

Your child has been sent home with a packet including this introduction letter, and a survey asking questions about your child’s sleep, behavior and other basic health information. The aim of the enclosed survey is to identify sleep problems in children grades pre K - 7 and to get information that may be useful for finding out if a child is able to participate in our project. Your participation in filling out this information is completely voluntary and in no way affects your child’s academic status at school. If you choose to fill out the questionnaires in this packet and would like your child to be considered for participation in our research project, you may leave your contact information at the bottom of this page. You may also complete the questionnaire and return it to school without providing any personal information.

The purpose of our research project is to determine the effectiveness of positive airway pressure (PAP) therapy on children who have breathing problems during sleep. PAP therapy is the use of an air mask and an air pressure machine during sleep to help a child breathe better. This project will be conducted at the Tucson Medical Center (TMC) Sleep Center and the University of Arizona College of Nursing. The project involves 6 total visits that occur over 6 months. These visits include three 2-night stays at TMC Sleep Center and 3 daytime visits to the College of Nursing for tests of your child’s behavior and thinking patterns. The overnight stays at the sleep center will occur two nights in a row and both a parent and the child will need to stay the whole night, both nights. Each visit to the College of Nursing will take about 3 ½ hours per session. Those children who are eligible and can participate in the project will receive compensation for their time and will be able to keep all PAP treatment devices (machine, mask, pillows, hoses, etc.) given to them during their participation in the project.

This project has been approved by Tucson Unified School District. All the information you provide will only be used only for research purpose, and will be kept strictly confidential. You have the right to not fill out the enclosed surveys. Thank you for your time and help with our project.

Sincerely,
Kristen Hedger Archbold RN, PhD

If you have any questions about this project, please feel free to contact Kristen Hedger Archbold at karchbold@nursing.arizona.edu, or (520) 300-1407. If you have questions and cannot reach the Principal Investigator or want to talk to someone other than the Investigator, you may contact University of Arizona Human Subjects Protection Program office at (520)626-6721 or online at http://orcr.vpr.arizona.edu/irb/contact.

I __________________ have read the introduction letter in full and would like to be contacted by research study personnel regarding my child ______________ participating in the “Neurobehavioral Effects of Positive Airway Pressure (PAP) Therapy in children with Obstructive Sleep Apnea” study. I understand that filling out the enclosed questionnaires is optional and participation in any portion of the project is voluntary. I give permission for the completed questionnaire to be used for research purposes.

Child’s Legal representative signature________________________ Date__________________

If you would like your child to be considered for participation in the study, kindly leave your preferred contact information so a project member can contact you.

Home phone number_________________ Best time to Call________

Cell phone number_________________ Best time to Call________

Email Address_____________________

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