SLEEP, PHYSICAL ACTIVITY, AND EXECUTIVE FUNCTION IN OBESE ADOLESCENTS WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA SYNDROME: A FEASIBILITY STUDY

A Dissertation in
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by
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ABSTRACT

BACKGROUND: Adolescents with obesity and obstructive sleep apnea syndrome (OSAS) are at substantially higher risk for poor physical and cognitive health outcomes than healthy counterparts.

PURPOSE: The purpose of this feasibility study was to acquire methodological and protocol insights for a subsequent, larger, study that will be fully powered to assess executive function in adolescents with obesity and OSAS and examine the effects of sleep duration and physical activity on executive function. The research questions were: (1) to determine the feasibility of recruiting and retaining a sample of obese adolescents (11-17 years of age) with and without-OSAS, (2) to pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation, (3) to explore executive function impairments as measured by the Global Executive Composite (i.e., overall summary score) and three subscales (i.e., Behavior Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index), within groups, compared to published normative data, and explore differences in executive function impairments between groups (obese adolescents with and without-OSAS), and (4) to describe differences in activity levels (frequency, intensity, time) and sleep duration (major sleep bout total sleep time), measured by 1-week actigraphy (objective measure of rest/activity and sleep) and self-report, between obese adolescents with and without OSAS and explore the relationship between activity levels and sleep duration with executive function (Global Executive Composite scores).

METHODS: A two-cohort, prospective study design was employed with a target population of adolescents with obesity (cohort 1) and obesity+OSAS (cohort 2). Participants were recruited, enrolled and consented/assented from an academic, tertiary medical center’s
sleep center and weight management clinic. Inclusion criteria were: age 11-17 years, BMI-for-age ≥95th percentile, presence or absence of OSAS determined by overnight PSG (diagnostic or split night study within the last year), apnea-hypopnea index ≥1.5 events/hour for clinically significant OSAS, parental consent and adolescent assent, reading level ≥5th grade, ability to read English, and anticipated performance of usual activities over a 1-week period after enrollment (e.g., no planned vacations, acute illnesses). Exclusion criteria were: age <11 or ≥18 years, BMI-for-age <95th percentile, overnight PSG >1 year ago, change in BMI greater than ± 2 kg/m2 since overnight PSG, acute or chronic physical injury or disability that impedes participation in physical activity, intellectual disabilities/learning disabilities that impact independent ability to respond to questionnaires, current treatment of OSAS, established diagnosis of other sleep-wake disorders that may disrupt sleep duration, including insomnia, restless legs syndrome, and narcolepsy, uncontrolled diabetes, disruptive behavioral disorders such as Attention Deficit Disorder (ADD), Attention Deficit Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD), established diagnosis of psychological disorders, including anxiety, schizophrenia, or personality disorders, or current use of psychotropic medications, uncontrolled mood disorders (depression, anxiety), and regular use (>3 days/week) of over the counter or prescribed medications that interfere with sleep. After baseline characteristic variables were collected by self-report questionnaire, one-week wrist-worn actigraphy and daily sleep and physical activity diaries were employed as measures of total nightly sleep time and physical activity including duration, frequency and intensity (tertiary outcomes). Executive function, the secondary outcome, was measured using the BRIEF®2. Feasibility outcomes, primary, included rates of recruitment, enrollment, retention and complete data; an end of study questionnaire measured participant acceptability of study protocol and instrumentation. Descriptive statistical
analysis and correlation tests were employed. Because of difficulty recruiting a group of obese adolescents’ without-OSAS, no tests for group differences were conducted.

**RESULTS:** It was not feasible to recruit obese adolescents without-OSAS given the recruitment plan; the study sample therefore included only a single cohort, adolescents with OSAS+obesity (n=20). Participants were largely white (n=15, 75%), non-Hispanic (n=19, 90%), adolescent (median= 14 years) males (n=11, 55%), with moderate obstructive sleep apnea syndrome (AHI median= 5.85, IQR 9.60). Face-to-face recruitment resulted in higher enrollment rates than mailed initiation letters. Complete data rates for one-week measures ranged from 75-90%. Ninety-five percent of participants completed the protocol and 90% of participants were interested in participating in another similar study. Obese adolescents with OSAS (n=20) had significantly worse executive function (by self- and parent-report) than a normative sample (p≤0.003); up to 30% had impaired executive function at thresholds considered clinically significant. No relationship was identified between sleep duration or physical activity and executive function. Participants did not meet national recommendations for sleep duration or physical activity and there was relatively minimal variability across participants for sleep duration or physical activity.

**CONCLUSION:** Alternative recruitment techniques are needed to obtain a sample of obese adolescents without-OSAS. Adolescents with obesity and OSAS have impaired executive function and do not meet recommended sleep or physical activity guidelines. Larger prospective studies are needed to determine if sleep duration and/or physical activity are associated with executive function in adolescents with OSAS and obesity.
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Chapter 1

Introduction

Background of the Problem

Obesity rates among children in the United States have dramatically increased in the past 30 years; at present, nearly 1 in 3 children are overweight (body mass index [BMI] $\geq 85^{th}$-$94^{th}$ percentile) or obese (BMI $\geq 95^{th}$ percentile) which indicates a quadrupling of prevalence in adolescents between the ages of 12-19 (Barlow, 2007; Ogden, Carroll, Kit, & Flegal, 2014). For the first time in history, the generation of children born in the 2000s are projected to have shorter life expectancies than their parents, due to the life-shortening effect of obesity (Olshansky et al., 2005). Severe obesity can reduce the length of life by an estimated 5-20 years (Fontaine, Redden, Wang, Westfall, & Allison, 2003) and this could be worsened in coming decades, as individuals are becoming obese at younger ages. With obesity onset at younger ages, associated health risks are acquired earlier in life which leads to adolescents entering adulthood with substantially higher morbidity risks (Olshansky et al., 2005). The economic consequences of childhood obesity are staggering, with an estimated $14.1 billion in direct healthcare costs attributable to childhood obesity (Trasande & Chatterjee, 2009). Children and adolescents who are obese are likely to become obese adults (Freedman et al., 2005; Freedman et al., 2009; Serdula et al., 1993; Whitaker, Wright, Pepe, Seidel, & Dietz, 1997) and the annual costs of treating obesity in adulthood is estimated at $147 billion (Finkelstein, Trogdon, Cohen, & Dietz, 2009).

Adolescence is an opportunistic and important time to intervene on obesity, as the chance of spontaneous remission of adolescent obesity is extremely low (Gordon-Larsen, Adair, Nelson, & Popkin, 2004). Analysis of the National Longitudinal Study of Adolescent Health, representative of approximately 15.6 million students, 13-20 years of age, at private and public
schools in the United States, indicates that 1.9 million adolescents developed obesity and an additional 1.5 million adolescents remained obese during the 5-year study period (Gordon-Larsen, Adair, et al., 2004). Childhood obesity is a public health epidemic, as it is a multisystem disease with many short- and long-term health risks. Immediate health risks are not to be taken lightly, as 70% of obese children between the ages of 5-17 years have at least one risk factor for cardiovascular disease, including high cholesterol and/or high blood pressure (Freedman, Mei, Srinivasan, Berenson, & Dietz, 2007). Additionally, obese children are more likely to have pre-diabetes (Li, Ford, Zhao, & Mokdad, 2009), bone and joint problems, obstructive sleep apnea, and social and psychological problems (Daniels et al., 2005; Dietz, 2004). Long-term risks include premature mortality and physical morbidity in adulthood (Reilly & Kelly, 2011) including neurological, psychosocial, pulmonary, cardiovascular, gastrointestinal, endocrine, renal, and musculoskeletal complications (Ebbeling, Pawlak, & Ludwig, 2002; Han, Lawlor, & Kimm, 2010).

Obesity is a strong risk factor for obstructive sleep apnea syndrome (OSAS); characterized by prolonged partial or complete upper airway obstructions that disrupt normal ventilation and sleep patterns (American Thoracic Society, 1996). A one standard deviation increase in BMI is associated with a 3.5-fold increased risk for OSAS (Kohler et al., 2009), and OSAS is present in up to 60% of obese children (Verhulst, Van Gaal, De Backer, & Desager, 2008). The relationship of obesity and OSAS is bi-directional, as obesity contributes to the development of OSAS and untreated OSAS contributes to obesity (Hargens, Kaleth, Edwards, & Butner, 2013). The etiology of OSAS in adolescents is complicated due to its multifactorial nature, including neuromuscular and anatomic factors (Yuan et al., 2013).
The association between obesity and OSAS is affected by differences in lymphoid tissue and airway size (Arens et al., 2011), reduction in upper airway reflexes with increasing age (Marcus et al., 2004), and developmental changes such as hormone secretion and fat deposition (Capdevila, Kheirandish-Gozal, Dayyat, & Gozal, 2008; Marcus, Brooks, et al., 2012). As with obesity, a multitude of complications are associated with OSAS during childhood and adolescence, including: cardiovascular, metabolic and neurobehavioral complications; deficits in cognition, neuropsychological function and somatic growth; and alterations in biomarkers of hormonal and inflammatory processes (Capdevila et al., 2008; Marcus, Brooks, et al., 2012).

OSAS and obesity, individually, can be detrimental across the span of childhood, a critical period of brain development and maturation (Blakemore & Choudhury, 2006). Adolescence is hallmarked by drastic hormonal, somatic, behavioral and cognitive changes, paralleled by changes in sleep physiology, architecture, and subsequent regulatory mechanisms (Brand & Kirov, 2011). As such, alterations to the restorative functions of sleep play a critical role in physiological, cognitive, and psychological processes during adolescence (Brand & Kirov, 2011).

Many children and adolescents with OSAS or obesity have prefrontal cortex dysfunction and neurocognitive impairments, leading to impaired executive function (Beebe & Gozal, 2002; Reinert, Po'e, & Barkin, 2013). In a randomized controlled trial of OSAS in children (N= 397; 5-9 years of age) randomized to tonsillectomy (n=194) or watchful waiting (n=203), wherein approximately 1/3 were obese and approximately half were obese or overweight per group, executive function was not significantly improved with tonsillectomy nor different between the randomized groups after exposure (p =0.16) (Marcus et al., 2013). Although the apnea hypopnea index (AHI) and other OSAS symptoms improved in the tonsillectomy group, executive function
remained stable, suggesting the potential lack of efficacy for executive function with stand-alone OSAS treatment approaches in obese/overweight children with OSAS (Marcus et al., 2013).

Executive function is an assembly of skills and higher order functions that control goal-directed behaviors, cognitive processes, and performance (Gioia, Isquith, Guy, & Kenworthy, 2015; Marcus, Brooks, et al., 2012). In OSAS, patients experience sleep disruptions and undergo intermittent hypoxemia and hypercarbia (Beebe & Gozal, 2002). This induces cellular and biochemical stress, and disrupts the restorative functions of sleep (Beebe & Gozal, 2002). As seen in Figure 1.1, dysfunctions of the prefrontal cortex are manifested behaviorally by executive dysfunction (Beebe & Gozal, 2002). In the model, the dotted arrow indicates that the executive system is an epiphenomenon (i.e., a secondary symptom or effect of the disease/condition), resulting from prefrontal cortex dysfunction, rather than a true effect (Beebe & Gozal, 2002). The executive system is composed of “behavioral inhibition, set-shifting, self-regulation of affect and arousal, working memory, analysis/synthesis, and contextual memory” (Beebe & Gozal, 2002, p. 2). Impairments to these functions result in maladaptive daytime behaviors including: difficulties mentally manipulating information, maintaining attention and motivation, poor planning, judgment, and decision making, disorganization, haphazard execution of plans, rigid-thinking, emotional lability, and impulsivity (Beebe & Gozal, 2002).
Mechanisms of obesity in the context of sleep disruptions (OSAS) and therefore sleep loss, include alterations in metabolic profiles (Leproult & Van Cauter, 2010). Alterations in hormones such as insulin, ghrelin, leptin, and cortisol, lead to increased hunger, decreased satiety, and insulin resistance (Leproult & Van Cauter, 2010). This is troublesome, as impaired glucose metabolism and insulin resistance have been linked to brain atrophy (Bruehl, Sweat, Tirsi, Shah, & Convit, 2011). Obesity has also been linked to decreased regional cerebral blood flow in the prefrontal cortex (Willeumier, Taylor, & Amen, 2011), decreases in regional gray
matter (Ou, Andres, Pivik, Cleves, & Badger, 2015) and lower total white matter volume (Yau, Kang, Javier, & Convit, 2014; Yokum, Ng, & Stice, 2012), and decreases in neuronal fiber bundle length contributing to brain atrophy (Raji et al., 2010).

Biological effects of obesity and disruptions in the restorative features of sleep independently influence executive function and impose substantial consequences for adolescents experiencing either of these conditions in isolation (Kheirandish-Gozal, Yoder, Kulkarni, Gozal, & Decety, 2014; Lau et al., 2015; Miller, Lee, & Lumeng, 2015; Xanthopoulos et al., 2015). The proposed adapted model (Figure 1.2) is based on the prefrontal model (Beebe & Gozal, 2002), however, takes both obesity and OSAS into consideration. The model suggests that the combination of OSAS and obesity is likely to heighten biological and cognitive risks, beyond those associated with either condition alone (Xanthopoulos et al., 2015). Adolescents with impaired executive function lack motivation, display an inability to initiate activity and have difficulties planning and carrying out goal-directed behaviors (Weaver & George, 2010). In adolescents with both OSAS and obesity, impaired executive function poses serious threats to their ability to engage in, adhere to, and benefit from obesity or OSAS treatment approaches (e.g., lifestyle modifications).
Figure 1.2. Adapted Model. Obesity and OSAS mechanisms leading to executive function impairments

Lifestyle modifications such as diet and physical activity are primary treatment recommendations for adolescents with obesity (Spear et al., 2007) and are also recommended for those with OSAS and obesity (Marcus, Brooks, et al., 2012). Recommendations for increased physical activity frequently accompany primary OSAS treatment with positive airway pressure therapy in adults (Epstein et al., 2009). However, these lifestyle modifications, specifically physical activity, have been given less attention in adolescents with OSAS and obesity. This is an important consideration, as preliminary evidence suggests physical activity is associated with reductions in OSAS severity, improved exercise capacity, and improvements in daytime
sleepiness, quality of life and mood state, even in the absence of significant weight loss (Hargens et al., 2013).

Though current U.S. guidelines state adolescents should participate in 60 minutes of physical activity per day (Physical Activity Guidelines for Americans, 2008), very few meet this benchmark (Song, Carroll, & Fulton, 2013). Findings from a nationally representative sample of students in grades 9-12 indicate only 27.1% achieve one or more hours of moderate-and/or vigorous-intensity physical activity daily (Centers for Disease Control and Prevention, 2015). As adolescents proceed toward adulthood, they become progressively more inactive (Caspersen, Pereira, & Curran, 2000; Gordon-Larsen, Nelson, & Popkin, 2004; Nelson, Neumark-Stzainer, Hannan, Sirard, & Story, 2006; Sallis, 2000). Children with OSAS and obesity are 4.2-times less likely to be involved in organized sports (Spruyt, Sans Capdevila, Serpero, Kheirandish-Gozal, & Gozal, 2010). The prevalence of inactivity, or sedentarism, is unfortunate, as physical activity decreases obesity and obesity-related complications (Aggeloussi et al., 2012; Bluher, Panagiotou, et al., 2014; Bluher, Petroff, et al., 2014; Vrablik, Dobiasova, Zlatohlavek, Urbanova, & Ceska, 2014) and improves both executive function (Davis et al., 2011; Ziereis & Jansen, 2015), and OSAS (C. L. Davis et al., 2011; Giebelhaus, Strohl, Lormes, Lehmann, & Netzer, 2000; Iftikhar, Kline, Hill, & Youngstedt, 2013; Kline et al., 2011; Sengul, Ozalevli, Oztura, Itil, & Baklan, 2011). Unfortunately, physical activity has not been extensively studied in adolescents with obesity and OSAS, a population at high risk for short- and long-term negative health consequences.

**Statement of the Problem**

Currently, obesity rates are remarkably high in the adolescent population and OSAS is increasingly prevalent among adolescents. Recommended treatments for OSAS are poorly
accepted and adhered to by adolescents (DiFeo et al., 2012; Marcus, Beck, et al., 2012; Marcus et al., 2006; Nixon, Mihai, Verginis, & Davey, 2011; Sawyer et al., 2011; Uong, Epperson, Bathon, & Jeffe, 2007). This lack of acceptance and adherence, results in exceedingly high numbers of cases of untreated OSAS. Untreated OSAS leads to adverse consequences including learning and attention difficulties, behavior problems, bed-wetting, retarded growth, hormonal and metabolic imbalances, and failure to thrive (Beebe & Byars, 2011; Chan, Edman, & Koltai, 2004; Marcus, Beck, et al., 2012; Marcus et al., 1995; Sawyer et al., 2011). Recommended treatments for pediatric OSAS include: surgical modification of the airway via adenotonsillectomy, continuous positive airway pressure therapy (CPAP), and/or lifestyle modifications. For children < 13 years of age, adenotonsillectomy is the first-line treatment; however, OSAS persists post-adenotonsillectomy in 33% to 88% of obese children (Costa & Mitchell, 2009; Lee, Hsu, Chang, Lin, & Kang, 2015; Marcus et al., 2013; Mitchell & Kelly, 2004, 2007). Adenotonsillectomy remains first-line treatment for adolescents ≥13 years, followed by CPAP, though effectiveness of CPAP is significantly limited by non-adherence (Marcus, Beck, et al., 2012; Marcus et al., 1995; Nixon et al., 2011; Sawyer et al., 2011).

My own preliminary data indicates that adolescents (ages 13-18 years) are less likely to attend follow-up appointments after completion of an overnight sleep study, and are therefore less likely to initiate positive airway pressure therapy (PAP; inclusive of CPAP and bilevel PAP but does not include any PAP with auto-adjustment or respiratory backup support) treatment than children ages 5-12 years (62% vs. 95%, respectively, p=0.016) (Figure 1.3) (Watach, Ciano, Mogle, & Sawyer, 2015). Objective PAP use (obtained from microprocessor record of the device) indicates lower adherence (adherence defined as use ≥4 hours/night) at both one-week (first week of treatment) and one-month (first month of treatment) among adolescents compared
to children (Figure 1.3) (Watach et al., 2015). Non-adherers in both the child and adolescent age groups show greater night-to-night and week-to-week variability in use (Figure 1.4) (Watach et al., 2015), predictive of poor long-term usage patterns in studies of adults (Budhiraja et al., 2007; McArdle et al., 1999; Rosenthal et al., 2000).

*Figure 1.3. Clinical follow-up and positive airway pressure therapy adherence in children and adolescents. Objective + provider reported use: 9 subject’s electronic medical records lacked a usage report, but provider reported use in chart as ≥ or < 4 hours at follow-up appointment (Watach et al., 2015).*
Because CPAP therapy is palliative rather than curative, lifestyle modifications are also recommended (Sawyer et al., 2011). The causal relationship of obesity and OSAS is well supported (Marcus et al., 2012) and a small but rigorous body of existing research indicates that weight reduction does hold promise as an effective treatment for OSAS in children and adolescents (Kalra et al., 2005; Tauman & Gozal, 2011; Van Hoorenbeeck et al., 2012; Verhulst, Franckx, Van Gaal, De Backer, & Desager, 2009). Given the poor CPAP adherence among adolescents with OSAS and the potential promising aspects of treatment by increasing physical activity to address both OSAS and obesity, research is needed to better inform clinical recommendations. Furthermore, adolescence is an optimal period for intervention as gains made in chronic disease management during childhood may be undone as a result of behavioral
changes during adolescence, potentially affecting long-term well-being and longevity (Rosina, Crisp, & Steinbeck, 2003; Steinbeck, Baur, Cowell, & Pietrobelli, 2009). Therefore, adolescence is a critical time when capacity for learning is ever increasing and new habits are being formed in the context of individual autonomy (Steinbeck et al., 2009).

**Purpose of the Study**

Due to poor physical health outcomes and sub-optimal neurocognitive performance that result from either obesity or OSAS in adolescents, it is imperative that we understand the physical and cognitive impact of the combination of obesity and OSAS in adolescents. By examining executive function outcomes and exploring physical activity levels and sleep patterns in a feasibility study, the results of the proposed research will first provide critical methodological and protocol insights for executing a subsequent, fully-powered cohort study; secondarily, results of the proposed feasibility study will also provide insights to the bidirectional relationship of obesity and OSAS. As a result, this line of inquiry will contribute to the relatively scant evidence addressing the field’s understanding of the health of adolescents with OSAS and obesity, and potentially offer insights for lifestyle modifications as potential future intervention opportunities in this population. The following aims will be addressed:

**Aim 1:** To determine the feasibility of recruiting and retaining a sample of obese adolescents (11-17 years of age) with and without-OSAS.

**Aim 2:** To pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation.

**Aim 3:** To explore executive function impairments as measured by the Global Executive Composite (i.e., overall summary score) and three subscales (i.e., Behavior Regulation
Index, Emotion Regulation Index, and Cognitive Regulation Index), within groups, compared to published normative data, and explore differences in executive function impairments between groups (obese adolescents with and without-OSAS).

**Aim 4:** To describe differences in activity levels (frequency, intensity, time) and sleep duration (major sleep bout total sleep time), measured by 1-week actigraphy (objective measure of rest/activity and sleep) and self-report, between obese adolescents with and without OSAS and explore the relationship between activity levels and sleep duration with executive function (Global Executive Composite scores).

**Definition of Key Terms**

- **Adolescent:** Adolescence is a period of growth and development that occurs between the ages of 10-19 (World Health Organization, 2016); one who is in this age range can be classified as an adolescent.
  - For the purposes of this study, adolescents are defined as those between the ages of 11 and 17 years old (see rationale in sample description, Chapter 3).
- **Obesity:** Defined as a BMI at or above the 95th percentile for adolescents of the same age and sex (Barlow, 2007; Han et al., 2010).
- **Obstructive Sleep Apnea Syndrome (OSAS):** Sleep disordered breathing characterized by prolonged partial or complete upper airway obstructions that disrupt normal ventilation and sleep patterns (American Thoracic Society, 1996).
  - In those < 18 years, apneas and hypopneas are scored using polysomnography; an apnea is scored when peak signal excursions drop by ≥ 90% from pre-event baseline and a hypopnea is scored when the peak signal excursions drop by ≥ 30% (Berry et al., 2012). The apneic and hypopneic events take place for ≥ the
duration of 2 breaths with either a ≥3% oxygen desaturation or an arousal (American Academy of Sleep Medicine, 2005, 2014). An apnea-hypopnea index (AHI) ≥ 1.5 events/hour, inclusive of obstructive events only, is considered abnormal (American Academy of Sleep Medicine, 2005, 2014).

- Executive Function (EF): An assembly of skills and higher order functions (i.e., skills required for organization, planning, and regulation), seated in the prefrontal cortex, that control cognitive processes and performance (Marcus, Brooks, et al., 2012).
- Physical Activity: Defined as “any bodily movement produced by skeletal muscles that requires energy expenditure” (World Health Organization, 2016).

**Assumptions**

Assumptions include:

- Obese adolescents will have impaired executive function.
- Obese adolescents with OSAS will exhibit greater impairments in executive function than obese adolescents without-OSAS.
- Adolescents will have shorter sleep duration than the currently recommended 8-10 hours per 24 hours (Hirshkowitz et al., 2015; Paruthi et al., 2016).
- Adolescents will be less active than the U.S. guideline recommendation of participation in 60 minutes of physical activity per day (*Physical Activity Guidelines for Americans*, 2008).
- Adolescents are a challenging population to recruit, retain, and complete the study/adhere to protocol activities.
Significance of Study

There have been significant increases in the prevalence of obesity among adolescents in recent years. As previously noted, there are strong, bidirectional links between obesity and OSAS; with evidence of increased BMI contributing to the development of OSAS and the mechanisms of OSAS further exacerbating the complications associated with obesity. The individual consequences of obesity and OSAS have far-reaching effects on multiple organs and body systems. However, for the focused purpose of the proposed study, this study seeks to examine the impact on the brain. Both obesity and OSAS cause impairments to the prefrontal cortex (see Figure 2), however, very little is known about the effects on executive function when obesity and OSAS are combined. There is reason to suspect that the combination of these conditions puts adolescents at higher risk for impaired executive function than experiencing either condition alone.

It is of great importance to explore this relationship, as identification of impairments to executive function may, in part, explain the lack of PAP treatment adherence in adolescents with OSAS, as individuals with impaired executive function display difficulties in processing and adapting to new situations and carrying out goal-directed behaviors. Therefore, impairments in executive function may make responding to new situations (i.e., PAP treatment) difficult. As adherence rates appear to be alarmingly low among adolescents, this causes a multitude of complications associated with untreated OSAS. Because of this, the field must explore options on how best to mitigate this issue.

Recently, physical activity interventions have shown promise for not only decreasing obesity, but also decreasing the severity of OSAS (reductions in AHI up to 50%), though most of these studies have been conducted in adult populations (Ackel-D'Elia et al., 2012; Aiello et al.,
Consistent research findings have also revealed that individuals who are more physically active experience less frequent and less severe OSAS than those who are less active or sedentary (Awad, Malhotra, Barnet, Quan, & Peppard, 2012; Peppard & Young, 2004). Obesity and OSAS impact the prefrontal cortex and therefore executive function, while physical activity has demonstrated improvements in executive function, obesity, and OSAS. However, before this avenue can be systematically examined, feasibility data is needed to ensure the success of the intended future inquiry as this appears to be a novel area of study in a potentially challenging target population.

**Chapter Summary**

Research findings have shown that adolescents are becoming more obese and more inactive during the years leading up to adulthood. This increase in obesity has led to a subsequent increase in the prevalence of OSAS in this population. OSAS and obesity independently cause biological and cognitive changes; this is a threat to normal and healthy development occurring during this transitional period to adulthood. Not only are these issues associated with increased health risks during adolescence, but are also linked with health risks that are carried into adulthood. Of great concern are impairments to the prefrontal cortex, leading to dysfunctions and impairments of executive functioning. These impairments are behaviorally manifested as: difficulties mentally manipulating information; maintaining attention and motivation; poor planning, judgment, and decision making; disorganization; haphazard execution of plans; rigid-thinking; emotional lability; and impulsivity. There is reason to suspect that the co-occurrence of obesity and OSAS may further impair children’s ability to engage in/benefit
from any goal-oriented behavior (i.e., physical activity, healthy sleep habits). This is especially concerning because physical activity has been shown to have a positive impact on obesity, OSAS, and executive function. The proposed feasibility study will provide methodological and protocol insights and preliminary data that will support a subsequent, fully-powered cohort study to determine differences in executive function between obese adolescents with and without-OSAS. The overall objective of this line of inquiry is to precisely estimate the impact of obesity and OSAS on executive function in adolescents and potential moderators/mediators. Long-term, this program of research will potentially lead to lifestyle modification interventions that address this public health problem.
Chapter 2

Literature Review

Introduction

In order to understand the current state of the science, identify gaps in the literature, and further justify the significance of the proposed study and future studies along this line of inquiry, multiple scientific content areas and their relationships will be addressed in this chapter. The relative novelty of the proposed research, combined with complexity due to the multi-layered, inter-relationships of numerous research variables specific to adolescence, obesity, OSAS, and executive function, necessitate a broad review of the literature. In order to understand the unique needs and developmental considerations in the care of adolescents, literature on the biological and psychosocial changes occurring during adolescence will be described. Due to the nature of this study, developmental changes related to sleep, body composition, and the brain will be highlighted. The state of the science addressing adolescent obesity, obstructive sleep apnea syndrome (OSAS), treatments, and their impact on adolescent health will also be examined. Thereafter, the core focus of this research and primary outcome of interest, executive function in adolescents with obesity and OSAS, will be explored with a more systematic and focused approach.

Methodology

Two different methods were chosen for the review of the literature due to the breadth, nature, and volume of science to be covered. The two methods presented in this chapter are a scoping review and a systematic review. A systematic review typically focuses on a well-defined question where specific study designs can be identified and collective results synthesized; whereas a scoping review addresses a breadth of scientific topics with many different study
designs that leads to new hypotheses/questions and/or identification of gaps in the current evidence (Arksey & O'Malley, 2005). Due to the breadth of topics being covered, the scoping review was chosen to (1) rapidly summarize the science, (2) assess key concepts in specific areas of adolescent health and development, obesity, OSAS, treatments, and (3) identify gaps in the existing literature.

With the scoping review methods, it is important to note that strict limitations are not placed on search terms from the outset in order to maintain a wide approach to generate a breadth of coverage. This process is more iterative than linear, requiring tactful maneuvering of the literature to ensure comprehensive coverage. Multiple databases were used for searching the literature and numerous combinations of search terms were used to identify literature related to the topical areas of interest in this chapter (Table 2.1). In addition to database searches, ancestry searching was also used as a means to locate primary research. Inclusion and exclusion criteria were set broadly, to ensure comprehensive searches. Search inclusion criteria were: primary research, reviews, textbooks, recommendations set out by organizations (based on research but outlined on websites), and English language. For purposes of this study, grey literature such as dissertations, conference abstracts, and private sector research was excluded. Though some of these sources may provide breaking new findings, inconsistent standards for peer-review and absence of editorial control and/or potential for bias in grey literature increase the risk of lower methodological quality than peer-reviewed published literature.
<table>
<thead>
<tr>
<th>Topical Areas*</th>
<th>Search Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescent Health</td>
<td>- Development, developmental changes, change, changes experienced, growth and development</td>
</tr>
<tr>
<td>Sleep Recommendations for Adolescents</td>
<td>- Sleep recommendations, recommended sleep, sleep health, sleep duration, sleep guidelines - Benefits, improved health, lack of sleep, consequences</td>
</tr>
<tr>
<td>Biological Influences on Sleep</td>
<td>- Sleep, Changes to sleep, biological process, biological changes, sleep-wake process, sleep pressure, circadian shift</td>
</tr>
<tr>
<td>Psychosocial Influences on Sleep</td>
<td>- Sleep, psychosocial influences, social jet-lag, screen time, electronics, bedtimes</td>
</tr>
<tr>
<td>Restricted and Inadequate Sleep</td>
<td>- Restricted sleep, inadequate sleep, sleep deprivation, sleep irregularities, sleep fragmentation, lack of sleep, short sleep, consequences</td>
</tr>
<tr>
<td>Policy Solutions</td>
<td>- School start times, delayed school start, sleep, policy,</td>
</tr>
<tr>
<td>Chronic Restricted/Inadequate Sleep and Body Composition</td>
<td>- Search terms used in “Restricted and Inadequate Sleep” + body composition, weight, obese, obesity, overweight, fat, fatness, BMI</td>
</tr>
<tr>
<td>Developmental Changes to the Brain</td>
<td>- Search terms used in “Adolescent Health” + brain, cognitive development, cognition, prefrontal cortex - Obese, obesity, overweight, sleep apnea, obstructive sleep apnea, obstructive sleep apnea syndrome</td>
</tr>
<tr>
<td>Obesity in Adolescents</td>
<td>- Weight, obese, obesity, overweight, fat, fatness, BMI - Effects, consequences, prevalence - Minority, low socioeconomic status - Lack of physical activity, low physical activity</td>
</tr>
<tr>
<td>Obesity’s Contribution to OSAS</td>
<td>- Obese, obesity, overweight, fat, fatness, BMI - Sleep apnea, obstructive sleep apnea, obstructive sleep apnea syndrome, OSA, OSAS</td>
</tr>
<tr>
<td>OSAS in Adolescents</td>
<td>- Sleep apnea, obstructive sleep apnea, obstructive sleep apnea syndrome, OSA, OSAS - Pathogenesis, risk, pathophysiology, etiology, treatment, efficacy - Positive airway pressure, use, non-adherence, underutilization</td>
</tr>
<tr>
<td>Consequences of Untreated OSAS</td>
<td>- Sleep apnea, obstructive sleep apnea, obstructive sleep apnea syndrome, OSA, OSAS - Untreated, consequences, risks, complications - Positive airway pressure, use, non-adherence, underutilization</td>
</tr>
<tr>
<td>Consequences of OSAS on the Adolescent Brain</td>
<td>- Sleep apnea, obstructive sleep apnea, obstructive sleep apnea syndrome, OSA, OSAS - Untreated, consequences, risks, complications - Brain, cognitive development, cognition, prefrontal cortex, neurocognitive impairments</td>
</tr>
<tr>
<td>OSAS + Obesity</td>
<td>- Search terms used in “Obesity’s Contribution to OSAS” + combination, shared, together, link, cause</td>
</tr>
<tr>
<td>Weight Loss Physical Activity</td>
<td>- Search terms used in “Obesity in Adolescents”, “OSAS in Adolescents” + physical activity, exercise, weight loss</td>
</tr>
</tbody>
</table>

Notes: *all topical area searches included a variation of the terms: adolescent, adolescents, adolescence, youth, teen (and pediatric on occasion); Databases used: PubMed, CINAHL, PsycINFO, The Cochrane Library, and The Web of Science; Other sources: Bibliographies and Penn State Library catalog (for books); OSA, obstructive sleep apnea; OSAS, obstructive sleep apnea syndrome; BMI, body mass index.
A systematic review approach is used to address this study’s primary outcome, executive function in obese adolescents with and without-OSAS. The objective of the systematic review is to summarize the scientific evidence regarding the effects of the combination of obesity and OSAS on executive function in adolescents. This systematic approach is applied in order to support the aims of the current study and highlight and explore future research agenda opportunities. The methodology of the systematic review is described later in this chapter (after discussion of the literature obtained in the scoping review).

**Scoping Review**

**Adolescent Health**

In the late 1700’s and early 1800’s there was a recognized need to specifically attend to the care of children differently than adults and a specialization in pediatrics evolved (Castiglioni & Krumbhaar, 1947). However, it was not until 1855 that the first pediatric hospital was founded and 1930 and 1933 that the American Academy of Pediatrics and American Board of Pediatrics were established, respectively (Luecke, 2004). The first adolescent symposium was held by the American Academy of Pediatrics in 1941, with the establishment of the Committee on Youth (currently, the Committee on Adolescence) in 1955 (Alderman, Rieder, & Cohen, 2003; Jenkins, 2016). In 1968, a group of academic faculty formed the Society for Adolescent Medicine, promoting the improvement of care and research for adolescents, and by the late 1970’s the Department of Health and Human Services funded multidisciplinary training programs in adolescent medicine (Alderman et al., 2003; Jenkins, 2016). It was not until 1991, only 25 years ago, that the American Board of Pediatrics recognized adolescent medicine as a board-certified entity (Alderman et al., 2003; Jenkins, 2016).
In comparison to the history of pediatrics, it is evident that the specific field of adolescent health and medicine is still relatively young. However, these historical events indicate that adolescence is recognized as a unique developmental period that needs to be given special consideration. Due to the many developmental changes occurring in this period, adolescents potentially appear to be physically child-like, or adult-like, but adolescents should not be treated as one or the other. Adolescence is defined as a period within the lifespan marked by critical transitions to a person’s biological, cognitive, psychological, and social characteristics (World Health Organization, 2016). During this time, adolescents are changing from what is typically considered child-like to what is considered adult-like (Lerner & Spanier, 1980).

In the midst of this development, perhaps the most commonly discussed developmental characteristics are puberty and sexual development. Though the sequence of this change is largely predictable, there is great individual variability that contributes to inter-individual differences, due in large part to genetics, social life events, socioeconomic status, body fat, and presence of other diseases or illnesses (American Psychological Association, 2002). In addition, social influences become more predominant, with physical appearance, body image, and the need to “fit in” becoming large concerns for adolescents which increase risks for depression and other psychological symptoms and disorders to emerge (American Psychological Association, 2002).

Recently, adolescent sleep health has become increasingly recognized as important to overall adolescent health. Along with the many changing body systems in adolescence, both altered intrinsic sleep mechanisms (i.e., biological processes/mechanisms) and psychosocial changes occur that alter sleep. Delayed sleep patterns (i.e., delayed sleep phase) of adolescence, a biologically-determined, normal phenomena, is recognized globally, across pre-industrial and
modern cultures (Carskadon, 2008; Gradisar, Gardner, & Dohnt, 2011); this circadian shift is inclusive of later bedtimes with propensity for later wake times. Yet, adolescents have stable, socioculturally-dictated early wake-times that reduce sleep opportunity and thereby total sleep time (Crowley, Tarokh, & Carskason, 2014).

**Sleep Recommendations for Adolescents**

Recently, the National Sleep Foundation (NSF) released recommendations that school age children (6-13 years) should sleep between 9-11 hours and teenagers (14-17 years) should sleep 8-10 hours (Hirshkowitz et al., 2015), though it is not defined whether this is hours per night or per 24-hours. These recommendations are based on a systematic review of 312 articles and authored by an 18-member panel, comprised of both sleep experts and experts in other areas of medicine, physiology, and science. For the first time, the American Academy of Sleep Medicine (AASM) has also released guidelines. These recommendations came after a panel of 13 sleep experts reviewed 864 published articles addressing the relationship between sleep duration and health in children (Paruthi et al., 2016). The AASM recommends that children 6-12 years of age should sleep 9 to 12 hours per 24 hours on a regular basis to promote optimal health and teenagers (13-18 years) should sleep 8 to 10 hours per 24 hours on a regular basis to promote optimal health (Paruthi et al., 2016). Though age groups defining the adolescent/teen years are different between the two sets of sleep recommendations (NSF 14-17 years; AASM 13-18 years), there is consensus that adolescents require at least 8 to 10 hours of sleep.

Regularly sleeping the recommended hours is associated with better physical and mental health outcomes such as: improved attention, learning, memory, mood/emotional regulation, behavior, and quality of life (Paruthi et al., 2016). Those who sleep less than 8 hours per night for prolonged periods compromise their health and well-being (Hirshkowitz et al., 2015).
Regularly sleeping less than, or more than, the recommended hours is associated with the aforementioned problems as well as increased risk of accidents, injuries, depression, suicide, hypertension, obesity, and diabetes (Becker, Langberg, & Byars, 2015; Paruthi et al., 2016).

**Biological Influences on Sleep**

There are multiple biological influences on sleep across the lifespan; for the purposes of this review, these influences will be discussed in the context of adolescence. As previously noted, adolescents around the globe experience developmental changes that influence sleep. One of the biological regulators of sleep is the homeostatic sleep-wake process, simply defined as a “pressure” to sleep (Jenni, Achermann, & Carskadon, 2005). Pressure to sleep increases as wakefulness is prolonged and dissipates during sleep. This pressure is shown to accumulate more slowly in adolescents than children, causing a natural ability to stay awake longer in the evening (Jenni et al., 2005). For example, at 11 p.m., the sleep pressure of an adolescent will be much less than that of a child or pre-pubertal adolescent. This is one potential mechanism explaining adolescent’s natural ability to delay sleep.

Another biological change in adolescence is a shift in the circadian rhythm, often referred to as the “internal clock.” This system influences sleep-wake patterns, but unlike the homeostatic sleep-wake process, it does not rely on previous sleep episodes. Adolescents begin to experience circadian phase delay (i.e., later sleep onset and offset) about the time of puberty (Carskadon, 1993; Carskadon & Acebo, 2002; Carskadon, Wolfson, Acebo, Tzischinsky, & Seifer, 1998). The master clock for the circadian system is the suprachiasmatic nuclei (SCN) of the hypothalamus (Crowley et al., 2014). The hormone melatonin, secreted by the pineal gland and regulated by the SCN, fluctuates with the circadian rhythm (i.e., low levels during the day and higher levels in the evening). In adolescents, more mature stages have been associated with later
onset and offset of melatonin, even when light exposure is fixed (Carskadon, Acebo, & Jenni, 2004; Crowley et al., 2014; Rofey, McMakin, Shaw, & Dahl, 2013). This phenomenon has been labeled delayed phase shift, reflective of the melatonin shift contributing to later sleep onset (Carskadon, 2008).

These biological processes appear to be consistent across cultures, as a meta-analysis of 13 studies from 9 countries indicated that weekend bedtimes are delayed by approximately 2.75 hours in those between the ages of 11-18 years (Gradisar et al., 2011). Further, these later sleep time preferences existed before the introduction of computers, internet, and cellphones (Carskadon, 2008), all current psychosocial influences on delayed sleep, or phase shifting.

**Psychosocial Influences on Sleep**

In addition to the biological influences that promote later sleep times in adolescents, there are numerous psychosocial influences to also take into consideration. Due to adolescents’ bodies not signaling them to sleep, they often stay awake to study, use electronic devices (e.g., television, videogames, cellphones), and/or socialize (Bartel, Gradisar, & Williamson, 2015; Gradisar et al., 2011; Hysing et al., 2015; Knutson & Lauderdale, 2009). A systematic review of 67 studies from 1999-2014 focused on the association between screen time and sleep outcomes among school-aged children and adolescents (Hale & Guan, 2015). Screen time was adversely associated with sleep outcomes, with evidence of shortened sleep duration and delayed sleep timing in 90% of the studies (Hale & Guan, 2015).

A poll by the National Sleep Foundation discovered that 89% of adults and 75% of children/adolescents have at least one electronic device in their bedrooms (National Sleep Foundation, 2014). Not only does this promote a gateway for distraction/delaying sleep, but there is also recent evidence that suggests the light emitted from these devices may further delay sleep
by delaying the circadian system and increasing alertness (Cajochen et al., 2011; Chang, Aeschbach, Duffy, & Czeisler, 2015). In addition, bedtime monitoring by parents becomes less common as children age, with only 35% of parents of 15-17 year olds enforcing bedtimes compared to 70% of parents of 6-11 year olds (National Sleep Foundation, 2014). Children, including adolescents, of parents who enforced bedtimes slept an average of 1.1 hours longer than children whose parents did not have similar rules (National Sleep Foundation, 2014).

**Restricted and Inadequate Sleep**

The combination of biological and psychosocial factors that promote delayed bedtimes often conflict with early school start times, leading to chronically restricted sleep. In the National Sleep Foundation poll, over half (58%) of 15-17 year olds reported sleeping 7 hours or less per night, and only 10% reported sleeping 9 hours or more (National Sleep Foundation, 2014). There are also discrepancies in sleep schedules between school days and weekends, and also between biological and social times, that cause social jetlag (Wittmann, Dinich, Merrow, & Roenneberg, 2006). Changes in sleep/wake times result in sleep irregularities for many adolescents (Crowley et al., 2014), with weekend time in bed averaging about 1 to 1.5 hours longer per night than week nights (Gradisar et al., 2011). Restricted and inadequate sleep poses a series of threats to adolescents, including: conferred risk for mental/emotional dysfunction including depression (Lovato & Gradisar, 2014; Shochat, Cohen-Zion, & Tzischinsky, 2014), obesity (Meldrum & Restivo, 2014; Owens, 2014), increased risk for impairments in memory, behavior, and school performance (Owens, 2014; Shochat et al., 2014; Wolfson & Carskadon, 2003), and increased engagement in injury-related risk behaviors (e.g. infrequent seatbelt use, drinking and driving, texting while driving) (Meldrum & Restivo, 2014; Wheaton, Chapman, & Croft, 2016) and fatal consequences such as automobile accidents (Owens, 2014). It is important to account for sleep
duration as a research variable in any study of obesity and OSAS in adolescents with the outcome of executive function, as executive function is potentially confounded by short sleep duration (Anderson, Storfer-Isser, Taylor, Rosen, & Redline, 2009).

**Policy Solutions**

With increasing evidence of the biological shifts that influence sleep during adolescence, multiple national level organizations have advocated for later school start times. For example, California’s U.S. Representatives introduced a bill in Congress called the Zzz’s to A’s Act ("Zzz's to A's Resolution," 2009), a grant incentive of $25,000 for school districts considering later start times. A petition arguing that schools should not start before 8 a.m. was brought to Congress during the 2012 National Sleep Awareness Week. Start School Later is a group of health professionals, educators, and researchers committed to raising public awareness surrounding proper sleep, advocating for the data-based benefits of later school start times (Start School Later, 2017; Wolfson & Johnson, 2014).

Later school start times correspond to increased sleep time. When school start times were delayed by 25-50 minutes across districts, total sleep time increased from 25-77 minutes on weeknights (Minges & Redeker, 2016). Additional benefits include improved attendance, decreased tardiness, increased alertness in the classroom, better grades, and fewer automobile accidents (Minges & Redeker, 2016; Vorona et al., 2011; Wheaton et al., 2016). Interestingly, a longitudinal study examining automobile accident rates in 17-18 year olds discovered that schools that implemented later start times had accident rates decrease 16.5%, whereas schools that did not implement the change had increases of 7.8% over the same 2-year time period (Danner & Phillips, 2008). Following substantial evidence illustrating adverse physical and psychological health consequences of inadequate sleep, The American Academy of Pediatrics
and The U.S. Centers for Disease Control and prevention support delaying school start times for middle and high school students, though actual implementation of these recommendations have been limited (Barnes et al., 2016).

**Chronic Restricted/Inadequate Sleep and Body Composition**

Recently, the relationship between sleep fragmentation and deprivation and body composition has been explored. There is compelling evidence linking sleep fragmentation and deprivation to the prevalence of childhood overweight (body mass index [BMI] ≥ 85th-94th percentile for adolescents of the same age and sex) and obesity (BMI ≥ 95th percentile) (Chahal, Fung, Kuhle, & Veugelers, 2013; Golley, Maher, Matricciani, & Olds, 2013; Jarrin, McGrath, & Drake, 2013; Marshall, Glozier, & Grunstein, 2008; Spruyt, Molfese, & Gozal, 2011; Wang & Beydoun, 2007). Further, there is a wealth of epidemiologic data supporting the association between short/inadequate sleep and being overweight or obese (Fatima, Doi, & Mamun, 2015; Grandner, Schopfer, Sands-Lincoln, Jackson, & Malhotra, 2015; Hart, Cairns, & Jelalian, 2011; Krueger, Reither, Peppard, Burger, & Hale, 2015; Miller, Lumeng, & LeBourgeois, 2015; Suglia, Kara, & Robinson, 2014). Many studies suggest that insufficient/lack of sleep places one at nearly twice the risk of being overweight or obese, with studies indicating obese children are 1.5- to 2-fold more likely to be short sleepers (Moraleda-Cibrian & O'Brien, 2014b; Padez, Mourao, Moreira, & Rosado, 2009; Taveras, Rifas-Shiman, Oken, Gunderson, & Gillman, 2008b). Using prospective cohort data from four waves (wave 1: 1994–95, mean age = 15.9; wave 2: 1996, mean age = 16.9; wave 3: 2001–02, mean age = 22.3; and wave 4: 2008–09, mean age = 28.8) of the National Longitudinal Study of Adolescent to Adult Health, Krueger and colleagues (2015) discovered those who slept -0.50 standard deviations less than the age specific average sleep hours, in all four waves of the study, had 1.45 times the odds of being obese. One
meta-analysis of 11 longitudinal studies, comprising 24,821 child and adolescent participants, revealed that subjects with short sleep duration had twice the risk of being overweight or obese (OR = 2.15; 95% CI 1.64, 2.81), providing evidence that chronic sleep restriction is associated with future overweight and obesity (Fatima et al., 2015).

Beyond sleep duration, social jetlag and psychosocial influences have been associated with increased rates of overweight or obesity. It is suggested that living “against the clock” may be another factor to consider when addressing the obesity epidemic (Roenneberg, Allebrandt, Merrow, & Vetter, 2012). Behavioral maladaptive habits such as increased high-calorie snacking and general increased food intake is also correlated with insufficient sleep (Brondel, Romer, Nougues, Touyarou, & Davenne, 2010; Chaput, 2016; Hogenkamp et al., 2013; Nedeltcheva et al., 2009). There is obvious negative impact on body composition as the result of chronically restricted or inadequate sleep. Additionally, the brain is negatively impacted by both inadequate amounts of restorative sleep and increased body weight.

**Developmental Changes to the Brain**

As normative changes to biological and psychosocial sleep mechanisms have been discussed, as well as their influence on body composition, it is also important to discuss the normative developmental changes to the brain during adolescence. Though there are inter-individual differences in cognitive development, the many developmental changes occurring during this period allow adolescents to engage in cognitive processes that were previously beyond their abilities (American Psychological Association, 2002). Adolescent brain maturation is characterized by the emergence of executive function, mediated by the prefrontal cortex, a region that undergoes significant changes across adolescence (Selemon, 2013). Perhaps one of the most prominent structural changes is the marked decline of cortical synapses, a process
referred to as neuronal pruning (Blakemore & Choudhury, 2006). The prefrontal cortex undergoes this process of pruning resulting in the reorganization of interacting neural networks and an increase in white matter (Caballero, Granberg, & Tseng, 2016; Willing & Juraska, 2015). With significant changes taking place during adolescence, the brain is particularly vulnerable to developmental insults (Caballero et al., 2016). These insults can include both obesity and OSAS, a sleep-disordered breathing syndrome characterized by prolonged partial or complete upper airway obstructions that disrupt normal ventilation and sleep patterns (American Thoracic Society, 1996). Obesity in adolescence is linked to detrimental developmental changes to the brain including: atrophy (Bruehl et al., 2011; Raji et al., 2010), decreased blood flow (Selim, Jones, Novak, Zhao, & Novak, 2008; Willeumier et al., 2011), and decreases in white matter (Yau et al., 2014). Additionally, systematic reviews have indicated consistent, inverse relationships between obesity and executive function in adolescents (Reinert et al., 2013; Smith, Hay, Campbell, & Trollor, 2011). OSAS also has significant impacts on the brain (as discussed in Chapter 1 and in further detail later). This is of great concern as insults and injuries to the prefrontal cortex during adolescence can disrupt normal brain maturation and thereby functioning through adulthood (Caballero et al., 2016).

**Obesity in Adolescents**

Obesity in children and adolescents is currently recognized as a significant public health problem that affects nearly every organ system in the body (Ng et al., 2014). Between 2007 and 2008, 31.7% of U.S. children between the ages of 2 and 19 were at or above the 85th percentile for weight (Ogden, Carroll, Curtin, Lamb, & Flegal, 2010); unfortunately, this statistic has remained relatively stable over recent years (Ogden et al., 2014). This percentage is a dramatic increase from decades ago, where the percentage of adolescents aged 12-19 years who were
Obese (BMI ≥ 95th percentile) increased from 5% to nearly 21% from 1980 to 2012 (Ogden et al., 2014). In addition to, and perhaps even as a result of the biological and psychosocial changes occurring during adolescence, sedentary lifestyles, a contributor to obesity, are adopted by many adolescents (Hobbs, Pearson, Foster, & Biddle, 2015). This is of great concern because up to 90% of children and adolescents who are obese become overweight or obese adults (American Psychological Association, 2002; Freedman, Khan, Dietz, Srinivasan, & Berenson, 2001; Freedman et al., 2005; Guo & Chumlea, 1999; Serdula et al., 1993; Singh, Mulder, Twisk, van Mechelen, & Chinapaw, 2008; Whitaker et al., 1997).

Those of low socioeconomic and/or ethnic minority status are at even greater risk for obesity. Diseases and adverse health consequences related to lack of physical activity, such as obesity and diabetes, are more common among these groups (American Psychological Association, 2002; Knowlden & Sharma, 2013; Ross, 2000). Among Hispanic adolescents ages 12-19 years, 38.1% are classified as overweight and 22.6% as obese (Ogden et al., 2014). Among African Americans, 39.8% overweight and 22.1% obese (Ogden et al., 2014). The prevalence of overweight and obesity are higher for ethnically/racially diverse adolescents than among non-Hispanic white adolescents, who have lower, but still alarmingly high prevalence of overweight (31.2%) and obesity (19.6%) (Ogden et al., 2014).

Inequality in the built environment (i.e., manmade surroundings that provide a setting for human activity; e.g., homes, buildings, streets, parks, green space in neighborhoods) may also play a large role in the differences in observed obesity prevalence, as the built environment influences a person’s level of physical activity (Ding, Sallis, Kerr, Lee, & Rosenberg, 2011; Ferdinand, Sen, Rahurkar, Engler, & Menachemi, 2012; Gordon-Larsen, Nelson, Page, & Popkin, 2006). Physical activity is lower, and screen time and sedentary time is higher, among
minority and low socioeconomic status children and adolescents (Eaton et al., 2010). This is an unfortunate and complicated issue, as there are fewer physical activity resources and more safety concerns for adolescents with these characteristics, further contributing to the chronic health disparities faced in minority adolescents and their families/communities (Lindgren et al., 2016; Lovasi, Hutson, Guerra, & Neckerman, 2009). Beyond the increased risk for diabetes, high blood lipids, hypertension, depression, and the numerous previously mentioned complications of obesity, OSAS risks are also increased in adolescents who are obese.

**Obesity’s Contribution to OSAS**

Obesity is a risk factor for sleep apnea (Gozal, 2014), as the risk of OSAS in obese adolescents is markedly increased (Arens & Muzumdar, 2010). However, there is also evidence that the presence of OSAS may promote or aggravate obesity mechanisms (Gozal, 2014). The trend of increased risk of OSAS among obese children and adolescents has been reported across many countries (Bixler et al., 2009; Kalra et al., 2005; Kohler et al., 2009; Kohler & van den Heuvel, 2008; Mathew & Narang, 2014; L. J. Mitchell et al., 2014; Verhulst et al., 2009; Verhulst et al., 2007; Wing et al., 2003). In fact, among obese children and adolescents, the risk for OSAS is increased 4-5-fold, with every 1 kg/m² increase in BMI, which increases the risk for OSAS by 12% in this young population (Redline et al., 1999).

The upper airway narrowing that takes place with obesity is thought to play a large role in the contribution of obesity to OSAS in adolescents. Pharyngeal narrowing results from fatty infiltration of the tongue and upper airway structures as well as subcutaneous fat deposits in the neck region, promoting increased collapsibility of the airway (Arens et al., 2011; White, Lombard, Cadieux, & Zwillich, 1985). Additionally, abdominal obesity may affect lung volumes, respiratory load, and diaphragmatic excursion (Abdeyrim et al., 2015; Fiorino &
Brooks, 2009). Obesity is accompanied by systemic inflammatory processes and alterations in appetite-regulating hormones such as decreases in circulating ghrelin and increases in circulating leptin due to peripheral and central leptin tissue resistance (Aygun, Gungor, Ustundag, Gurgoze, & Sen, 2005; Celi et al., 2003; Klok, Jakobsdottir, & Drent, 2007; Miller, Lee, et al., 2015; Reinehr, Kratzsch, Kiess, & Andler, 2005; Tschop et al., 2001). Leptin resistance dampens the natural respiratory stimulant properties of leptin, resulting in weakened respiratory reflexes, particularly during sleep (Arens & Marcus, 2004; Pan & Kastin, 2014). Additionally, the fragmented sleep associated with obesity can increase the arousal threshold, possibly aggravating the duration of obstructions (Beebe et al., 2007).

**OSAS in Adolescents**

One recognized difficulty in any attempt to synthesize literature on OSAS in adolescents is the often-large age span included in pediatric OSAS studies, with very few focusing on just adolescents (Andersen, Holm, & Homoe, 2016). The pathogenesis of OSAS is different in children versus adolescents, with the risk of developing OSAS due to being overweight or obese primarily found among adolescents age ≥ 12 years (Arens & Marcus, 2004; Beebe, 2006; Marcus, Brooks, et al., 2012; Yuan et al., 2013). However, regardless of the cause, OSAS can produce serious cardiovascular and neurobehavioral impairments via sleep fragmentation and gas exchange abnormalities (Katz & Marcus, 2014).

The disease process of OSAS has been long recognized and was initially described by Dr. Mackenzie over a century ago (Mackenzie, 1880). However, it was not recognized in children until the mid-1970’s (Guilleminault, Eldridge, Simmons, & Dement, 1976); the first reported non-surgical treatment for OSAS, nasal continuous positive airway pressure was first described in 1986 (Guilleminault, Nino-Murcia, Heldt, Baldwin, & Hutchinson, 1986).
OSAS typically has two peaks; the first occurs in children 2-8 years of age, and a second
during adolescence with relation to weight gain (Chang & Chae, 2010). Adenotonsillar
hypertrophy is the most common etiology of OSAS in children, making surgical treatment the
first-line treatment (Marcus, Brooks, et al., 2012; Tal, 2014). Many children experience
significant improvement in OSAS, defined by a decrease in apnea-hypopnea index (AHI),
following surgery (Tal, Bar, Leiberman, & Tarasiuk, 2003). However, the residual risk of OSAS
(i.e., persistently elevated AHI) after adenotonsillectomy is markedly higher in obese children
than non-obese children (Bhattacharjee et al., 2010; Mitchell & Kelly, 2004; Tagaya et al.,
2012). Because surgery is less successful at resolving OSAS in obese children (Andersen et al.,
2016; Friedman, Wilson, Lin, & Chang, 2009), continuous positive airway pressure (CPAP)
therapy is commonly recommended (Capdevila et al., 2008; Li, Celestin, & Lockey, 2016;
Marcus, Brooks, et al., 2012). CPAP therapy is a highly efficacious treatment for OSAS in
children and adolescents and results in significant (all p <0.001) improvements in respiratory and
sleeps parameters (i.e., AHI, oxygen saturation [SpO₂]) (Marcus et al., 2006).

Unfortunately, underutilization and non-adherence (use of ≤4 hours/night on 70% of
nights) is an issue with CPAP therapy (Marcus, Beck, et al., 2012; Marcus et al., 2006; Nixon et
al., 2011; Sawyer et al., 2011; Simon, Duncan, Janicke, & Wagner, 2012; Uong et al., 2007).
Many studies evaluating CPAP use in pediatric populations provide evidence for CPAP
underutilization and non-adherence. In one study, one third of children dropped out before 6
months and those that were adherent only had a mean use of 5.3 hours per night (Marcus et al.,
2006). And though this usage level is clinically defined as adherent based on common clinical
criteria of ≥ 4 hours/night of use, children should be sleeping no less than 8 hours per night; a
significant portion of every major sleep bout is therefore untreated. Another study found that
adherence was suboptimal, with an average use of 3 hours per night on 22 days per month (DiFeo et al., 2012). Additionally, initial CPAP usage during the first week of use is often predictive of subsequent use (Budhiraja et al., 2007; McArdle et al., 1999; Nixon et al., 2011; Rosenthal et al., 2000) which means early CPAP failure or suboptimal use, lessens the likelihood for long-term adherence and thereby lower CPAP effectiveness as a long term treatment of OSAS. It is clear that despite the efficacy and safety of CPAP therapy, treatment adherence is a major challenge for the field of pediatric sleep medicine. This is unfortunate, as the therapy has an extraordinary ability to reduce childhood comorbidities and adult cardiovascular disease (Davidson Ward & Perez, 2014; Gozal, 2014).

Consequences of Untreated OSAS

Left untreated, OSAS can lead to increased mortality and contribute to significant cardiovascular, metabolic, and cognitive complications (Capdevila et al., 2008; Hargens et al., 2013; Marcus, Brooks, et al., 2012; Redline et al., 2007). However, the exact threshold/severity of OSAS associated with these adverse consequences remains unclear, as there are individual traits and widespread normative developmental changes across childhood (Katz & D'Ambrosio, 2008; Katz & Marcus, 2014). Though there are numerous cardiovascular and metabolic consequences of untreated OSAS, the consequences on the brain will be discussed in detail due to the focus of the proposed research.

Consequences of OSAS on the Adolescent Brain

Characteristics of OSAS, such as intermittent hypoxia and sleep fragmentation, have significant negative effects on the brain (Tal, 2014), specifically the prefrontal cortex and the behavioral and cognitive manifestations of impairments to this region (Beebe, 2006; Beebe & Gozal, 2002; O'Brien, 2014). This is especially concerning as the brain is very vulnerable in the
adolescent period (Caballero et al., 2016). The role of inflammation and oxidative stress as mechanisms for cellular neuronal changes in children with OSAS have been suggested, as animal studies have shown that intermittent hypoxia leads to cellular damage and impaired behavioral outcomes similar to those observed in OSAS (Gozal, 2009; Hambrecht et al., 2009; Li et al., 2015; Zhou, Cai, Zhang, Jia, & Gong, 2009). The increased recognition of subtle neurocognitive impairments in those with variations of sleep disordered breathing has forced practitioners to address threshold levels of disease that require intervention (Katz & Marcus, 2014).

Because there are differences in the epidemiology and pathophysiology of OSAS in children and adolescents, there has been debate regarding the scoring of respiratory events in adolescents, with little information to guide which scoring rules should be applied for PSG in adolescent’s ages 13-18 years old (Tapia et al., 2008). Even the American Academy of Sleep Medicine states there is no consensus for scoring respiratory events for this age group (Berry et al., 2012). Although adult scoring criteria are commonly applied in adolescents, there are a few major differences between the pediatric and adult scoring. One of particular importance is the duration of the apneas and hypopneas; in adults, they are only scored if they are ≥ 10 seconds in duration, whereas in children they are scored if they are ≥ 2 breaths duration (even if its < 10 seconds) (Berry et al., 2012). This is due to children having increased respiratory rates and lower residual capacities, meaning they are more likely to desaturate during brief apneas that may last < 10 seconds (Beck & Marcus, 2009).

Though adolescent OSAS may appear more adult like in relation to OSAS etiology, there is support for the use of pediatric scoring criteria in adolescents. Accardo et al. (2010) scored PSG’s in healthy, non-obese adolescents (ages 13-18 years, n= 101) and found far lower mean AHI when using the adult scoring criteria versus pediatric (AHI= 0.4/hr vs. AHI=1.7/hr,
respectively, p < 0.001). This indicates that far fewer adolescents would meet OSAS diagnostic criteria if adult scoring were used (i.e., AHI ≥ 5/hr). Similarly, another study compared pediatric and adult scoring criteria in healthy, non-obese children and adolescents (ages 8-18 years, n= 68) (Tapia et al., 2008). Because this was a healthy sample, median AHI was 0/hr using either scoring criteria, however, hypopneas would be scored in 15 out of 32 adolescents using pediatric rules while only 2 would be scored using adult criteria (Tapia et al., 2008). While this difference was statistically significant (p=0.043), it was not clinically relevant due to the low AHI of the sample (Tapia et al., 2008). Yet in evaluations of OSAS in adolescents, there is relatively consistent evidence to support application of pediatric respiratory event scoring criteria (Accardo et al., 2010; Aurora et al., 2011; Tapia et al., 2008), as children tend to exhibit complications of OSAS with a lower AHI than adults (Beck & Marcus, 2009).

The Combination; OSAS + Obesity

Based on this scoping review, obesity and OSAS have many similar health implications, including cardiovascular, metabolic, and neurocognitive consequences. On top of the comorbidities associated with these conditions, the normal developmental changes that occur during the adolescent period are impaired by both obesity and OSAS. The adolescent stage is very sensitive and important for the transition to adulthood, and the negative effects of obesity and OSAS are increasingly recognized as imparting risks for unhealthy transition to adulthood. Though we may know a respectable amount about the individual effects of these conditions, there is not much known about the effects of their combination in adolescents (Mathew & Narang, 2014). However, similar to obesity, OSAS is recognized as a low-grade systemic inflammatory disease, and the coexistence of the two conditions is suspected to further exacerbate inflammatory responses (Gozal, 2009; Gozal et al., 2010; Gozal, Serpero, Sans
It is known that children with the combination of obesity and OSAS tend to be older, have an etiology of OSAS that is linked to obesity rather than tonsillar or adenoidal hypertrophy, and are at greater risk for cardiovascular and metabolic dysfunction than their lean counterparts with OSAS (Dayyat, Kheirandish-Gozal, Sans Capdevila, Maarafeya, & Gozal, 2009; Redline et al., 2007). Those with the combination of obesity and OSAS have increased severity of OSAS. In one study, OSAS (AHI >2/hr) was more prevalent (78% v. 61.7%) in snorers (4-17 years of age) who were obese/overweight, as compared to non-obese subjects and the relative risk for OSAS was significantly higher among obese children compared to non-obese children (OR= 3.05; 95% CI, 1.78 to 5.25; p < 0.0001) (Kheirandish-Gozal, Sans Capdevila, Kheirandish, & Gozal, 2008). Additionally, those who were obese had more severe OSAS (AHI 9.6/hr v. 7.2/hr; p < 0.0001) (Kheirandish-Gozal et al., 2008). Another study looking at the effects of OSAS and obesity found that 53% of subjects (4.2-18 years) who were obese had an AHI >1/hr, compared to 29% of non-obese subjects (Reade et al., 2004). Similarly, out of 91 children and adolescents (6-16 years of age), all of whom were overweight (n=27) or obese (n=64), only 54% had a normal PSG (Verhulst et al., 2007). A study seeking to compare BMI’s of those with and without-OSAS (5-15 years of age; n= 288) found that obesity was observed in 7% of non-OSAS cases as compared to 37% of the OSAS cases (Barone et al., 2009). In yet another study comparing BMI between children with obesity and OSAS and obese children without OSAS, BMI was higher in those with OSAS compared to those without OSAS (43.9 ± 13.9 kg/m² v. 35.4 ± 11.2 kg/m², respectively; p= 0.04) (Canapari et al., 2011).
Despite a strong link between obesity and OSAS based on epidemiologic and observational studies, treatment of OSAS in the obese adolescent population remains problematic. There is only a 59.8% success rate in the treatment of OSAS with adenotonsillectomy and the treatment is even less effective in those who are obese (Andersen et al., 2016; Costa & Mitchell, 2009; Friedman et al., 2009; Li et al., 2016; R. B. Mitchell & Kelly, 2007; Tagaya et al., 2012; Tauman et al., 2006). A recent systematic review examining the effect of different OSAS treatment options found that the prevalence and persistence of OSAS ranged from 33 to 76% in obese children and adolescents as compared to 15 to 37% in non-obese children and adolescents post-adenotonsillectomy (Andersen et al., 2016). However, it was noted that the definition of OSAS, degree of obesity, and age of the study populations varied across the included studies. In studies that involved PAP therapy, two out of the three studies included in the review reported mean nightly usage as <4 hours (Andersen et al., 2016), indicating suboptimal use. Of importance, this review also examined the effect of weight loss on OSAS and found that OSAS improved significantly after intervention and the prevalence of persistent OSAS varied between 10 and 38% with weight loss interventions (Andersen et al., 2016).

**Weight Loss and Physical Activity in Obesity and OSAS**

Weight loss should be addressed and included as part of the treatment plan when OSAS is weight related (Alonso, 2014; Alonso-Alvarez et al., 2014; Marcus, Brooks, et al., 2012). However, the current body of evidence surrounding the effectiveness of this strategy in reducing OSAS in the pediatric population is somewhat limited (Alonso, 2014). Existing studies (Alqahtani, Elahmedi, & Al Qahtani, 2014; Kalra et al., 2005; Siegfried, Siegfried, Rabenbauer, & Hebebrand, 1999; Tuomilehto et al., 2009; Verhulst et al., 2009; Willi, Oexmann, Wright,
Collop, & Key, 1998) found that a weight loss intervention (both surgical and/or behavioral) significantly improved OSAS in obese adolescents. These studies have demonstrated significant AHI reductions (>50%), OSAS resolution, and relatively low OSAS persistence rates (<38%) following weight loss. Not only do weight loss and lifestyle interventions (i.e., exercise, diet) benefit adolescents in terms of OSAS outcomes, but their cardiovascular, metabolic, and neurocognitive health improves as well.

Initiative to partake in physical activity to promote weight loss is difficult, particularly in the obese OSAS population as OSAS causes daytime sleepiness and daytime sleepiness is further amplified in those who are obese (Spruyt et al., 2010). The presence of excessive daytime sleepiness is likely to reduce overall daily physical activity (Gozal & Kheirandish-Gozal, 2009; Spruyt et al., 2010). As obesity and OSAS often coincide, it is important to further investigate the relationship between weight loss and OSAS; especially as the current OSAS treatment recommendation (i.e., PAP) is poorly received or underutilized, resulting in sub-par treatment for the adolescent OSAS population.

Further, the adolescent population experiencing obesity, OSAS, or both obesity and OSAS are likely to experience additional benefits from physical activity. Physical activity has potential to positively influence cognitive performance by enhancing multiple aspects of adolescent’s cognitive functioning; all of which are important for healthy cognitive development (C. L. Davis et al., 2011; Gomes da Silva & Arida, 2015). Though many studies have been published on the broad benefits of exercise on cognition, few studies have specifically focused on executive function as an outcome. In a meta-analysis of 19 studies (n=586) examining the effects of acute physical activity (10-40 minutes) on executive function in preadolescent children (6-12 years), adolescents (13-17 years) and young adults (18-35 years), there was a significant
overall effect of acute physical exercise on executive function (d=0.52, 95% CI 0.29-0.76, p<0.001), though it should be noted that only 3/19 of these studies were conducted in adolescents ages 13-17 years of age (Verburgh, Konigs, Scherder, & Oosterlaan, 2014).

Despite the well-documented health benefits of physical activity both in the general adolescent population and OSAS/obese adolescent population, physical activity levels decline across adolescence (Janssen & Leblanc, 2010; Reiner, Niermann, Jekauc, & Woll, 2013). Enrollment in physical education drops from 79% to 37% in 12th grade students (American Psychological Association, 2002) and the Youth Behavioral Risk Factor Survey indicates that only 27% of public high school students meet national recommendations of performing at least 60 minutes of physical activity per day (Centers for Disease Control and Prevention, 2013). So although the health benefits of physical activity are profound (Warburton & Bredin, 2016), even generally healthy adolescents don’t follow current recommendations. When obesity and OSAS are coupled with the complexity of adolescent development, physical activity is likely to be severely curtailed in the target populations of interest in this study. Yet, it is important to account for physical activity as a research variable in any study of obesity and OSAS in adolescents with the outcome of executive function, as executive function is potentially confounded by physical activity (Verburgh et al., 2014).

Conclusion

This scoping review provides a basic but necessary understanding of many components of adolescent development. The scoping review was strategically organized to provide foundational knowledge and demonstrate a logical pathway of reason for the purposes of conducting this study. The net result of the scoping review is a comprehensive description of the
mechanisms of adolescence, obesity, and OSAS on the brain, sleep, and health outcomes in adolescents.

Obesity and OSAS often coincide. Obesity and OSAS not only individually impact cardiovascular, metabolic, and neurocognitive health, but also are likely to magnify these effects when experienced in combination. Due to the apparent lack of evidence addressing the effects of the combination of obesity and OSAS, the goal of this study is to begin to investigate the combination of obesity and OSAS in adolescence with specific focus on executive function outcome. As executive function is impaired in both conditions (obesity and OSAS, individually), there is reason to believe the combination of obesity and OSAS magnifies this impairment. Executive function is a neurocognitive outcome, and as such is an important consideration, as the ability to self-regulate and organize generate from this function. The prefrontal cortex (i.e., house of executive function) is vulnerable during the adolescent period, especially when exposed to injury or insult (i.e., obesity or OSAS). These disruptions can cause executive dysfunction, which may be permanent and lifelong, hence, the need to address this in young populations. It is important to understand the impact of the combination of obesity and OSAS on executive function, as understanding these potential impairments may assist in identifying pathways of adolescent’s resistance to adhere to interventions used to treat obesity or OSAS.

**Systematic Review: Effects of Obesity & OSAS on Executive Function in Adolescents**

To define the state of the science addressing the effects of the combination of obesity and OSAS on executive function, a systematic review was conducted in accordance to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009).
Literature Search

The search was conducted using online databases including PubMed, CINAHL, PsycINFO, The Cochrane Library, and The Web of Science. These databases were selected *a priori* with the following rationale: PubMed was selected for its leading role in citations and abstracts for biomedical research, as well as its broad array of subject and discipline coverage ("Databases by Description," 2016). Additionally, coverage is worldwide and updated weekly ("Databases by Description," 2016). CINAHL was utilized due to its focus on nursing and allied health. This database provides citations for book chapters, nursing dissertations, association publications, conference proceedings, patient education materials, research instruments, standards of practice, and clinical innovations ("Databases by Description," 2016). PsycINFO was chosen for its worldwide respectability in quality; this database includes literature from a wide array of disciplines such as psychology, medicine, nursing, and social work ("Databases by Description," 2016). The Cochrane Library, known as a database for evidence-based medicine tools was beneficial by its inclusion of systematic reviews, abstracts of reviews, clinical trials, methods studies, technology assessments, and economic evaluations ("Databases by Description," 2016). Lastly, The Web of Science was utilized for its collection of articles from thousands of journals and indexes of citations within those articles ("Databases by Description," 2016); this feature allows the reader to view which papers have cited a core paper, as well as how many times a paper was cited. Grey literature such as dissertations, conference abstracts, and private sector research was excluded for this systematic review due to its inconsistency for peer-review and absence of editorial control and/or lack of control in commercial publishing, as these are likely to heighten risk of lower methodological quality than peer-reviewed published literature.
Database searches were carried out using keywords or medical subject headings (MeSH). The search terms were selected to focus on the population and topic of interest to answer the question: How does the combination of obesity and OSAS affect executive function in adolescents? The keywords and MeSH terms used include: obstructive sleep apnea, obstructive sleep apnea syndrome, OSA, OSAS, adolescent, adolescence, teen, youth, obese, obesity, overweight, executive function, executive functions, and executive functioning (Table 2.2).
Table 2.2. Systematic Review Search Terms and Results

<table>
<thead>
<tr>
<th>Database</th>
<th>Search Terms &amp; Limits</th>
<th>Citations Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>PubMed</td>
<td>((((sleep apnea, obstructive[MeSH Terms]) AND adolescent[MeSH Terms]) AND executive function[MeSH Terms])) AND pediatric obesity[MeSH Terms]</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>((((obstructive sleep apnea OR obstructive sleep apnea syndrome OR OSA OR OSAS)) AND (adolescent OR adolescence OR teen OR youth)) AND (obese OR obesity OR overweight)) AND (executive function OR executive functions OR executive functioning)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Limit: English</td>
<td></td>
</tr>
<tr>
<td>CINAHL</td>
<td>(obstructive sleep apnea OR obstructive sleep apnea syndrome OR OSA OR OSAS) AND (adolescent OR adolescence OR teen OR youth) AND (obese OR obesity OR overweight) AND (executive function OR executive functions OR executive functioning)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Limit: English</td>
<td></td>
</tr>
<tr>
<td>PsycINFO</td>
<td>(obstructive sleep apnea OR obstructive sleep apnea syndrome OR OSA OR OSAS) AND (adolescent OR adolescence OR teen OR youth) AND (obese OR obesity OR overweight) AND (executive function OR executive functions OR executive functioning)</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Limit: English</td>
<td></td>
</tr>
<tr>
<td>The Cochrane Library</td>
<td>(obstructive sleep apnea OR obstructive sleep apnea syndrome OR OSA OR OSAS) AND (adolescent OR adolescence OR teen OR youth) AND (obese OR obesity OR overweight) AND (executive function OR executive functions OR executive functioning)</td>
<td>0</td>
</tr>
<tr>
<td>Web of Science</td>
<td>(obstructive sleep apnea OR obstructive sleep apnea syndrome OR OSA OR OSAS) AND (adolescent OR adolescence OR teen OR youth) AND (obese OR obesity OR overweight) AND (executive function OR executive functions OR executive functioning)</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Limit: English</td>
<td></td>
</tr>
<tr>
<td>Total Articles</td>
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<td></td>
</tr>
<tr>
<td>Relevant Articles</td>
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<td></td>
</tr>
<tr>
<td>Duplicates Removed</td>
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<td></td>
</tr>
<tr>
<td>Remaining Articles</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
Eligibility Criteria

Studies meeting the following criteria were considered for inclusion: (1) OSAS determined by overnight polysomnography (PSG); (2) study defined obesity criteria and at least a proportion of the sample was obese (particularly those with OSAS); and (3) ages ≥10 years to ≤18 years. Studies were excluded for the following reasons: (1) participant age range was < 10 years or >18 years; (2) study did not include participants with PSG determined OSAS; (3) study did not include participants who were obese; and (4) study included participants with other conditions known to impair executive function (e.g., attention-deficit hyperactivity disorder, depression, schizophrenia, autism, fetal alcohol syndrome, brain injury).

Search Results

The collective total of database searches provided 20 articles for review (Table 2.2; Figure 2.1). After assessing for relevance and inclusion and exclusion criteria, 14 articles were fully reviewed. After removing duplicates, four published studies were included in the systematic review.
Of the four papers included in the review, three (Hannon et al., 2012; McNally, Shear, Tlustos, Amin, & Beebe, 2012; Xanthopoulos et al., 2015) self-identified as cross-sectional and one other (Tan, Healey, Schaugency, Dawes, & Galland, 2014) is also classified as cross-sectional based on reported methodology (i.e., no indication of longitudinal or multi-time point data collection). Only one study (Xanthopoulos et al., 2015) identified as a case-control study, while two others (Hannon et al., 2012; Tan et al., 2014) are assumed to be cross-sectional cohort studies, as they compared two groups (OSAS and non-OSAS) with relatively small samples sizes (n= 37, n=31, respectively). McNally and colleagues (2012) labeled their study as a cross-sectional correlative study. A methodological evidence level and quality assessment (using the Johns Hopkins Nursing Evidence Based Practice Evidence Rating Scales) (Newhouse, Dearholt,
Poe, Pugh, & White, 2005) indicates that all five studies are level III evidence (Table 2.3). The studies included in this review are assessed to be of high or good methodological quality (Table 2.3) (Newhouse et al., 2005).

**Table 2.3. Evaluation of Methodological Quality Using Johns Hopkins Nursing Evidence Appraisal System (Newhouse et al., 2005)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Evidence Type</th>
<th>Quality Appraisal of Research Studies</th>
<th>Evidence Rating Level*</th>
<th>Quality**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xanthopolous et al. (2015)</td>
<td>Cross-sectional case control</td>
<td>11 with Yes</td>
<td>III</td>
<td>High</td>
</tr>
<tr>
<td>Tan et al. (2014)</td>
<td>Cross-sectional cohort study</td>
<td>11 with Yes</td>
<td>III</td>
<td>High</td>
</tr>
<tr>
<td>Hannon et al. (2012)</td>
<td>Cross-sectional pilot study</td>
<td>7 with Yes</td>
<td>III</td>
<td>Good</td>
</tr>
<tr>
<td>McNally et al. (2012)</td>
<td>Cross-sectional correlative study</td>
<td>10 with Yes</td>
<td>III</td>
<td>High</td>
</tr>
</tbody>
</table>

*Level I: experimental study/randomized controlled trial (RCT) or meta-analysis of RCT; Level II: quasi-experimental; Level III: non-experimental study, qualitative study, or meta-synthesis; Level IV: opinion of nationally recognized experts based on research evidence or expert consensus panel (systematic review or clinical practice guidelines); Level V: opinion of individual expert based on non-research evidence (case studies, literature reviews, organizational experience e.g., quality improvement and financial data, clinical expertise, or personal experience.

**High Quality:** consistent results with sufficient sample size, some control, fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence

**Good Quality:** reasonably consistent results, sufficient sample size, adequate control, and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence

**Low quality or major flaws:** little evidence with inconsistent results, insufficient sample size, conclusions cannot be drawn

**Sample Description**

The age of study participants ranges from 10-18 years, with mean age (years) ranging from 13.1 ± 2.3 (Tan et al., 2014) to 14.04 ±1.85 (McNally et al., 2012) across all studies (Table 2.4). The percentage of males in the studies ranges from 41% (McNally et al., 2012) to 85%
(Xanthopoulos et al., 2015) of participants. Per inclusion criteria, all studies were required to have participants that are classified as obese. Obesity is defined as a BMI > 95th percentile for age and sex (McNally et al., 2012; Xanthopoulos et al., 2015), > 97th percentile for age and sex (Hannon et al., 2012), or as having a BMI conceptually equivalent to a BMI ≥30 kg/m² at age 18 using Cole cut-off criteria (Tan et al., 2014). Per inclusion criteria for the systematic review, in all 4 studies, the OSAS group is obese. OSAS severity classifications based on PSG-derived AHI varied across studies; AHI ≥ 5/hr (Hannon et al., 2012; Xanthopoulos et al., 2015), AHI >2/hr (Tan et al., 2014), or AHI 1-5/hr as mild OSAS and AHI > 5 as moderate to severe OSAS (McNally et al., 2012).
Table 2.4. Description of Included Studies (n=4)

<table>
<thead>
<tr>
<th>Author/Year/Site</th>
<th>Design/Sample Size (N)</th>
<th>Study Groups</th>
<th>OB Criteria</th>
<th>OSAS Criteria</th>
<th>Characteristics OB+OSAS</th>
<th>Characteristics OB (non-OSAS)</th>
<th>Characteristics Lean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xanthopolous et al. 2015 USA</td>
<td>Cross-section case control N=95</td>
<td>OB OB+OSAS Lean 12-16y</td>
<td>&gt;95th % for age and sex</td>
<td>AHI ≥ 5 events/hr</td>
<td>Age: 14.3 ± 1.4  %Male: 76.3 BMI(z): 2.4±0.4 AHI: 10.3(4.9,143.4) n= 38</td>
<td>Age: 14.0 ± 1.5  %Male: 95.2 BMI(z): 2.2 ±0.3 AHI: 0.5 (0, 1.3) n= 21</td>
<td>Age: 14.6 ± 1.5  %Male: 88.9 BMI(z):0.1 ±0.9 AHI:0.3 (0,1.6) n= 36</td>
</tr>
<tr>
<td>Tan et al. 2014 New Zealand</td>
<td>Cross-sectional cohort study N=31</td>
<td>OB OB+OSAS 10-18y</td>
<td>Cole cut-off criteria; BMI equivalent to ≥30 kg/m² at age 18</td>
<td>AHI &gt; 2 events/hr</td>
<td>Age: 13.1 ± 2.3  %Male: 60 BMI(z):2.9±0.7 AHI, median (IQR): 4.7 (2.4-8.3) n= 15</td>
<td>Age: 14.3 ± 1.4  %Male: 88 BMI(z): 3.1±0.4 AHI, median (IQR): 0.9 (0.5-1.2) n= 16</td>
<td>N/A</td>
</tr>
<tr>
<td>Hannon et al. 2012 USA</td>
<td>Cross-sectional pilot N=37</td>
<td>OB OB+OSAS 12-18y</td>
<td>&gt;97th % for age and sex</td>
<td>AHI ≥1.5 events/hr</td>
<td>Age: 14.9 ± 0.4  %Male: NR; 54% for whole study BMI: kg/m² 41.8 ± 2.2 AHI: NR n= 17</td>
<td>Age: 14.3 ± 0.4  %Male: NR BMI: kg/m² 37.4 ± 1.5 AHI: NR n= 20</td>
<td>N/A</td>
</tr>
<tr>
<td>McNally et al. 2012 USA</td>
<td>Cross-sectional correlative study N=111</td>
<td>OB+noOSAS OB+mildOSAS OB+ModSevOSAS 10-16.9y</td>
<td>&gt;95th % for age and sex</td>
<td>OB+ noOSAS: AHI &lt;1 event/hr OB+mild: AHI 1-5 events/hr OB+Mod Sev: AHI &gt;5 events/hr</td>
<td>Mild: Age: 13.59 ± 2.08  %Male: 37.2 BMI(z): 2.49±0.27 AHI: 2.16 (1.06) n= 43</td>
<td>Age: 13.29±1.94  %Male: 21.62 BMI(z): 2.37±0.26 AHI: 0.46 (.31) n= 37</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Notes. OB: Obesity; OSAS: Obstructive Sleep Apnea Syndrome; N/A: Not Applicable; NR: Not Reported; BMI: Body Mass Index; BMI(z): Body Mass Index z-score; AHI: Apnea-Hypopnea Index; IQR: Interquartile Range; mildOSAS: Mild Obstructive Sleep Apnea Syndrome; ModSevOSAS: Moderate to Severe Obstructive Sleep Apnea Syndrome
Executive Function Assessment Description

Across studies, executive function was measured using different instruments (Table 2.5). Two studies used the Behavioral Rating Inventory of Executive Function (Gioia, Isquith, Guy, & Kenworthy, 2000), a questionnaire that yields summary performance scores which indicate presence of impairments to executive function. The included studies used parent report (Tan et al., 2014; Xanthopoulos et al., 2015) and teacher report (Tan et al., 2014) forms. The Stroop Color and Word Test (Stroop, 1935) was used by Hannon and colleagues (2012). This is a task measure with three components; a word task, a color task, and a color-word task. Performance on each of these tasks is used to assess executive function by determining ability to inhibit stimulus-bound responses as well as deal with interferences. One other study (McNally et al., 2012) assessed executive function using the Iowa Gambling Task (Bechara, Damasio, Damasio, & Anderson, 1994), a task completed in the form of a card game. During the card game, subjects are exposed to choices that are associated with risk and reward, with executive function non-impaired individuals demonstrating improved decisions over time.
Table 2.5. *Description of Executive Function Outcomes*

<table>
<thead>
<tr>
<th>Author/Year/Site</th>
<th>EF Measure</th>
<th>EF Outcome for Group OB+OSAS</th>
<th>EF Outcome for Group OB</th>
<th>EF Outcome for Group Lean</th>
<th>Summary of EF Outcomes</th>
</tr>
</thead>
</table>
| Xanthopolous et al. 2015 USA | BRIEF - Parent report | GEC $\geq 65$; n=8 (22.3%)  
BRI $\geq 65$; n=8 (22.3%)  
MI $\geq 65$; n=8 (22.3%) | GEC $\geq 65$; n=0 (0%)  
BRI $\geq 65$; n=0 (0%)  
MI $\geq 65$; n=0 (0%) | GEC $\geq 65$; n=1 (2.9%)  
BRI $\geq 65$; n=0 (0%)  
MI $\geq 65$; n=0 (0%) | OSAS+OB had worse executive function compared to OB (p <.001) and lean (p <.001)  
Mediation analysis based on 5000 resamples found effect of BMI z-score on AHI was significant (p $\leq$ 0.017)  
**OB+OSAS = WORSE EF** |
| Tan et al. 2014 New Zealand | BRIEF - Parent report & Teacher report | Parent:  
GEC: 63.3 (55.5-71.1)  
BRI: 62.5 (53.9-71.1)  
MI: 62.4 (55.5-69.3)  
Teacher:  
GEC: 70.4 (59.1-81.9)  
BRI: 65.7 (52.1-79.3)  
MI: 70.5 (61.0-79.9) | Parent:  
GEC: 63.0 (56.6-69.4)  
BRI: 57.7 (50.6-64.8)  
MI: 62.1 (56.0-68.2)  
Teacher:  
GEC: 62.8 (52.0-73.6)  
BRI: 59.8 (50.9-66.6)  
MI: 65.6 (54.0-77.3) | N/A | Both OSAS and non-OSAS were $>$1 SD above normative sex & age normed means; however, not in the clinical range  
Cohen’s d (OSAS compared to non-OSAS):  
Parent:  
GEC: 0.03  
BRI: 0.35  
MI: 0.03  
Teacher:  
GEC: 0.44  
BRI: 0.43  
MI: 0.28  
all p $\geq$ 0.300  
**NO SIGNIFICANT DIFFERENCE BETWEEN OSA & NON-OSAS** |
<table>
<thead>
<tr>
<th>Author/Year/Site</th>
<th>EF Measure</th>
<th>EF Outcome for Group OB+OSAS</th>
<th>EF Outcome for Group OB</th>
<th>EF Outcome for Group Lean</th>
<th>Summary of EF Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hannon et al. 2012</td>
<td>Stroop Color &amp; Word Test</td>
<td>Score/mean: 42.5 ± 2.3</td>
<td>Score/mean: 44.2 ± 2.0</td>
<td>N/A</td>
<td>Cohen’s d (OSAS compared to non-OSAS): d= -0.18</td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No between-group differences (p=.602)</td>
</tr>
<tr>
<td>McNally et al. 2012</td>
<td>Iowa Gambling Task (IGT)</td>
<td>Showed little change in pattern of choices</td>
<td>Made better decisions as task progressed</td>
<td>N/A</td>
<td>OSAS significant effect (p=.02) on rate of change in IGT performance (slope) even after taking into account SES &amp; puberty level.</td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td>Mild OSAS: slope = 0.31; p = 0.33</td>
<td>Slope = 1.04; p &lt; .01</td>
<td></td>
<td>No-OSAS group made better choices (i.e., improvement) as task progressed (slope: 1.04; p&lt;0.01). Mild &amp; Mod-Severe OSAS showed little change (slope: 0.31, 0.16, respectively; p=0.33, 0.70, respectively).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate-Severe OSAS: slope = 0.16; p = 0.70</td>
<td></td>
<td></td>
<td>BMI was not related to IGT (r² = .08, p=.62)</td>
</tr>
</tbody>
</table>

**Notes.** EF, Executive Function; OB, Obesity; OSAS, Obstructive Sleep Apnea Syndrome; BRIEF, Behavioral Rating Inventory of Executive Function; GEC, Global Executive Composite; BRI, Behavior Rating Index; MI, Metacognition Index; BMI, Body Mass Index; AHI, Apnea-Hypopnea Index; N/A, Not Applicable; SES, Socioeconomic Status
**Discussion: Effects of Obesity and OSAS on Executive Function**

Two of four studies indicate that those with OSAS and obesity performed significantly worse on measures of executive function than non-OSAS controls; \( p \leq 0.017 \) (Xanthopoulos et al., 2015), \( p = 0.02 \) (McNally et al., 2012). In the two remaining studies that found no significant differences between groups (Hannon et al., 2012; Tan et al., 2014). Tan, et al. (2014) reported that executive function was >1 standard deviation above normative age and sex means (higher score = impairment) in both the obese and obese+OSAS group (\( p \geq 0.300 \)) (Tan et al., 2014); Hannon, et al. (2012) reported both the obese and obese+OSAS groups displayed “normal” levels of executive function with no significant difference between groups (\( p = 0.602 \)) (Hannon et al., 2012). Given these inconsistent findings, the small sample sizes in the studies included in the review, and the relatively limited set of evidence (n=4 studies), it is difficult to draw definitive conclusions about the effect of obesity and OSAS on executive function. Definitive systematic review conclusions are also predicated on methodological inconsistencies including variation in measurement of the primary outcome and variation in comparison groups.

Underpowered studies can have significant effects on the results. With small sample sizes, underpowered studies increase the risk of Type II error; *a priori* power analysis can reduce concerns for Type II error when a power analysis is calculated based on the primary outcome, or in some cases, multiple outcomes. With multiple outcomes, the risk of Type I error increases substantially, necessitating significance adjustment or prioritizing an outcome variable as primary and other outcomes as secondary. However, there is high value in small pilot studies in that effect size determination contributes to adequately powering future studies. Reporting effect size allows for quantification of differences between groups (small, moderate, large) and emphasizes the size of the difference. Calculating effect size does not require the large number of
participants that are required to find statistically significant differences between groups. Further, this statistical test allows for determining if the findings are clinically relevant and allows for identification of sample sizes needed to provide adequate power for detecting statistical differences. The included systematic review studies were inclusive of mostly small pilot studies, wherein effect size determination was an objective.

Tan and colleagues (2014) stated their study was powered at 80% to detect differences in academic assessment scores and outright indicated that “the study may not have been powered strongly enough to detect between group differences” for executive function and other cognitive measures (Tan et al., 2014, p. 18). For this reason, they chose to report effect sizes in addition to p-values (Table 2.5). Similarly, Hannon and colleagues (2012) chose to report effect sizes (Cohen’s d) due to the small sample size of their pilot study, and did not indicate if executive function was their primary outcome. Xanthopolous and colleagues (2015) did not mention that their study was powered for the outcome of executive function; however, they indicate that because there were multiple outcome variables of interest (sleepiness, mood and behavior, and executive function), the p-value was adjusted for multiple comparisons, requiring p≤0.017 for statistical significance; this adjustment decreases the risk of Type I error but does not fully address power concerns for the primary outcome. McNally and colleagues (2012) indicate the Iowa Gambling Task was added to the protocol of a larger study investigating broad neurobehavioral effects of OSAS, so the study was not specifically powered to detect differences in executive function. Overall, the studies were not adequately powered to detect group differences in executive function. In order that subsequent studies address this limitation, determining effect sizes in pilot studies to guide subsequent sample size decisions is necessary to more precisely determine the effect of OSAS and/or obesity on executive function.
Another limitation of the included systematic review studies is the inconsistency in instrumentation for the primary outcome, executive function (Table 5). A variety of measures were used to measure executive function, including: the Behavioral Rating Inventory of Executive Function questionnaires (parent and teacher forms; Gioia, Isquith, Guy, & Kenworthy, 2000), The Stroop Color and Word Test (Stroop, 1935), and the Iowa Gambling Task (Bechara et al., 1994). Because these instruments measure executive function on different scales and different scoring rules were applied across studies, comparing or pooling results across the literature is challenging. For this reason, a consistent measure of executive function in subsequent studies should be employed so the phenomenon can be better understood.

Additionally, comparison groups varied across studies (Tables 2.4 and 2.5). Only one study (Xanthopoulos et al., 2015) included a lean control group for comparison, and another (Tan et al., 2014) compared findings to normative sex- and age-normed means. In order to fully understand the individual and combined effects of obesity and OSAS on executive function, it is imperative that future studies compare executive function to a “healthy control” group. For this pilot study, executive function in obese and obese+OSAS adolescents will be compared to normative published data for the Behavioral Rating Inventory of Executive Function questionnaires (Gioia et al., 2015). In a future adequately powered study, a 3-cohort design will be employed to detect differences between groups, inclusive of a non-obese, non-OSAS group (i.e., healthy controls).

Perhaps one of the largest issues unveiled in the process of this systematic review is the actual variability in the use of the term executive function across studies and the absence of a study-provided operational definition of executive function in the published studies. With lack of clarity for how studies conceptualized and defined the primary outcome, executive function,
there is ambiguity across the systematic review evidence set for measurement (operational definition) of executive function. As previously outlined in Chapter 1, executive function is composed of “behavioral inhibition, set-shifting, self-regulation of affect and arousal, working memory, analysis/synthesis, and contextual memory” (Beebe & Gozal, 2002, p.2). Though there are 6 domains described in the Prefrontal Model (Figure 1.1), the multiple processes encompassed in executive function lead to difficulty operationalizing a single measure of executive function. Because of the multifaceted nature of executive function, a number of measures can be found in the literature that suggest the assessment of executive function, even if only a select few domains are being measured. This can be potentially misleading if the study or instrument does not evaluate the complete executive function system. An incomplete understanding of executive function is generated when published primary studies measure only one domain of executive function. By first, conceptually defining the intended primary outcome (i.e., executive function) and then incorporating a well-aligned operational definition of executive function with a comprehensive measurement approach for this complex outcome, the field will be better positioned to develop knowledge about executive function.

In the proposed study and intended subsequent work, the Behavioral Rating Inventory of Executive Function is an optimal measure of executive function to use, as it is comprehensive in its assessment of the conceptually-defined domains of executive function. For example: the parental form includes 9 clinical scales (domains): Inhibit, Self-Monitor, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Task-Monitor, and Organization of Materials (Gioia et al., 2000). The self-report form consists of 7 clinical scales: Inhibit, Self-Monitor, Shift, Emotional Control, Task Completion, Working Memory, and Plan/Organize. Further, the clinical scales within each form compose a Global Executive Composite (GEC) score and three indices:
the Behavior Regulation Index (BRI), the Emotional Regulation Index (ERI), and the Cognitive Regulation Index (CRI). An additional and important benefit for using the Behavioral Rating Inventory of Executive Function is the availability of published normative data; the availability of such normative data permits comparison of study results to normative data for adolescents, even in the absence of a study control group.

**Conclusion**

This chapter has provided a comprehensive overview of the important developmental aspects of adolescence, sleep, physical activity, obesity, OSAS, and executive function. By performing both a scoping review as well as a systematic review, a clear gap in the literature has been identified. This gap is the understanding of the combined effects of obesity and OSAS on executive function in adolescents. This void in scientific knowledge has a long road ahead in order to make any definitive conclusions about the combined effect of obesity and OSAS on executive function in adolescents. The proposed study will contribute to the existing literature by exploring executive function impairments in obese adolescents with OSAS and importantly, establish critical preliminary evidence to support a subsequent, fully-powered three-cohort study. This broad area of scientific focus has the potential to reduce obesity and OSAS morbidity in adolescence as well as provide insights for potential interventions for obesity and OSAS in adolescence that will impact the overall health states of adolescents and promote their successful, healthy transition to adulthood.
Chapter 3

Research Design and Methods

Introduction

This chapter will outline the study design, sample and setting, measures, study protocol, data collection and management, and analysis. The purpose of the study is to:

**Aim 1:** To determine the feasibility of recruiting and retaining a sample of obese adolescents (11-17 years of age) with and without-OSAS.

**Aim 2:** To pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation.

**Aim 3:** To explore executive function impairments as measured by the Global Executive Composite (i.e., overall summary score) and three subscales (i.e., Behavior Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index), within groups, compared to published normative data, and explore differences in executive function impairments between groups (obese adolescents with and without-OSAS).

**Aim 4:** To describe differences in activity levels (frequency, intensity, time) and sleep duration (major sleep bout total sleep time), measured by 1-week actigraphy (objective measure of rest/activity and sleep) and self-report, between obese adolescents with and without OSAS and explore the relationship between activity levels and sleep duration with executive function (Global Executive Composite scores).

**Study Design**

This study is a feasibility study employing a two-cohort study design with a prospective 1-week measurement protocol. A cohort design allows for comparison of two cohorts,
determining the risk and incidence of a condition/outcome (Mann, 2003); in this study, determining if the combination of obesity and OSAS puts adolescents at heightened risk for impaired executive function. A case-control design was not selected, as this design type focuses on factors that predispose a patient to a disease/outcome, while reflecting retrospectively on factors that differ between the case and control groups (Song & Chung, 2010). Because this study has a cross-sectional design, a cohort study is the more appropriate choice (Mann, 2003). This study is designed to first identify the disease or condition (e.g., obesity, OSAS + obesity) and then look forward to the outcome of interest, executive function. The forward-looking approach is designed to permit the evaluation of potential mediators/moderators (i.e., physical activity, sleep duration) of the outcome; though forward-looking by design, this study is a cross-sectional design as no baseline-outcome comparisons are intended.

This study is not powered to detect statistically significant differences between groups (see Sample and Setting, sample size justification) as this is a feasibility study. Employing a cross-sectional cohort design, the feasibility study allows for the study aims to be addressed: (1) determining feasibility of recruiting and retaining adolescents with obesity and OSAS, (2) determining participant acceptability of instrumentation and complete data resulting from protocol, (3) exploring executive function impairments within groups as compared to published normative data, and (4) exploring group differences in physical activity levels and sleep duration. The overarching objective of the proposed research is to provide preliminary data to support a future, larger study that will systematically examine the cognitive health implications of obesity and OSAS in adolescents. In future studies, between-group comparisons will be necessary to determine if the combination of obesity and OSAS puts adolescents at heightened risk for cognitive impairments, specifically impairments to executive function. The results of this
feasibility study provide critical preliminary data and design/protocol insights for a future study intended to examine the following between-group differences: 1) executive function, 2) physical activity levels and sleep duration and 3) the relationship and influence of physical activity levels and sleep duration on executive function.

There are several benefits of conducting a feasibility study. Conducting a feasibility study prior to a larger study can enhance the likelihood of success in the subsequent study, while also determining potential challenges (Thabane et al., 2010). Positive feasibility study results (e.g., high rates of participation, sample retention, and complete data) suggest that the population of interest will positively receive the study and that the protocol is feasible for subsequent implementation. Alternatively, negative results (e.g., missing data, high drop-out rates, low participant acceptability) are also insightful for detecting necessary changes in the study protocol for a future, larger study. The experience gained by the investigator with regard to the measures used in this study allows for more efficient and skillful data collection, management, and interpretation in subsequent studies. Additionally, perhaps one of the main benefits in conducting this feasibility study is to estimate effect sizes needed for sample size calculations for a future, larger study.

**Sample and Setting**

This feasibility study employed a cross-sectional, two-cohort study design targeting enrollment of obese (BMI ≥95th percentile) adolescents (ages 11-17 years) with (n=12) and without (n=12) OSAS. There were two recruitment sites. Obese (BMI ≥95th percentile) adolescents, ages 11-17 years, scheduled for overnight polysomnography (PSG) at a suburban tertiary academic medical center, and patients of a pediatric weight loss clinic were invited to participate. Convenience sampling was used at the medical center. For recruitment from the
weight loss clinic, a cohort discovery method (i2b2), a Clinical and Translational Science Institute investigator resource, was used to identify potentially eligible participants. Adolescent was defined as ≥11 to ≤ 17 years and adolescents were classified as having clinically significant OSAS if overnight-PSG indicated an apnea-hypopnea index (excluding central events) ≥1.5 events/hour. Adolescents were eligible to be assigned to the without-OSAS group if they had a negative PSG (AHI < 1.5) within the last year and a stable BMI (± 2 kg/m²) since their PSG. Per federal guidance defining vulnerable research populations ("Protection of Human Subjects," 2009), adolescent participants in this study are considered children as they were <18 years of age.

Inclusion criteria for the study were: age 11-17 years; BMI-for-age ≥95th percentile; presence or absence of OSAS determined by overnight PSG (i.e., sleep study; diagnostic or split night study) within the last year; apnea-hypopnea index ≥1.5 events/hour for clinically significant OSAS; parental consent and adolescent assent; reading level ≥5th grade; ability to read English; and anticipated performance of usual activities over a 1-week period after enrollment (e.g., no planned vacations, acute illnesses). Exclusion criteria were: age <11 or ≥ 18 years; BMI-for-age <95th percentile; overnight PSG >1 year ago; change in BMI greater than ± 2 kg/m2) since overnight PSG; acute or chronic physical injury or disability that impedes participation in physical activity; intellectual disabilities/learning disabilities that impact independent ability to respond to questionnaires; any current treatment of OSAS; established diagnosis of other sleep-wake disorders that may disrupt sleep duration, including insomnia, restless legs syndrome, and narcolepsy; uncontrolled diabetes; disruptive behavioral disorders such as Attention Deficit Disorder (ADD), Attention Deficit Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD); established diagnosis of psychological disorders,
including anxiety, schizophrenia, or personality disorders, or current use of psychotropic medications; uncontrolled mood disorders (depression, anxiety); and regular use (>3 days/week) of over the counter or prescribed medications that interfere with sleep (e.g., melatonin, sedative-hypnotics such as zolpidem, stimulant agents such as modafanil and methylphenidate).

**Recruitment**

Adolescents being seen at the medical center were approached on the night of their scheduled diagnostic PSG. Potential subjects were queried by a PSG technologist to determine if the patient was willing to speak with a researcher about participating in the study. Patients are scheduled to arrive approximately 2-3 hours prior to the start of PSG for acclimatization to the laboratory environment and preparation for their diagnostic PSG. If both the adolescent and legal guardian were interested in additional details of the study, or participating in the study, the principal investigator was introduced to the patient/guardian for study protocol description, pre-enrollment eligibility screening, and informed consent/assent.

Recruitment procedures for the adolescents of the weight loss clinic were different. Potential participants were mailed an IRB-approved invitation letter, signed by the Director of the pediatric weight loss program, Director of the pediatric sleep program, and the PI. If the patient contacted the PI and was interested in learning more about the study, the PI provided a more detailed description of the study protocol by telephone. If still interested, a pre-enrollment eligibility screening questionnaire, approved by the IRB, was conducted via phone. If they were eligible to participate, the PI scheduled to meet with the potential participant at the medical center or weight loss clinic. Or, if the potential participant had an upcoming clinical visit, the PI coordinated to meet with them directly after their scheduled clinic visit to discuss the study and proceed with informed consent/assent if agreeable. Recruitment efforts were conducted with the
utmost respect, including the minimization of language addressing weight status (i.e., obesity) and emphasis placed on the study’s intent to explore adolescent well-being and health-habits.

**Protocol**

The study protocol incorporated two research visits with a one-week data collection period between research visits (Table 3.1).

**Table 3.1. Study Protocol**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Visit 1</th>
<th>Visit 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-enrollment Eligibility Screening Questionnaire</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Diagnostic polysomnography (PSG)*</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Subject Characteristics Questionnaire</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Modified Epworth Sleepiness Scale (Melendres, Lutz, Rubin, &amp; Marcus, 2004)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Physical Activity/ Sleep Measures. Instruction &amp; distribution of:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Consensus Sleep Diary (Carney et al., 2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Previous Day Physical Activity Recall (Weston, Petosa, &amp; Pate, 1997)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Executive Function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• BRIEF®2 (Self-Report and Parent-Report) (Gioia et al., 2015)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Return Devices and Diaries</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>End of Study Survey</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

* if being seen on night of PSG
A self-report pre-enrollment eligibility screening questionnaire was used at the time of recruitment (details provided in “Measures”). The screening questionnaire was delivered in person on night of PSG or via phone if patients were recruited using mailed invitation letter. If patients met eligibility requirements, they were introduced to the consent/assent process or scheduled for an in-person research visit to meet with the PI and complete informed consent/assent and participate in visit 1. The PI described the consent/assent procedure in a quiet, private environment. Participants and their parent/guardian confirmed their understanding of the study and their rights as a research participant, demonstrated both verbally to the PI as well as by signature (Appendix B).

After consent/assent, participants had an objective measure of height (by stadiometer) and weight (calibrated digital electronic scale) by a trained, licensed RN (PI) in a private environment. BMI was calculated by dividing weight in kilograms by the square of height in meters. For adolescents, BMI is age- and sex-specific and referred to as BMI-for-age. Weight status is determined using an age- and sex-specific percentile for BMI rather than BMI categories used for adults due to adolescent body composition variation by age, as well as by gender. The adolescent was eligible for study participation if they were considered to be obese (defined as BMI ≥ 95th percentile for the same age and sex adolescents).

Participants then completed the modified Epworth Sleepiness Scale (Melendres et al., 2004) and a subject characteristic questionnaire to obtain demographic information. Participants were provided with a quiet environment (e.g., private exam room) to complete all study-related procedures. All questionnaires in this study included written instructions and the investigator additionally provided verbal instructions. Participants were also provided the opportunity to ask questions. Completed questionnaires were then collected by the investigator after completion and
reviewed for missing responses. If any missing items were discovered, respondents were asked to go back and answer the skipped or missed items. If the respondent purposefully chose to skip item(s), the PI made note of this in the research file.

After completion of the modified Epworth Sleepiness Scale (Melendres et al., 2004) and the subject characteristic questionnaire, participants were provided a standardized set of verbal and written instruction for the use of the wrist-worn Philips Respironics Actiwatch 2 or Actiwatch Spectrum ("Actiwatch 2," 2017; "Actiwatch Spectrum," 2017) as well as the diaries (i.e., Consensus Sleep Diary (Carney et al., 2012) and Previous Day Physical Activity Recall (Weston et al., 1997)). Participants were engaged in the study for one week (including one weekend inclusive of at least two traditional weekend days [Friday/Saturday; or Saturday/Sunday]) from visit 1 to visit 2; see Table 3.1. According to the American Academy of Sleep Medicine, actigraphy monitoring should occur for at least seven days with both work/school and free (i.e., weekend) days included within monitoring period (American Academy of Sleep Medicine, 2005, 2014). In order to increase compliance with the diary, participants and their guardian signed a release form, indicating their permission to receive daily text message reminders at 8 p.m. for the 7-day period. Participants were instructed that the wrist-worn Philips Respironics Actiwatch 2 or Actiwatch Spectrum ("Actiwatch 2," 2017; "Actiwatch Spectrum," 2017) should be worn 24-hours per day, as it is intended to measure sleep. The only time the device is required to be removed is in the instance of water submersion greater than 1 meter for more than 30 minutes ("Actiwatch 2," 2017; "Actiwatch Spectrum," 2017).

Data collection points were at baseline/visit 1 and at visit 2 with a one-week “at home” measurement period of physical activity and sleep duration. Visit 1 and visit 2 occurred at either clinic location. At visit 2, participants and their guardian completed their respective BRIEF® 2
questionnaire (self-report form or parent-report form) (Gioia et al., 2015), used to measure executive function, the modified Epworth Sleepiness Scale (Melendres et al., 2004), and the end-of-study survey to determine participant acceptability of the study experience. At this time, sleep and activity diaries were collected and assessed for completeness. Actigraphy devices were downloaded and data was assessed for completeness.

**Measures**

**Pre-enrollment Eligibility Screening Questionnaire (Appendix C)**

A pre-enrollment eligibility screening questionnaire was used at the time of recruitment. The self-report questionnaire queried potential participants on the following criteria: age; current treatment for OSAS; established diagnosis of other sleep-wake disorders that may disrupt sleep duration, including insomnia, restless leg syndrome, and narcolepsy; new or existing bodily injury or disability that hinders ability to participate in physical activity; anticipation of disruption of usual activities over the coming week (i.e., vacation, surgery, staying awake for extended periods of time for school charities), and diagnosis of behavioral disorders such as ADD, ADHD, or ODD.

**Polysomnography (PSG)**

For the purposes of this study, PSG was not a research-specific measure but a clinical procedure. Overnight, in-laboratory diagnostic PSG, performed and scored using standard criteria (American Academy of Sleep Medicine, 2014; Berry et al., 2012), provided data that characterized participants as with-OSAS or without-OSAS, for cohort inclusion. Data extracted from the clinical PSG scored report included: apnea hypopnea index (AHI; events/hr), apnea index, hypopnea index, O₂ Nadir, minutes and percent of total sleep time spent at <92% O₂.
saturation, and minutes and percent of total sleep time spent with end tidal PCO$_2$ (partial pressure of carbon dioxide) ≥ 50mmHg.

**Subject Characteristic Questionnaire (Appendix D)**

This self-report questionnaire (designed by the PI) included items that addressed study participants’ demographic characteristics. Content included, age, gender, race, ethnicity, grade in school, and involvement in extracurricular activities such as sports or clubs.

**Modified Epworth Sleepiness Scale (Appendix E)**

The Epworth Sleepiness Scale is an 8-item questionnaire used to measure a person's general level of daytime sleepiness by assessing propensity to fall asleep during commonly encountered situations (Johns, 1992). Scores can range from 0 to 24 and an Epworth Sleepiness Scale score >10 indicates increased daytime sleepiness (Johns, 1992). The modified version used in the current study was modified in order to be more applicable to children (Melendres et al., 2004). The mention of alcohol was deleted in question 7 and question 8 was altered to specify that the subject was a passenger in the car rather than a driver (Melendres et al., 2004). In the current study, the modified Epworth Sleepiness Scale score data was used as a descriptive variable for sample characteristics.

*Psychometrics:* Internal consistency of the 8-items in the modified Epworth Sleepiness Scale was assessed in a retrospective review of 192 records of Chinese children who underwent overnight PSG and had a completed modified Epworth Sleepiness Scale questionnaire (Melendres et al., 2004), by Cronbach’s alpha ($\alpha = 0.85$) (Chan et al., 2009). No differences between the modified Epworth Sleepiness Scale (Melendres et al., 2004) score among patients with mild (AHI 1-4/hr), moderate (AHI 5-9/hr), and severe (AHI ≥10/hr) OSAS was identified; the modified Epworth Sleepiness Scale score of those with OSAS was statistically higher than
the score of control subjects (8.1 ± 4.9 vs 5.3 ± 3.9, p<.001) (Melendres et al., 2004) suggesting the instrument is sensitive to sleepiness in pediatric OSAS. Spearman’s correlation test between modified Epworth Sleepiness Scale scores and low AHI (≤5/hr) and high AHI (≥5/hr) reached statistical significance (rho = 0.124, 95% CI = 0.004 to 0.281) (Chan et al., 2009). It should be noted that the strength of the identified association was weaker than that reported in adults (correlation coefficient = 0.12 versus 0.55 in adult studies) (Johns, 1992). The weak correlation, as compared with adults, may be related to sleep architecture in children with OSAS (Goh, Galster, & Marcus, 2000). It is suggested that sleep architecture is preserved in pediatric OSAS; although the arousal index is elevated, only a portion of the respiratory events will be associated with a cortical arousal (Goh et al., 2000). Another study found that shortened sleep latencies occur in children with OSAS, but daytime sleepiness is infrequent; however, daytime sleepiness was more likely to occur in severe OSAS and/or obese patients (Gozal, Wang, & Pope, 2001). The adult-like etiology of OSAS observed in obese adolescents, as well as the measurement of aspects of cognition (executive function), warranted the assessment of daytime sleepiness in this study.

**Behavior Rating Inventory of Executive Function, Second Edition (BRIEF®2; Appendix F)**

The Behavior Rating Inventory of Executive Function, Second Edition (BRIEF®2; Gioia et al., 2015) is the first revision of the Behavior Rating Inventory of Executive Function (BRIEF®; Gioia et al., 2000). This instrument is used to assess everyday behaviors associated with executive functions in home and school environments. This instrument was chosen for this study as it provides an ecological assessment of executive function and the two editions have been used in more than 1000 peer-reviewed studies worldwide (Gioia et al., 2015), allowing for comparison of study results to the extant literature. No new items were added to the second
edition, allowing for consistency of reported results between the two versions (Gioia et al., 2015). Further, this measure of executive function allowed for a comparison to a large, nationally stratified standardization sample that is matched to the U.S. Census (Gioia et al., 2015).

The authors describe executive function as “a collection of interrelated functions, or processes, that are responsible for goal-directed behavior and cognitive activity—that is, as the ‘conductor of the orchestra’ that controls, organizes, and directs cognitive activity, behavior, and emotional responses” (Gioia et al., 2015, p. 2). In this study, the BRIEF®2 variables (parent-report and self-report [see below]) were the primary outcome variables. The BRIEF®2 (both parent-report and self-report) requires a fifth grade reading level and is to be completed by parents of school-age children 5-18 years, and by adolescents aged 11-18 years. The BRIEF®2 parent-form contains 63 items with nine theoretically and empirically derived, well-validated, clinical scales to measure domains of executive function. The domains include: Inhibit, Self-Monitor, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Task-Monitor, and Organization of Materials. The parental report augments the adolescent self-report. The adolescent self-report form provides additional information about the level of awareness and perceptions of their executive function. The self-report consists of 55 items with seven clinical scales that parallel the Parent form: Inhibit, Self-Monitor, Shift, Emotional Control, Task Completion, Working Memory, and Plan/Organize. The clinical scales within each form compose three indices: (1) the Behavior Regulation Index (BRI), representing one’s ability to regulate and monitor behavior effectively, (2) the Emotion Regulation Index (ERI), representing one’s ability to regulate emotional responses, including response to changing situations, and (3) the Cognitive Regulation Index (CRI), representing one’s ability to control and manage cognitive
processes and problem solve efficiently. In addition, there is an overall summary score, the Global Executive Composite (GEC), a reflection of the individual’s executive dysfunction level.

The BRIEF®2 parent-form (paper/pencil) was completed by the parent or guardian. This form contains 63 items and typically takes less than 10 minutes to complete (Gioia et al., 2015). Written instructions emphasize the importance of responding to all items; verbal instructions were provided verbatim from the instrument manual to ensure consistency (Gioia et al., 2015, p. 12). The BRIEF®2 self-report form (paper/pencil) was completed by the adolescent participant. This form contains 55 items and typically takes less than 10 minutes to complete. Written instructions emphasize the importance of responding to all items; verbal instructions were provided verbatim from the instrument manual to ensure consistency (Gioia et al., 2015, p. 13).

**Scoring:** The item responses are: Never (1), Sometimes (2), and Often (3). The raw scores are summed for each clinical scale. This raw score is then converted to a T-score using the appropriate normative tables provided in the manual (Gioia et al., 2015). Using a linear transformation of the raw scale scores ($M=50$, $SD=10$), T-scores ≥ 60 are considered clinically significant (i.e., abnormal). Sample percentiles are also calculated to identify the percentage of children in the standardization sample who fall below a given raw score. For all BRIEF®2 clinical scales and indices, T-scores between 60-64 are considered mildly elevated, 65-69 potentially clinically elevated, and 70 or above clinically elevated or clinically significant (Gioia et al., 2015).

**Missing items:** If more than 12 items (parent form) or more than 10 items (self report) are missing in total, the BRIEF®2 cannot be scored. If more than 2 items are missing for any clinical scale (e.g., Inhibit), the scale should not be scored. If only 1 item per scale is missing, the missing item is assigned a score of Never (N), or 1, and the raw score (sum) can be calculated.
**Psychometrics:** The BRIEF®2 demonstrates appropriate reliability and strong evidence of validity (Gioia et al., 2015). The internal consistency of the BRIEF®2 is high for all index scores, with all parent-form Cronbach’s alpha coefficients > .90 and the self-report forms in the mid .80s to high .90s. Coefficients across all individual scales were .80 or higher for both parent and self-report. The interrater reliability between parent and adolescent raters are moderate, with overall mean correlations of .62 for the typically developing sample and .30 for the clinical sample. Effect sizes for mean differences between raters for each scale ranges from .08-.18 in the typically developing sample and .05-.49 in the clinical sample. Correlations between two parent raters were moderate, with a mean correlation of .77 for the typically developing sample (effect size: .01-.13) and .59 for the clinical sample (effect size: .08-.24). Test-retest reliability correlation coefficient for Parent Forms was .79 across clinical scales over an average interval of 2.9 weeks. Test-retest coefficients for the indices and composite scores were also high (>0.82). Within self-report forms, the mean test-retest correlation across clinical scales was .74 over an average interval of 3.7 weeks with correlations for indexes and composites ≥ .75.

The validity of the BRIEF®2 is based on evidence of content, internal structure, and its relation to measures of other similar and dissimilar variables. Large, detailed descriptions are available in (Gioia et al., 2015). Collectively, correlational and exploratory factor analyses provide consistent strong support for valid interpretation of BRIEF®2 scores based on their relationship to other well-established behavioral, emotional, social, and attentional functioning rating scales. The patterns of strong correlations between the BRIEF®2 and behavior rating scales measuring similar constructs (e.g., BRIEF®2 Inhibit Scale with BASC-2 Hyperactivity/impulsivity scale) provide convergent evidence, whereas lower correlations
between scales measuring different constructs provide discriminant evidence for the validity of the BRIEF®2.

**Wrist-worn Actigraphy: Philips Respironics Actiwatch 2™ and Actiwatch Spectrum™**

An actigraph is a small, wrist-watch sized device used to measure sleep/wake by an internal accelerometer (i.e., motion sensor). Actigraphy provides the advantage of having objective information on sleep habits and patterns while allowing the participant to remain in their natural sleep environment (Martin & Hakim, 2011). This objective measure of sleep is of value, as self-reported sleep duration is often over estimated (Arora, Broglia, Pushpakumar, Lodhi, & Taheri, 2013). The data is collected and translated into epochs (typically 30 seconds to one minute) of activity; using proprietary validated algorithms; epochs are then scored as sleep or wake in order to provide estimates of sleep/wake duration. In this study, wrist-worn actigraphy, Philips Respironics Actiwatch 2 and Actiwatch Spectrum ("Actiwatch 2," 2017; "Actiwatch Spectrum," 2017), were used to objectively measure average sleep durations (i.e., primary variable, major sleep bout total sleep time; exploratory variable, total sleep time per 24-hours) across one week (including one weekend). Though two different models of Actiwatches were used, details and specifications of the accelerometer are identical for the two devices (Actiware 6.0.4 Manual; ("Actiwatch 2," 2017; "Actiwatch Spectrum," 2017). Additionally, the device settings and proprietary algorithms for scoring sleep versus wake were the same across both devices. Therefore, for the purpose of this study, use of two different device models did not affect the quality of the data. The Actiwatch was worn on the non-dominant wrist and was used in unison with a subjective measure of sleep/wake (see Consensus Sleep Diary; (Carney et al., 2012). The purpose of this objective measure of sleep was to describe differences in sleep
duration (major sleep bout total sleep time) between obese adolescents with and without-OSAS and additionally explore the relationship between average sleep duration and executive function.

**Scoring:** In the absence of a well-established standardized approach to actigraphy measures in children across previously conducted studies (Meltzer, Montgomery-Downs, Insana, & Walsh, 2012), there are not specific currently available normative values for pediatric populations (Meltzer, Montgomery-Downs, et al., 2012). Given these limitations, study decisions were based on provided justifications. A comprehensive review of 228 studies using actigraphy for assessment of sleep in pediatric populations guided the decision making for scoring actigraphy data (Meltzer, Montgomery-Downs, et al., 2012). Interval options selected in the Actiware scoring program included: set automated rest intervals, only one rest interval per day, use markers, and convert off-wrist to exclude data. The Actiwatches were configured to collect data at 30 second epochs with the activity thresholds set to “low”, the sleep interval detection algorithm set to immobile minutes, and sleep onset and offset set to 10 minutes. Automated scoring was used (Actiware 6.0.4), wherein the Actiware algorithm automatically assigns rest intervals to the data based on the configuration parameters selected. In instances where automated scoring needed to be overridden and/or automated parameters needed to be adjusted, actograms were scored using a combination of sleep diaries and visual scoring. Diaries data used to guide scoring included: time in bed, time sleep initiated, time awake, and time out of bed. These reported times assisted scoring sleep/wake periods. Additionally, rest interval start times were able to be visually identified by a significant, sustained drop in activity levels or identified if the participant used the event marker button on the device to indicate, for example, “in bed,” “initiate sleep,” “awake,” and/or “out of bed.” Sleep onset was initiated at the first minute of 10 consecutive minutes scored as sleep, with one full minute of activity allowed within the 10-
minute time frame (Meltzer, Walsh, & Peightal, 2015). Overriding automated scoring was indicated, for example, by the Actiware algorithms failing to detect rest intervals, despite an apparent drop in activity, or, in instances where the participant appeared to have two separate rest intervals throughout the evening; for example, a sustained period of wakefulness between sleep bouts, wherein the automated scoring did not identify the second rest interval due to setting of “only one rest interval per day” being selected.

**Psychometrics:** Sensitivity is considered the proportion of epochs scored as sleep using PSG that is accurately identified by actigraphy (Meltzer, Montgomery-Downs, et al., 2012). Specificity is the proportion of PSG scored wake epochs accurately identified as wake by actigraphy (Meltzer, Montgomery-Downs, et al., 2012). Both of these components are important in measuring sleep/wake, as incorrect scoring of sleep/wake episodes can lead to under or overestimations of sleep parameters such as total sleep time. Another technique to determine the sensitivity or specificity is the Bland-Altman concordance technique (Altman & Bland, 1983; Bland & Altman, 1986), determined by providing a visual representation and plotting data against the gold-standard to assess standard deviations/deviations from the ideal (Meltzer, Montgomery-Downs, et al., 2012).

Actigraphy has been shown to provide valid estimates of sleep patterns in adolescents (O’Driscoll, Foster, Davey, Nixon, & Horne, 2010; Sadeh, Sharkey, & Carskadon, 1994) and has good sensitivity to detect sleep when compared with the gold standard measure of sleep, PSG, in pediatric populations (83–97 %) (Meltzer, Montgomery-Downs, et al., 2012). However, 55% of pediatric validation studies have reported specificity values under 60% for detecting sleep after wake onset, resulting in inflated estimates of sleep duration (Meltzer, Montgomery-Downs, et al., 2012). One example includes actigraphy comparison to PSG in a group of 115 subjects (ages
Data for the Mini-Mitter Actiwatch-2 was collected at 1-minute epochs and the Sadeh algorithm (most commonly reported analysis for children and adolescents), was examined as the primary algorithm with the Cole-Kripke algorithm as secondary (Meltzer, Walsh, Traylor, & Westin, 2012). No significant differences between PSG and Mini-Mitter Actiwatch-2 were found for total sleep time when controlling for age and sleep disordered breathing status; however, the Actiwatch 2 ("Actiwatch 2," 2017) device overestimated wake after sleep onset by 10 minutes (Meltzer, Walsh, et al., 2012). The sensitivity (0.89-0.97) indicates the device has good sensitivity to detect sleep, but poorer specificity (0.54-0.77) to detect wake (Meltzer, Walsh, et al., 2012). In a study assessing the Actiware auto rest detection algorithm against sleep diaries in 10 normal, healthy adults for at least 150 nights of sleep, automated scoring was more likely to produce consistent results with less variation in sleep parameters than when scored with diary data alone (Respironics Inc., 2007).

**Missingness:** In order for actigraphy data to be considered complete for this study, the record must include five full nights of actigraphy data, including two weekend days (Friday/Saturday/Sunday). This decision was made based on the extant literature, where studies have agreed that at least 4 days of monitoring (with complete data) are necessary to achieve a reliability of 0.80 pediatric populations (Trost, McIver, & Pate, 2005). A complete day is considered ≥10 hours of data (excluding periods when the device removed for sleep/bathing) in order to obtain a reliability of 0.80 (Corder, Ekelund, Steele, Wareham, & Brage, 2008; Tudor-Locke et al., 2015)

**Consensus Sleep Diary (Appendix G)**

The concurrent use of a sleep diary during actigraphy recording is necessary and consistent with established guidelines (American Academy of Sleep Medicine, 2014). Sleep
diaries provide a backup for data in the event of device malfunction, a relatively rare and unanticipated problem, and also help to differentiate sleep/wake periods or on/off times when the actigraphy data appears ambiguous (Martin & Hakim, 2011; Meltzer, Montgomery-Downs, et al., 2012). However, one concern to keep in mind when using this subjectively reported data is that diaries may over-report sleep time; a study of 385 adolescents (age 13-18 years) found that actigraphic estimates of total sleep time were substantially less than sleep diary (6h 51min actigraphy vs. 8h 16min sleep diary (Short, Gradisar, Lack, Wright, & Carskadon, 2012). As such, the actigraphy data provided the primary source of sleep duration while diary data provided guidance in scoring the primary sleep/wake data (i.e., actigraphy). The diary data additionally provides a descriptive self-report variable of total sleep time and sleep-related behaviors for subsequent post-hoc analysis.

Because this study recorded sleep onset/offset and sleep durations, caffeine intake needed to be considered. High caffeine consumption has the potential to delay bedtimes and is associated with shorter sleep durations and increased daytime sleepiness (Aepli, Kurth, Tesler, Jenni, & Huber, 2015; Owens, 2014). As such, regular caffeine users tend to develop a cycle in which disturbed sleep (attributable to caffeine) leads to daytime sleepiness, leading to increased caffeine consumption (Roehrs & Roth, 2008). Further, energy drink consumption has tripled (from 4% to 12%) between 2000-2008 (Han & Powell, 2013) and the 2007-2010 National Health and Nutrition Examination Survey found an intake of at least 25-50 mg/d of caffeine is evident in approximately 75% of adolescents (Ahluwalia & Herrick, 2015).

Until recently, there has been a lack of standardization in sleep diaries, contributing to an inability to compare findings (Carney et al., 2012). In response to this, the field of sleep medicine convened an expert panel to compare multiple sleep diaries and develop a consensus sleep diary.
This consensus diary allows for inter-study comparisons by accruing consistent data for variables commonly examined in sleep. To ensure sleep diary results from this study are comparable to future literature adopting the consensus diary, a modified version was used in this study. The Core Consensus Sleep Diary (Carney et al., 2012) contains nine items that were considered to be most critical parameters by the expert panel. These items include: time of getting into bed, time at which the individual attempted to fall asleep, sleep onset latency, number of awakenings, duration of awakenings, time of final awakening, final rise time, perceived sleep quality (via Likert scale), and additional space for open ended comments from the respondent. Due to the above-mentioned relationship of caffeine and sleep/sleepiness, two items from The Expanded Consensus Sleep Diary for Evening (Carney et al., 2012) were included in the study sleep diary. These two questions address the number of caffeinated drinks consumed and time of last caffeinated drink prior to sleep onset. An additional two items from the Expanded Consensus Sleep Diary for Evening (Carney et al., 2012) were added to the diary for this study. These items include: number of naps/dozing episodes and duration of the naps/dozing episodes. Including this subjective report provides additional information for any ambiguous data points in the actigraphy data and provides exploratory data for total sleep time per 24 hours in addition to the primary total sleep time variable, major sleep bout total sleep time.

**Psychometrics:** Unfortunately, due to the nature of sleep and its night-to-night variability, test-retest reliability cannot be reported. Additionally, because the sleep diary is not intended to measure one construct, testing the internal consistency of the measure is also not feasible. Because of these issues, no formal reliability and validity data are available (Carney et al., 2012).

**Missingness:** In order for sleep diary data to be considered complete, the record must include five full days of diary data including two weekend days (Friday/Saturday/Sunday).
Activity Diary - Previous Day Physical Activity Recall (PDPAR; Appendix H)

According to the youth physical activity guidelines (Physical Activity Guidelines for Americans, 2008), adolescents should be active at least 60 minutes per day with most of the 60 minutes or more at a moderate- or vigorous-intensity. For the purposes of this study, activity frequency is defined as the number of days per week that adolescents are active at a moderate- to vigorous- level of activity for 30-minutes (to account for gym classes) and the recommended 60 minutes. Intensity of activity is important in determining the level of exertion in performing different activities. For example, walking to the bus stop requires a different level of exertion than playing softball; these two activities will have differing intensities. Intensity of activity is reported as: low-light, high-light, moderate, and vigorous. These intensities are determined based on the metabolic equivalent of task (MET) value associated with the reported activity. MET’s are useful for describing energy expenditure of certain activities. For example, an activity that is a 3 MET activity requires 3 times the energy of a 1 MET activity, such as sitting still.

Time (minutes per day), or duration, of activity will be reported for all intensity levels. The purpose of including activity time measurement is to describe differences in activity levels (frequency, intensity, time) between obese adolescents with and without-OSAS and, additionally, to explore the relationship between activity levels and executive function. This data also provides a description of participant’s physical activity that can be examined from the perspective of current recommendations (i.e., how much time is spent in low intensity activities and if adolescents are meeting the recommended physical activity guidelines). Frequency, intensity and time will be examined as descriptive variables to explore the potential relationship between activity and the primary outcome, executive function. A physical activity dairy was chosen as the primary measure for physical activity as opposed to obtaining physical activity data from the
Actiwatch. Waist-worn accelerometers for physical activity, and wrist-worn actigraphy for sleep prove to have better sensitivity, specificity, and accuracy at the respective locations based on accepted algorithms for the respective devices (Hjorth et al., 2012; Kohl et al., 2000; Meltzer, Montgomery-Downs, et al., 2012; Slater, 2015; Toon et al., 2016). Though devices are being tested to determine the ability to measure both physical activity and sleep using one device/location, these investigations are preliminary (Hjorth et al., 2012; Rosenberger, Buman, Haskell, McConnell, & Carstensen, 2016) and therefore were not deemed appropriate for a feasibility or dissertation study.

The Previous Day Physical Activity Recall (PDPAR) (Weston et al., 1997) is a self-report measure intended to document after school (3 p.m. – 11:30 p.m.) physical activity. Responses are time-based recall aliquots of 30-minute segments. There is a list of numbers (1-33) associated with commonly performed activities (e.g., cooking, sleeping, homework, shopping, swimming, etc.), in which respondents place the numbered activity in the appropriate cell designating the time of the activity. Respondents are also asked to rate the intensity of the activity by four levels (very light, light, medium, or hard). Each activity has corresponding MET values for all levels of intensity to calculate energy expenditure (Ainsworth et al., 2011). For the purpose of this study, the instrument has been adjusted for a 24-hour recall period, as actigraphy data collection was concurrently collected over 24-hours across seven days.

Psychometrics: Weston and colleagues (1997) tested the validity and reliability of the PDPAR with pedometers and accelerometers in students’ grades 7-12. This study reported high test-retest reliability (within 1-hour) (r=0.98), high inter-rater reliability (r=0.99), and correlations between the pedometer and Caltrac monitor (accelerometer) to be high (r=0.88 and r=0.77, respectively) (Weston et al., 1997). Another study examined the concurrent reliability of the PDPAR with the
CSA 7164 accelerometer (Trost, Ward, McGraw, & Pate, 1999). This study found a modest correlation between MET from PDPAR and accelerometer counts was 0.57 for each 30-minute time block (Trost et al., 1999). Similar to the instrument adaptation in this study, a prior study adapted the instrument to account for a 24-hour recall period; the recall period was modified from 3:30 p.m. to 11:30 p.m. to 9:00 a.m. to 9:00 a.m. (Trost, Marshall, Miller, Hurley, & Hunt, 2007) and was tested against pedometers measuring step counts. However, the study by Trost and colleagues (2007) excluded midnight to 5:00 a.m. from the questionnaire. Modest correlations (r=0.29 to 0.34; \( p < 0.05 \)) between step counts and mean METs, 30-minute blocks of vigorous physical activity and moderate-vigorous activity were identified for the modified instrument; these results are in contrast to the previously reported correlations between the instrument and Caltrac monitor accelerometer (Weston et al., 1997). It should be noted that the modified instrument constructs of mean METs, 30-minute blocks of vigorous activity, 30-minute blocks of moderate-vigorous activity, and 30-minute blocks of screen based-activities were examined in relationship to a pedometer that does not measure intensity of activity, unlike accelerometers that were used in the prior studies to establish concurrent validity (Trost et al., 2007).

**Missingness:** In order for PDPAR diary data to be considered complete, the participant must be missing no more than four, 30-minute blocks per day. If more than 10% of the activity data are considered missing, the statistical analysis is likely to be biased (Bennett, 2001; Dong & Peng, 2013). For this reason, if the participant was missing more than 2 hours of data per day, the diary data for that day was considered to be incomplete. For the diary to be complete, it had to contain five complete days of PDPAR diary data, inclusive of any two weekend days (Friday/Saturday/Sunday).
End of Study Survey (Appendix I)

The end of study survey assessed participant acceptability of the study experience. This included participant feedback on instrumentation and protocol acceptability. The purpose of this survey was to determine participants’ acceptability and challenges of the current protocol; specifically, acceptability and attitudes toward continuous activity/sleep tracking devices and diaries was sought to impart insights for subsequent study design. The survey, inclusive of 13 items, addressed the likelihood/willingness of participants to participate in a similarly designed study, aspects participants would like to see changed (e.g., electronic diary vs. paper), and open-ended feedback. The survey item responses were either binary (i.e., yes/no), ordinal based on a Likert scale response set (i.e., very dissatisfied, somewhat dissatisfied, somewhat satisfied, very satisfied) or open-ended in response to a single item. In addition to participant reported satisfaction with the study protocol and instrumentation, acceptability of protocol nuances specific to the wearable device (i.e., actigraphy) and diaries (i.e., sleep and activity), a feasibility domain, was also addressed by the end of study survey measure.

Data Collection and Management

The following instruments were paper/pencil versions: Pre-enrollment eligibility screening questionnaire, subject characteristic questionnaire, modified Epworth Sleepiness Scale, sleep & activity diaries, BRIEF®2 (Parent Report and Self-Report), and the end-of-study survey. All paper forms were maintained in participant research files, labeled only by a unique study ID.

Philips Respironics Actiwatch 2 and Actiwatch Spectrum are electronic data collection instruments ("Actiwatch 2," 2017; "Actiwatch Spectrum," 2017). All electronic data was maintained on a study-specific, IRB-approved, HIPAA compliant server. Electronic data files
were labeled by a unique study ID. Access to electronic data was managed by the PI and mentor; access permission was provided for PI/mentor and study biostatistician.

All study participants were assigned a randomly-generated study ID number. All study records were labeled only by the unique study ID number; no private, identifiable labels (e.g., name, Medical Record number) were used. A master participant list, linking study ID number and participant private, identifiable data (name, address, phone number, DOB, mobile number or email) was maintained by the PI. The master participant list was secured on the sleep server, accessible only to the PI and mentor. At the completion of all planned analyses, the master participant list will be electronically shredded.

During conduct of the study, all paper research files were stored in a locked, fireproof filing cabinet at the study site. Only the PI and mentor have access to the filing cabinet. At completion of all study activities, including the analysis, all paper research files will be transported from the study site to the College of Nursing (CON) in an IRB-approved mobile record storage system. Long-term storage at the CON will be in a locked, fireproof filing cabinet in a locked office (mentor, A. Sawyer; Nursing Sciences Building, 307C, University Park). Long-term storage of records will be for 3 years, as required by IRB.

Data preparation for analysis was conducted by the PI with oversight by the mentor. Participant data was double-entered by the PI in a study database (Excel) in preparation for analysis. All entries were reviewed for inaccuracies and missing data was labeled by (.) and later translated to an empty cell for analysis. A master, de-identified database was prepared for analysis; individual level data was associated with only study ID number.
Potential Hazards and Precautions

Loss of confidentiality was a risk of participating in this research. Precautions were taken by assigning unique ID numbers to ensure no personal identifiers could be connected with the data. A unique study ID number was assigned to each participant and a log accessible only to the PI, study biostatistician, and mentor, linked the study identification number to personal identifiers. Another potential risk included subjects experiencing psychological distress with completion of questionnaires; questions were estimated to be relatively benign and the risk was expected to be minimal. There was potential for participants to experience initial problems sleeping with wrist actigraphy, though it was anticipated that this would only occur during the first night.

Analysis

The distribution of all research variables were examined by measures of central tendency. For continuous variables, means, standard deviation or medians and interquartile ranges (IQR) were examined and for categorical variables, frequencies were examined. Distribution of data was also graphically examined using stem-and-leaf plots and histograms. Outliers were identified by examining stem-and-leaf plots for any data points that fell outside of the IQR. Because this was a small feasibility study, outliers in the data were retained. This study aimed to compare differences between obese adolescents with and without-OSAS. Because of difficulty recruiting a group of obese adolescents’ without-OSAS, no tests for group differences were conducted to address study aims three and four. All study analyses conducted were on the single cohort of obese adolescents with OSAS. Descriptive analysis by characteristic variables (e.g., age, gender) was completed. Distributions of continuous characteristic and research variables were first evaluated for approximate normality, and then reported as mean/SD or median (IQR), as
appropriate. Missing data was assumed missing at random (no imputation); missing data was summarized by variable. The following analyses address the study aims:

**Aim 1:** To determine the feasibility of recruiting and retaining a sample of obese adolescents (11-17 years of age) with and without-OSAS.

For this aim, recruitment rate \(\frac{\# \text{invited to participate}}{\# \text{agreed to speak to researcher}}\), eligibility rate \(\frac{\# \text{eligible to participate}}{\# \text{participated}}\), participation rate \(\frac{\# \text{participated}}{\# \text{eligible to participate}}\), and study completion rate \(\frac{\# \text{completed protocol}}{\# \text{consented}}\) are summarized using descriptive statistics.

**Aim 2:** To pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation.

Complete data rates \(\frac{\# \text{subjects with complete data}}{\# \text{consented}}\) are reported for actiwatches ("Actiwatch 2," 2017; "Actiwatch Spectrum," 2017), Consensus Sleep Diaries (Carney et al., 2012), and the PDPAR (Weston et al., 1997) for physical activity and summarized by descriptive statistics. A descriptive analysis of data from the end-of-study survey (frequencies) is reported. Open-ended responses are narratively summarized. Consistent themes, as is possible with a small sample size, are identified and summarized.

**Aim 3:** To explore executive function impairments as measured by the Global Executive Composite (i.e., overall summary score) and three subscales (i.e., Behavior Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index), within groups, compared to published normative data, and explore differences in executive function impairments between groups (obese adolescents with and without-OSAS).
Clinical subscale scores (indices) and the Global Executive Composite (i.e., overall summary score) are reported as T-scores. The individual T-scores of the participants are summarized using mean/SD. Sample data is compared to the normative published data (Gioia et al., 2015) using one-sample t-tests within-groups.

The individual T-scores of the participants are compared to the normative data for categorization, with T-scores < 60 considered normal, between 60-64 considered mildly elevated, 65-69 potentially clinically elevated, and 70 or above clinically elevated or clinically significant (Gioia et al., 2015).

**Aim 4:** To describe differences in activity levels (frequency, intensity, time) and sleep duration (major sleep bout total sleep time), measured by 1-week actigraphy (objective measure of rest/activity and sleep) and self-report, between obese adolescents with and without OSAS and explore the relationship between activity levels and sleep duration with executive function (Global Executive Composite scores).

Activity level, time (total duration of activity/day in minutes), is prioritized as the primary activity variable for this aim. This decision is based on the national guidelines/recommendations for physical activity, designated as time (e.g., 60 minutes/day of activity) (*Physical Activity Guidelines for Americans*, 2008). The activity time (mean ± SD; median [IQR]) and intensity is explored. Activity frequency is defined as bouts, or number, of activity sessions in a one-week period. In applying this definition, activity frequency (count data) is also examined for exploratory analysis.

Sleep duration, or major sleep bout total sleep time (continuous variable) is summarized using descriptive statistics (mean ± SD; median [IQR]). Sleep duration is summarized for 7-day measurement period and is comprised of at least two weekend days (Friday/Saturday;
Saturday/Sunday). Graphical summary of sleep duration and physical activity is also explored (histogram).

To explore the associations between activity level (time), sleep duration (mean/median total sleep time for 7 day period, and Global Executive Composite score (executive function outcome), scatterplots are examined, and Spearman rank correlation coefficients are estimated along with corresponding 95% confidence intervals. By a priori defining the priority variables for exploratory correlations, risk of Type I error is reduced.

**Methodological Considerations**

A potential problem with a cohort study design with a prospective 1-week measurement protocol is the loss of subjects to follow-up (Mann, 2003; Song & Chung, 2010). Because participants only completed two research visits (baseline/visit 1 and after 1 week at visit 2), a low attrition rate was anticipated. Participants were provided non-coercive compensation for participation. Compensation was provided for participant time burden relative to protocol data collection; compensation was provided at visit 1 and visit 2. Though the compensation at visit 2 was expected to also support the retention rate in this study, there was risk for incomplete data with the continuous measurement of activity and sleep (i.e., actigraphy) over the one-week protocol period. As a technology-based measurement device was employed in this study, risks are relative to device performance and participant adherence to the protocol. Additionally, participant completion of sleep and activity diaries is required for accurate scoring of sleep and activity. Risk of incomplete data with diary completion was assessed as moderate at the outset of the study. To mitigate this potential problem, diaries provided clear and simple instructions with easy to complete forms.
Chapter Summary

This chapter has defined the aims of this study, the study design, recruitment, sample and setting, study protocol, measures/instrumentation, data collection and management, statistical analysis, and methodological considerations. The details outlined in this chapter have provided sufficient information on the logistics of the study which support replication of the study if desired. Decisions made regarding the study design, sample, protocol, measures, analysis, and methodological considerations are supported by the extant published literature.
Chapter 4

Results

Introduction

The purpose of this study was to examine executive function outcomes and explore physical activity level and sleep duration in obese, OSAS adolescents in a feasibility study to provide critical methodological and protocol insights for executing a subsequent, fully-powered cohort study. Secondarily, results of the feasibility study also provide insights on executive function, physical activity level, and sleep duration in adolescents with obesity and OSAS, contributing to the relatively scant evidence addressing the field’s understanding of the health of adolescents with obesity and OSAS. The following aims were addressed:

**Aim 1:** To determine the feasibility of recruiting and retaining a sample of obese adolescents (11-17 years of age) with and without-OSAS.

**Aim 2:** To pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation.

**Aim 3:** To explore executive function impairments as measured by the Global Executive Composite (i.e., overall summary score) and three subscales (i.e., Behavior Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index), within groups, compared to published normative data, and explore differences in executive function impairments between groups (obese adolescents with and without-OSAS).

**Aim 4:** To describe differences in activity levels (frequency, intensity, time) and sleep duration (major sleep bout total sleep time), measured by 1-week actigraphy (objective measure of rest/activity and sleep) and self-report, between obese adolescents with and
without OSAS and explore the relationship between activity levels and sleep duration with executive function (Global Executive Composite scores).

**Feasibility Results**

**Aim 1:** To determine the feasibility of recruiting and retaining a sample of obese adolescents (11-17 years of age) with and without-OSAS.

**Sample Recruitment**

Those who received mailed invitation letters were identified using the institutional cohort discovery platform, i2b2; sixty-one potentially eligible participants, identified by i2b2, were mailed study invitation letters (Figure 4.1). Fifteen adolescents who were mailed letters contacted the investigator to express interest in study enrollment. After completion of the pre-enrollment eligibility screening questionnaire, nine adolescents were eligible to participate and research visit 1 was scheduled. Six adolescents were deemed ineligible due to the following reasons: change in BMI greater than ± 2 kg/m2 since PSG (n=1), diagnosis of ADHD or ADD (n=2), diagnosis of narcolepsy (n=1), and current OSAS treatment (n=2). Of the nine adolescents who were eligible, one adolescent did not attend visit 1, resulting in eight adolescent participants who were recruited and enrolled by means of an invitation letter. Six of the adolescents recruited by invitation letter and thereafter enrolled in the study had OSAS as indicated by PSG (AHI ≥ 1.5 events/hr); two participants did not meet OSAS AHI criterion.
Figure 4.1. Recruitment and enrollment using i2b2 and mailed invitation letters

Notes. i2b2, Informatics for Integrating Biology & the Bedside; BMI, body mass index; PSG, polysomnography; ADHD, attention deficit hyperactivity disorder; ADD, attention deficit disorder; tx, treatment; OSAS, obstructive sleep apnea syndrome; AHI, apnea hypopnea index

One hundred twenty eight adolescents between the ages of 11-17 years were scheduled for a diagnostic PSG during the recruitment phase of this study (duration of 4 months; Figure 4.2). One hundred adolescents did not meet eligibility criteria. Of 28 adolescents that were eligible, eight adolescents cancelled their scheduled PSG and three adolescents did not show up for scheduled research visits. Of the remaining 17 adolescents that were approached regarding interest in participation, 16 enrolled and one declined participation. Of the 16 enrolled
adolescents, 15 had OSAS and one had an AHI < 1.5 events per hour, categorizing them as without-OSAS. One adolescent was later excluded from the analysis due to incomplete data (i.e., unable to complete the protocol due to personal transportation issues).

**Figure 4.2.** Recruitment and enrollment on night of scheduled PSG

*Notes:* Categories are not mutually exclusive; PSG, polysomnography; BMI, body mass index; ADD, attention deficit disorder; ADHD, attention deficit hyperactivity disorder; ODD, oppositional defiant disorder; OCD, obsessive compulsive disorder; AHI, apnea hypopnea index
The sampling plan for this study was intended to provide a sample inclusive of two groups of adolescents; one group with obesity and OSAS, the other with obesity but without-OSAS. After two months of recruitment, the challenge of recruiting/enrolling obese adolescents without-OSAS became evident with only 2 adolescents without-OSAS recruited using i2b2 and only 1 without-OSAS recruited on the night of PSG. Therefore, a de-identified ancestry search of the sleep center’s PSG acquisition database was conducted to determine the feasibility of obtaining an adolescent obese, without-OSAS cohort at the recruitment site. PSG results for the nine months prior to the start of this study’s recruitment and enrollment phase were hand searched. Of 206 adolescent records identified in that time frame, incomplete records for cancellation and PSG no-show were excluded (n=20); 186 complete PSG results were available for de-identified review (Figure 4.3). Of those, only 22 (11.8%) had an AHI <1.5 events/hour, of which only four (2%) had a BMI categorized as obese (BMI ≥ 95th percentile). Based on these data, the investigator determined that feasibility of recruiting/enrolling a study cohort of obese adolescents without-OSAS, employing the study recruitment plan, was not feasible.
Figure 4.3. De-identified search of PSG’s prior to study enrollment phase

Notes. PSG, polysomnography; BMI, body mass index; AHI, apnea hypopnea index

Sample Recruitment, Enrollment, and Retention Rates: Feasibility Outcomes

Recruitment rate was calculated as \( \frac{\# \text{ agreed to speak to researcher}}{\# \text{ invited to participate}} \). Because two separate recruitment strategies were used for the study, two separate recruitment rates are reported. Using i2b2, 15 subjects agreed to speak to a researcher out of 61 potentially eligible subjects invited to participate, resulting in a recruitment rate of 24.6%. For the PSG recruitment strategy, 16 subjects agreed to speak to a researcher out of 17 that were invited to participate; this resulted in a recruitment rate of 94.1%. The eligibility rate was calculated as \( \frac{\# \text{ eligible to participate}}{\# \text{ participated}} \). For
i2b2, nine subjects were eligible to participate out of the eight that participated; one eligible subject did not complete visit 1. On the night of PSG, 17 subjects were eligible out of 16 that participated; one subject declined participation, as this adolescent was not interested in being a research participant. The participation rate was calculated as \( \frac{\text{# participated}}{\text{# eligible to participate}} \). For i2b2, eight subjects participated out of nine subjects who were eligible to participate in the study. This resulted in a participation rate of 88.9%. On the night of PSG, 16 subjects participated out of 17 who were eligible to participate. This resulted in a participation rate of 94.1% on the night of PSG. The study completion rate \( \frac{\text{# completed protocol}}{\text{# consented}} \) was 95%; 20 participants completed the protocol (visit 1 and visit 2) out of 21 consented.

**Participant Characteristics**

Study participant characteristics are shown in Table 4.1; means and standard deviations, as well as medians and interquartile ranges are reported due to the small sample size. Distribution of continuous characteristic variables was analyzed by boxplots (Figure 4.4; and polysomnographic characteristics, Figure 4.5). The box represents the IQR (i.e., 25th-75th percentile) and the line within the box represents the median (i.e., the 50th percentile). The whiskers on the box plot indicate the minimum and maximum values of the majority of the data, with any data points outside of these lines being labeled as outliers. Because of the small sample size, outliers were frequent across variables and the data was not normally distributed (Figure 4.4; Figure 4.5). For this reason, median (IQR) provides a more accurate representation of participant characteristics for this study and is prioritized for describing the sample.

The majority of study participants were white (n=15; 75%), non-Hispanic (n=18; 90%), males (n=11; 55%), with a median age of 14 (IQR, 2) years. As participants needed to have a BMI $\geq 95^{\text{th}}$ percentile to be enrolled in the study, median BMI was expectedly high, at 36.45
kg/m² (IQR, 4.6), with a median BMI z-score of 2.47 (IQR, 0.3). Most participants (n=9; 45%) were in the 8th or 9th grade and based on insurance type, may be considered to be of low socioeconomic status (n=13; 65%). Study participants had asthma (n=8; 40%), pre-hypertension (n=4; 20%), and excessive daytime sleepiness (n=5; 25%) with a median modified-ESS (Melendres et al., 2004) score of 8 (IQR, 5.5). Very few worked on school days (n=1; 5%) or weekends (n=1; 5%) and few were currently involved in a sport (n=3; 15%), school club (n=7; 35%), or non-school affiliated club (n=3; 15%).

The median apnea hypopnea index (excluding central events) indicated participants experienced a median of 5.85 (IQR, 9.6) events/hr, 0.30 (IQR, 0.9) apneic events/hour, and 5.00 (IQR, 8.7) hyponeic events/hour (Table 4.1). This indicates that the majority of OSAS in this sample is based on greater frequency of hypopneic events than apneic events. Median lowest oxygen saturation during PSG was 91% (IQR,8), with 0.10 (IQR, 18.2) minutes and 0% (IQR, 3.3) of their total sleep time spent at <92% oxygen saturation. End-tidal PCO₂ median was also low due to extreme outliers, with zero (IQR, 10.7) minutes spent at ≥ 50mmHg and 0% (IQR, 2.2) of total sleep time.
Table 4.1. Participant characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11 (55)</td>
</tr>
<tr>
<td>Female</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Grade</td>
<td></td>
</tr>
<tr>
<td>5th</td>
<td>1 (5)</td>
</tr>
<tr>
<td>6th &amp; 7th</td>
<td>6 (30)</td>
</tr>
<tr>
<td>8th &amp; 9th</td>
<td>9 (45)</td>
</tr>
<tr>
<td>10th &amp; 11th</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>15 (75)</td>
</tr>
<tr>
<td>African American</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>18 (90)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Excessive Sleepinessa</td>
<td>5 (25)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>8 (40)</td>
</tr>
<tr>
<td>Pre-hypertension</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Public insurance</td>
<td>13 (65)</td>
</tr>
<tr>
<td>Extracurricular activities</td>
<td></td>
</tr>
<tr>
<td>Working school days</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Working on weekends</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Currently in a sport</td>
<td>3 (15)</td>
</tr>
<tr>
<td>In a school club</td>
<td>7 (35)</td>
</tr>
<tr>
<td>In a non-school club</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Age, years</td>
<td>13.45 (1.61)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>36.02 (5.20)</td>
</tr>
<tr>
<td>BMI-z-score</td>
<td>2.42 (0.26)</td>
</tr>
<tr>
<td>Modified-ESS score</td>
<td>8.75 (4.35)</td>
</tr>
<tr>
<td>PSG characteristics</td>
<td></td>
</tr>
<tr>
<td>AHI (events/hr)</td>
<td>9.64 (11.77)</td>
</tr>
<tr>
<td>Apnea Index</td>
<td>1.16 (3.03)</td>
</tr>
<tr>
<td>Hypopnea Index</td>
<td>8.28 (9.52)</td>
</tr>
<tr>
<td>O₂ Nadir</td>
<td>87.95 (6.13)</td>
</tr>
<tr>
<td>&lt;92% O₂, minutes</td>
<td>18.7 (38.25)</td>
</tr>
<tr>
<td>&lt;92% O₂, %TST</td>
<td>3.73 (7.76)</td>
</tr>
<tr>
<td>End tidal PCO₂, minutes</td>
<td>38.96 (103.14)</td>
</tr>
<tr>
<td>End tidal PCO₂, % TST</td>
<td>7.18 (18.30)</td>
</tr>
</tbody>
</table>

Notes. a score >10 using the modified Epworth Sleepiness Scale. BMI, body mass index; ESS, Epworth Sleepiness Scale; PSG, polysomnogram; AHI, apnea hypopnea index; O₂, oxygen; O₂ Nadir, lowest oxygen saturation; TST, total sleep time; PCO₂, partial pressure of carbon dioxide.
Figure 4.4. Boxplots for participant characteristics

Notes. Age expressed in years; BMI, body mass index
Figure 4.5. Boxplots for polysomnographic variables

Notes. AHI, apnea hypopnea index; O₂ Nadir, lowest oxygen saturation
Aim 2: To pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation.

Complete Data Rates for 1-Week Measures

An aim of this feasibility study was to pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation. In order for watch and sleep diary data to be
considered complete, five full days of data, including two weekend days (Friday/Saturday/Sunday), was required. Complete data rates were calculated as

\[
\frac{\text{# subjects with complete data}}{\text{# consented}}
\]

Using this formula, the following were complete data rates for the sleep and physical activity measures: wrist worn actigraphy (n=15; 75%), Consensus sleep diaries (n=18; 90%), and PDPAR physical activity diaries (n=18; 90%). Missing actigraphy data was due to participant removal of device/non-wear (n=3) and device error (n=2). Device errors included the messages: “The Actiwatch experienced a battery reset. Data may or may not have been corrupted” and “There was an unexpected error when converting the Actiwatch data, resulting in no data being retrievable. (Decode Result: 3)”. Subjects with missing data were excluded from the analysis, where appropriate.

**Acceptability of Instrumentation and Protocol**

An end-of-study survey provided insights regarding adolescent’s acceptance of both study instrumentation and the protocol. As this was a feasibility study, questions were also designed to gain insight for participant’s willingness to participate in a future similar study as well as provide adolescent self-reported opinions and preferences to aid in future study design. A descriptive analysis of the responses to the questionnaire revealed that adolescents were generally satisfied with their involvement in the study and did not perceive the instrumentation to be too burdensome (Table 4.2; Table 4.3). In order to gain additional insights, responses to open-ended questions were analyzed using thematic analysis.
Table 4.2. *End of Study Survey; Dichotomous Responses (Yes/No)*

<table>
<thead>
<tr>
<th>Questions</th>
<th>Yes Responses n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Would you participate in another study that used a daily diary?</td>
<td>20 (100)</td>
</tr>
<tr>
<td>2. Did you have difficulty remembering to complete the diary on a daily basis?</td>
<td>4 (20)</td>
</tr>
<tr>
<td>3. Would you prefer the diary to be available for your entries on an app (smartphone, tablet, computer, etc.)?</td>
<td>15 (75)</td>
</tr>
<tr>
<td>4. You wore a wrist-worn device for a 7-day period in this study. Did you remove the device at any time?</td>
<td>16 (80)</td>
</tr>
<tr>
<td>4.2. If you removed the device, did you put it back on?</td>
<td>16 (80)</td>
</tr>
<tr>
<td>5. Would you be willing to participate in a study that asked you to wear the same device and maintain a diary for a longer period of time?</td>
<td>16 (80)</td>
</tr>
<tr>
<td>6: Would you be willing to wear a small device at your waist at the same time as wearing the wrist-worn device?</td>
<td>16 (80)</td>
</tr>
<tr>
<td>7. Would you be interested in receiving/viewing your sleep and activity information?</td>
<td>18 (90)</td>
</tr>
<tr>
<td>8. Would you be willing to participate in another study similar to this one in the future?</td>
<td>18 (90)</td>
</tr>
</tbody>
</table>

All participants (100%) stated they would participate in another study that used a daily diary. Only 20% (n=4) of adolescents stated they had trouble remembering to complete the diary on a daily basis. An open-ended question following this question asked: “If yes, what did you do to help you remember?” A thematic analysis of the responses indicated things that helped those who had trouble remembering to complete the diaries included: receiving text message reminders (n=2), parental reminders (n=1), and keeping the diary in sight (n=1). Seventy-five percent of participants (n=15) stated they would prefer the diaries to be available on an app (smartphone, tablet, computer, etc.). Eighty percent of participants (n=16) reported removing the device at some point over the 7-day period. For those who answered “yes” to removing the device, an
open-ended question asked: “If yes, in what situations did you remove the watch?” A thematic analysis of responses indicated of those who removed the watch, reasons for removing it included: grooming/bathing (n=9), needing a break from it being on their wrist (n=3), or removing it due to requirements (sports/gym) (n=3), and “because of a rash” (n=1).

When asked if they put the watch back on, 80% (n=16) said yes; 5% (n=1) said no, 15% (n=3) did not respond suggesting they did not take it off. An open-ended question asked: “What helped you to remember to put it back on?” A thematic analysis revealed the prompts that reminded them included: seeing it lying around (n=4), parental reminder (n=3), or that it “felt weird” because they got used to it being on their wrist (n=3), self-reminders (n=3), “nothing” (n=2), and “had a mark from it” (n=1).

Eighty-percent (n=16) stated they would be willing to participate in a study that asked them to wear the same device and maintain a diary for a longer period of time. Eighty percent (n=16) of participants stated they would be willing to wear a waist-accelerometer simultaneously with the wrist-worn watch. Ninety percent of participants (n=18) stated they would be interested in receiving sleep and activity information from the watch during research participation. An open-ended question asked why they would be interested in receiving this information. A thematic analysis of responses included the following reasons for wanting to receive this information and included: personal curiosity/interest (n=15), comparison to peers (n=1), to help to improve habits (n=1), and “don’t want one” (n=1). A few examples of responses include:

- “I would like to know because I want to know if I do as much physical activity as a average teen”
- “It would be interesting to know”
- “It would be interesting to see the data of my sleep”
• “So I know how much I slept”
• “Yes because all of these things can be beneficial for me and for doctors”
• “I would like to see my progress”
• “Because it would improve my habits”

Ninety percent of participants (n=18) stated they would be willing to participate in another study similar to this one in the future; 5% (n=1) stated they would not participate in another similar study and one response was eliminated from analysis due to the participant answering both “yes” and “no”.

Overall, adolescents who participated in the study were “very satisfied” (n=9; 45%), “somewhat satisfied” (n=10; 50%) or “very dissatisfied (n=1; 5%) with their involvement in the study (Table 4.3). No adolescents rated their involvement as “somewhat dissatisfied”.

Participants reported that it took them “less than 5 minutes” (n=7; 35%), “5-15 minutes” (n=12; 60%) and “15-30 minutes” (n=1; 5%) to complete their daily dairies (inclusive of both the physical activity diary and sleep diary). No participants claimed it took them more than 30 minutes. Eighty-five percent of participants (n=17) claimed that the frequency of study-provided daily text message reminders were “a good amount” (n=17; 85%), “too frequent” (n=1; 5%) and “not enough” (n=2; 10%). Participants reported that they would like to receive text reminders “twice per day” (n=4; 20%), “once per day” (n=15; 75%), or “every other day” (n=1; 5%), with no participants preferring the “every third day” option (0%). The study-provided daily text message reminders were sent at 8:00 P.M., Eastern Standard Time. Participants stated they would prefer to receive the text messages at: morning 6a-8a (n=3; 15%), late morning 9a-11a (n=0; 0%), afternoon 12p-3p (n=4; 20%), early evening 4p-6p (n=4; 20%), evening 7p-9p (n=8; 40%), or late evening 10p-midnight (n=0; 0%). Eighty-percent of participants (n=16) stated they
would be willing to be enrolled in a similar study for longer than one week. When queried about what an “acceptable amount of time” to be engaged in a similar study would be, adolescent participants reported 2 weeks (n=5; 25%), 3 weeks (n=4; 20%), 4 weeks (n=2; 10%), or >4 weeks (n=5; 25%).
Table 4.3. *End of Study Survey: Likert-scale Responses*

<table>
<thead>
<tr>
<th>Questions</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Overall, are you satisfied with your involvement in the study?</td>
<td></td>
</tr>
<tr>
<td>Very dissatisfied</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Somewhat dissatisfied</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Somewhat satisfied</td>
<td>10 (50)</td>
</tr>
<tr>
<td>Very satisfied</td>
<td>9 (45)</td>
</tr>
<tr>
<td>2. On days that you used the diary, how long do you estimate it took you</td>
<td></td>
</tr>
<tr>
<td>to complete the diary each day?</td>
<td></td>
</tr>
<tr>
<td>Less than 5 minutes</td>
<td>7 (35)</td>
</tr>
<tr>
<td>5-15 minutes</td>
<td>12 (60)</td>
</tr>
<tr>
<td>15-30 minutes</td>
<td>1 (5)</td>
</tr>
<tr>
<td>More than 30 minutes</td>
<td>0 (0)</td>
</tr>
<tr>
<td>3. You received a text message every evening to remind you to fill out</td>
<td></td>
</tr>
<tr>
<td>the diaries. Were these text messages: too frequent, a good amount,</td>
<td></td>
</tr>
<tr>
<td>not enough?</td>
<td></td>
</tr>
<tr>
<td>Too frequent</td>
<td>1 (5)</td>
</tr>
<tr>
<td>A good amount</td>
<td>17 (85)</td>
</tr>
<tr>
<td>Not enough</td>
<td>2 (10)</td>
</tr>
<tr>
<td>4. How often would you prefer to receive the text reminder?</td>
<td></td>
</tr>
<tr>
<td>Twice per day</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Once per day</td>
<td>15 (75)</td>
</tr>
<tr>
<td>Every other day</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Every third day</td>
<td>0 (0)</td>
</tr>
<tr>
<td>5. What time would you prefer to receive the text message?</td>
<td></td>
</tr>
<tr>
<td>Morning, 6a-8a</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Late morning, 9a-11a</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Afternoon, 12p-3p</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Early evening, 4p-6p</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Evening, 7p-9p</td>
<td>8 (40)</td>
</tr>
<tr>
<td>Late evening, 10p-midnight</td>
<td>0 (0)</td>
</tr>
<tr>
<td>6. If you are willing to participate for a longer period of time, how</td>
<td></td>
</tr>
<tr>
<td>long would you be willing to be involved in a similar study?</td>
<td></td>
</tr>
<tr>
<td>2 weeks</td>
<td>5 (25)</td>
</tr>
<tr>
<td>3 weeks</td>
<td>4 (20)</td>
</tr>
<tr>
<td>4 weeks</td>
<td>2 (10)</td>
</tr>
<tr>
<td>&gt;4 weeks</td>
<td>5 (25)</td>
</tr>
</tbody>
</table>
The last question of the survey was optional, asking respondents to provide any “positive or negative feedback”, stating their contributions would “help us plan future studies”. Participants provided valuable feedback. Some of the most meaningful responses with regard to the purpose of the question are shown below:

- “I didn’t mind the watch I forgot it was even there. I would of liked the smartphone app instead of the journal better so I could go back and erase if needed. I love that I am getting paid to do something so simple.”
- “I think the watch could be a bit more, like, pretty looking. I liked how the text message was sent and stuff to be reminded to fill out the diary.”
- “It was not that difficult. It did not bother me throughout the day.”
- “[t] really wasn’t that bad and if you think that people will judge you [for wearing the watch] they didn’t even notice till the last day.”
- “The watch wasn’t too annoying to wear, but it would be better without it.”
- “Make the watch smaller.”

**Executive Function**

**Aim 3: To explore executive function impairments as measured by the Global Executive Composite (i.e., overall summary score) and three subscales (i.e., Behavior Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index), within groups, compared to published normative data, and explore differences in executive function impairments between groups (obese adolescents with and without-OSAS).**

**Executive Function Score; Self- and Parent-Report**

Because an obese, without-OSAS group was not feasibly recruited/enrolled in the current study, group differences were not evaluated. For the obese, OSAS cohort (n=20), descriptive analysis included boxplots to visualize outliers and assess normality of BRIEF®2 score distribution (Figure 4.6).
Figure 4.6. BRIEF®2 Global Executive Composite and Summary Indexes Scores: Self-report and parent-report

Notes. GEC, Global Executive Composite; BRI, Behavior Rating Index; ERI, Emotion Regulation Index; CRI, Cognitive Regulation Index

There were no outliers observed; both self-report and parent-report scores were normally distributed, and means were consistently above the normative standardization sample mean ($M = 50$) (Table 4.4). The normative standardization sample for the BRIEF®2 consists of 3,603 total ratings matched by age, gender, ethnicity, and parent education level to the U.S. Census (Gioia et al., 2015). Clinical subscale scores (indices) and the Global Executive Composite (i.e., overall summary score) are reported as T-scores, with higher scores indicating more impairment. The
individual T-scores of the participants are summarized using mean (SD). The individual T-scores of the participants were compared to the categorized normative data, with T-scores < 60 considered normal, between 60-64 considered mildly elevated, 65-69 potentially clinically elevated, and 70 or above clinically elevated or clinically significant (Gioia et al., 2015). Descriptive statistics (mean [SD]) and frequencies for executive function impairment (i.e., BRIEF®2 T-score ≥ 60) were examined for self-report and parent-report measures for 4 different indices (Table 4.4).

**Table 4.4. Assessment of Executive Function Using the Behavior Rating Inventory of Executive Function, Second Edition (BRIEF®2)(n=20)**

<table>
<thead>
<tr>
<th>BRIEF®2 Indices</th>
<th>mean (SD)</th>
<th>n(%) ≥ 60-64</th>
<th>n(%) ≥ 65</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Self</td>
<td>Parent</td>
<td>Self</td>
</tr>
<tr>
<td>Global Executive Composite</td>
<td>58.2 (9.9)</td>
<td>57.8 (10.4)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Behavior Regulation Index</td>
<td>58.0 (11.2)</td>
<td>55.5 (12.0)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Emotion Regulation Index</td>
<td>56.8 (7.5)</td>
<td>59.0 (12.0)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Cognitive Regulation Index</td>
<td>58.0 (10.4)</td>
<td>57.0 (9.4)</td>
<td>1 (5)</td>
</tr>
</tbody>
</table>

*Notes.* a scores ≥ 60-64 are considered mildly elevated; b scores ≥ 65 are considered clinically elevated; Self = self-report; Parent = parent-report

Self-report mean scores were higher than parent-report mean scores for three of four BRIEF®2 indices (GEC, 58.2 v. 57.8; BRI, 58.0 v. 55.5; CRI, 58.0 v. 57.0, respectively). Parent-report mean scores were higher for the ERI than self-report mean scores (ERI, 59.0 v. 56.8, respectively). BRIEF®2 scores were examined as categorical variables (i.e., mildly elevated
Twenty percent of participants (n=4) had GEC scores meeting the mildly elevated criteria, 20% (n=4) on the BRI, 15% (n=3) on the ERI, and 5% (n=1) on the CRI. By parent report, 10% of participants (n=2) had GEC scores meeting the mildly elevated criteria, 5% (n=1) on the BRI, 5% (n=1) on the ERI, and 25% (n=5) on the CRI. When examining BRIEF®2 scores as categorical variables to assess for clinically elevated scores (i.e., score ≥ 65), 25% (n=5) of participants had GEC scores meeting the clinically elevated criteria, 30% (n=6) on the BRI, 15% (n=3) on the ERI, and 35% (n=7) on the CRI. By parent-report, 30% (n=6) of participants had GEC scores meeting the clinically elevated criteria, 30% (n=6) on the BRI, 35% (n=7) on the ERI, and 20% (n=4) on the CRI.

To test for statistically significant differences between self-report and parent-report mean scores for all BRIEF®2 indices, paired-sample t-tests were used. This test was chosen as the means were derived for a single group of subjects. Mean GEC scores for the self-report and parent-report had a moderate-strong correlation (r= 0.573, p=0.008). Mean GEC scores for self-report were, on average, 0.4 points higher (95% CI [-3.999, 4.799]) than parent-report scores; mean scores between self-report and parent-report were not significantly different (t_{19}=1.90, p=0.851). Self-report BRI scores were, on average, 2.55 points higher (95% CI [-1.927, 7.027]) than parent-report and had a moderate-strong correlation (r= 0.660, p=0.002); mean BRI self-report and parent-report scores were not significantly different (t_{19}=1.192, p= 0.248). Self-report ERI scores were, on average, 2.20 points lower (95% CI [-6.649, 2.249]) than parent-report; self-report and parent-report ERI scores had a moderate-strong correlation (r= 0.617, p=0.004) and were not significantly different (t_{19}=-1.035, p= 0.314). Self-report CRI scores were, on average, 1.00 point higher (95% CI [-3.770, 5.770]) than parent-report and had a moderate correlation (r= 0.60}
0.472, p=0.035); CRI scores, self-report and parent-report, were not significantly different (t_{19}=0.439, p= 0.666).

**Executive Function Compared To Normative Sample**

Participant data was compared to the normative published data (Gioia et al., 2015) using one-sample t-tests within-groups. The mean BRIEF®2 scores for all four indices of the self-report and three of four parent-report indices were significantly different than the standardization sample (self-report, all p ≤ 0.05; parent-report, BRI p = 0.056) (Table 4.5).

### Table 4.5. T-test Results Comparing Participant BRIEF®2 Scores to Normative Sample

<table>
<thead>
<tr>
<th>All (n=20), df=19</th>
<th>Mean difference</th>
<th>95% CI</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Self-Report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GEC</td>
<td>8.20</td>
<td>3.56, 12.84</td>
<td>3.697</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>BRI</td>
<td>8.00</td>
<td>2.78, 13.22</td>
<td>3.209</td>
<td><strong>0.005</strong></td>
</tr>
<tr>
<td>ERI</td>
<td>6.75</td>
<td>3.22, 10.28</td>
<td>4.001</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>CRI</td>
<td>7.95</td>
<td>3.08, 12.82</td>
<td>3.415</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td><strong>Parent-Report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GEC</td>
<td>7.80</td>
<td>2.93, 12.67</td>
<td>3.352</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>BRI</td>
<td>5.45</td>
<td>-0.16, 11.06</td>
<td>2.034</td>
<td>0.056</td>
</tr>
<tr>
<td>ERI</td>
<td>8.95</td>
<td>3.30, 14.60</td>
<td>3.314</td>
<td><strong>0.004</strong></td>
</tr>
<tr>
<td>CRI</td>
<td>6.95</td>
<td>2.57, 11.33</td>
<td>3.322</td>
<td><strong>0.004</strong></td>
</tr>
</tbody>
</table>

**Notes.** df, degrees of freedom; CI, confidence interval; GEC, Global Executive Composite; BRI, Behavior Rating Index; ERI, Emotion Regulation Index; CRI, Cognitive Regulation Index
The GEC (i.e., summary score) was prioritized as the primary outcome for comparing self-reported and parent-reported executive function to the standardized normative sample. Self-report mean GEC scores were higher than the standardized normative sample (58.2 v. 50.0; $SD$, 9.9 v. 10.0, respectively, $t = 3.697, p = 0.002$). Based on parent-report, mean GEC scores were higher than the standardized normative sample (57.8 v. 50.0; $SD$, 10.8 v. 10.0, respectively, $t = 3.352, p = 0.003$).

**Aim 4: To describe differences in activity levels (frequency, intensity, time) and sleep duration (major sleep bout total sleep time), measured by 1-week actigraphy (objective measure of rest/activity and sleep) and self-report, between obese adolescents with and without OSAS and explore the relationship between activity levels and sleep duration with executive function (Global Executive Composite scores).**

**Physical Activity and Sleep Duration**

Group differences between those with and without-OSAS were not evaluated in absence of obese, without-OSAS group.

**Frequency, Intensity, and Time Spent Engaging in Physical Activity**

Self-reported physical activity was descriptively analyzed among those with complete Previous Day Physical Activity Recall (PDPAR) (Weston et al., 1997) diary data (n=18). Intensity, frequency, and time of physical activity were measured and results reported herein.

**Intensity.** Intensity of activity was classified using the Compendium of Physical Activities (Ainsworth et al., 2011). All activities recorded on the PDPAR (Weston et al., 1997) diary by participants were assigned corresponding metabolic equivalent (MET) values based on the Compendium of Physical Activities (Ainsworth et al., 2011). These MET values were then categorized by intensity as follows: “low-light” (1- <2 METS), “high light” (2- <3 METS),
“moderate” (3-<6 METS), and “vigorous” (≥6 METS). Because national physical activity guidelines address a combined category of moderate and vigorous activity, the moderate and vigorous categories were also combined to account for all activity at ≥3 METS (Table 4.7).

Frequency. Activity frequency was defined as bouts, or number, of activity sessions in a one-week period. For the purposes of this study, frequency was defined as the number of days per week that the adolescent reported being active in a ≥3 MET-associated activity for at least 30 minutes; activity frequency was also examined as the number of days per week adolescents reported being active in a ≥3 MET-associated activity for at least 60 minutes. Participants with complete data (n=18) were largely inactive (Table 4.6). No adolescent participants met the national guidelines of performing ≥60 minutes of moderate-vigorous activity (i.e., ≥3 MET associated activity) on 7 days/week.

Table 4.6. Number of Days per Week Engaged In Moderate-Vigorous Activity for 30 or 60 Minutes (n=18)

<table>
<thead>
<tr>
<th># Days/Week with Moderate-Vigorous Activity</th>
<th>≥30 minutes (n[%])</th>
<th>≥60 minutes (n[%])</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Days</td>
<td>4 (22.2)</td>
<td>6 (33.3)</td>
</tr>
<tr>
<td>1 Day</td>
<td>2 (11.1)</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>2 Days</td>
<td>6 (33.3)</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td>3 Days</td>
<td>1 (5.6)</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>4 Days</td>
<td>2 (11.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>5 Days</td>
<td>2 (11.1)</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>6 Days</td>
<td>1 (5.6)</td>
<td>1 (5.6)</td>
</tr>
<tr>
<td>7 Days</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
Time. Time spent in various intensities of physical activities was calculated as minutes per day at each intensity level, as this provides more meaningful data than minutes per week when comparing to national recommendations which are expressed in minutes per day (e.g., 60 minutes/day of activity) (Physical Activity Guidelines for Americans, 2008). Due to the small sample size, descriptive analysis includes mean (SD) and median (IQR) (Table 4.7). The distributions of minutes per day spent in various intensities of physical activity were examined for outliers using boxplots (Figure 4.7).

<table>
<thead>
<tr>
<th>Physical Activity</th>
<th>mean (SD)</th>
<th>median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-light intensity activity per day (mins)</td>
<td>823.73 (113.65)</td>
<td>835.72 (108.57)</td>
</tr>
<tr>
<td>High-light intensity activity per day (mins)</td>
<td>48.62 (62.44)</td>
<td>30.86 (49.28)</td>
</tr>
<tr>
<td>Moderate intensity activity per day (mins)</td>
<td>44.05 (67.18)</td>
<td>23.57 (47.17)</td>
</tr>
<tr>
<td>Vigorous intensity activity per day (mins)</td>
<td>3.33 (10.14)</td>
<td>0.00 (1.07)</td>
</tr>
<tr>
<td>Moderate + vigorous activity per day (mins)</td>
<td>47.38 (67.28)</td>
<td>34.29 (56.78)</td>
</tr>
</tbody>
</table>

Notes. SD, standard deviation; IQR, interquartile range
Figure 4.7. Distribution of minutes per day spent in varying intensities of physical activity

Notes. PDPAR, Previous Day Physical Activity Recall; lowlt, low-light intensity activity; highlight, high-light intensity activity; mod, moderate intensity activity; vig, vigorous intensity activity; modvig, moderate to vigorous intensity activity
The outliers were then removed to determine if the data would become normally distributed (Figure 4.8).
Figure 4.8. Distribution of minutes per day spent in varying intensities of physical activity, outliers removed

Notes. PDPAR, Previous Day Physical Activity Recall; lowlt, low-light intensity activity; highlight, high-light intensity activity; mod, moderate intensity activity; vig, vigorous intensity activity; modvig, moderate to vigorous intensity activity
With outliers removed, the data still remained highly skewed and the number of data points were reduced at all intensity categories which prohibited descriptive tests for the vigorous activity category (boxplot indicated 4 outliers). Descriptive statistics for the data with outliers removed are shown in Table 4.8.

**Table 4.8. Minutes per Day Spent in Various Intensities of Physical Activity, Outliers Removed**

<table>
<thead>
<tr>
<th>Physical Activity</th>
<th>mean (SD)</th>
<th>median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-light intensity activity per day (mins), n=15</td>
<td>865.05 (66.48)</td>
<td>848.57 (94.29)</td>
</tr>
<tr>
<td>High-light intensity activity per day (mins), n=16</td>
<td>30.11 (26.85)</td>
<td>25.71 (41.78)</td>
</tr>
<tr>
<td>Moderate intensity activity per day (mins), n=16</td>
<td>24.91 (24.90)</td>
<td>19.29 (41.79)</td>
</tr>
<tr>
<td>Vigorous intensity activity per day (mins)*</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Moderate + vigorous activity per day (mins), n=17</td>
<td>33.53 (33.75)</td>
<td>25.71 (51.43)</td>
</tr>
</tbody>
</table>

*Notes. *Not enough data points, error when outliers removed; SD, standard deviation; IQR, interquartile range

When outliers were removed, average minutes per day were reduced in all intensities, with the exception of low-light intensity activity. With the exception of low-light intensity activity, these results indicate that few participants reported time spent in activity intensities other than the low-light intensity category, wherein the sample mean is located.

**Relationship between Moderate-Vigorous Physical Activity and Executive Function**

The relationship between physical activity and executive function was evaluated at the various physical activity intensities using Spearman’s rank correlation coefficient. Correlations were weak (all, $r_s \leq 0.284$) and non-significant (all, $p \geq 0.253$) (Table 4.9).
### Table 4.9. Relationship between Minutes per Day Spent in Various Intensities of Physical Activity and Executive Function As Measured By Self-Report GEC Scores

<table>
<thead>
<tr>
<th>Physical Activity</th>
<th>$r_s$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-light intensity activity per day (mins)</td>
<td>0.284</td>
<td>0.253</td>
</tr>
<tr>
<td>High-light intensity activity per day (mins)</td>
<td>0.109</td>
<td>0.668</td>
</tr>
<tr>
<td>Moderate intensity activity per day (mins)</td>
<td>-0.079</td>
<td>0.756</td>
</tr>
<tr>
<td>Vigorous intensity activity per day (mins)</td>
<td>-0.061</td>
<td>0.809</td>
</tr>
<tr>
<td>Moderate + vigorous activity per day (mins)</td>
<td>-0.097</td>
<td>0.703</td>
</tr>
</tbody>
</table>

Notes. $r_s$ = Spearman’s rank correlation; SD, standard deviation; IQR, interquartile range

The relationship between moderate-vigorous activity time and executive function (measure by self-report GEC score) was examined. Spearman’s rank correlation ($r_s = -0.097$, $p=0.703$) (Figure 4.9) was weak and not statistically significant.

![Figure 4.9. Relationship between moderate-vigorous physical activity and executive function](image)

**Notes.** GEC-T= Self-reported GEC T-score; PDPAR_modvig_perday= minutes spent in moderate-vigorous intensity activity per day.
**Average Total Sleep Time of Participants**

Group differences for total sleep time between those with and without-OSAS were not evaluated. One-week of complete data for wrist-worn actigraphy provided objective measures of total sleep time (n=15). For the purposes of this study, total sleep time is expressed as average minutes per night (i.e., major sleep bout), rather than total minutes per week due to national recommendations expressed as “per night”. A descriptive analysis, including mean (SD) and median (IQR) and boxplots were examined to assess for outliers and determine normality of the data (Figure 4.10).

The mean number of minutes slept per night was 408.31 (SD, 58.1) and median number of minutes was 412.21 (IQR, 59.29) (n=15). This translates to approximately 6.8 hours per night and 6.9 hours per night, respectively. The distribution of total sleep time is shown in Figure 4.10.

![Boxplot of total sleep time](image)

**Figure 4.10.** Distribution of total sleep time

**Notes.** TST_SUM_AVG= average number of minute spent sleeping per night across one week
The above noted outlier was removed and the descriptive analysis was repeated. The mean number of minutes slept per night was 419.87 (SD, 38.43) and median number of minutes was 412.39 (IQR, 59.08) (n=14). This translates to approximately 7 hours per night and 6.9 hours per night, respectively. The distribution of total sleep time is shown in Figure 4.11.

![Figure 4.11. Distribution of Total Sleep Time, outlier removed](image)

Notes. TST_SUM_AVG= average number of minute spent sleeping per night across one week

**Relationship between Total Sleep Time and Executive Function**

The relationship between total sleep time and executive function was evaluated using Spearman’s rank correlation coefficient. The correlation between total sleep time and executive function was weak and non-significant ($r_s = 0.002$, p=0.995) (Figure 4.12).
Figure 4.12. Relationship between total sleep time and executive function  

Notes. GEC-T = Self-reported GEC T-score; TST_SUM_AVG = average number of minutes/night spent sleeping (across one week)  

**National Recommendations for Physical Activity and Sleep**

Engagement in moderate-vigorous physical activity and sleep duration were examined relative to the recommendations set forth in the U.S. national recommendations (Hirshkowitz et al., 2015; Paruthi et al., 2016; *Physical Activity Guidelines for Americans*, 2008) (Figure 4.13). Nearly 27% of participants (n=4) had zero nights of sleep for at least eight hours; in other words, nearly 27% of participants slept less than eight hours per night on all days of data collection. Approximately 33% (n=5) slept ≥ 8 hours per night on one night per week, 33% (n=5) on two nights per week, and 6% (n=1) on three nights per week. No participants slept ≥ 8 hours per night on 4 or more nights per week.

Of those with complete PDPAR diary data (n=18), approximately 33% (n=6) of participants engaged in moderate-to-vigorous intensity activity for at least 60 minutes on zero
days per week; in other words, 33% of participants (n=6) did not engage in moderate-to-vigorous intensity activity for at least 60 minutes on any days of data collection. Approximately 11% (n=2) engaged in moderate-to-vigorous intensity activity for ≥ 60 minutes on one day per week, 27.8% (n=5) on two days per week, 11.1% (n=2) on 3 days per week, 0% (n=0) on 4 days per week, 11.1% (n=2) on 5 days per week, 5.6% (n=1) on 6 days per week, and 0% (0) on 7 days per week.

Figure 4.13. Total sleep time and moderate-vigorous physical activity by national recommendation thresholds

Notes. aTST, n=15; Mod+Vig activity, n=18; TST, total sleep time
As evidence of the short sleep duration observed in this group of participants, an exploratory analysis aimed to determine the number of nights per week adolescents were sleeping less than seven hours per night, as this threshold is known to contribute to a multitude of issues, as explained in Chapter 2. Of the 15 participants with complete sleep data, 6.7% (n=1) slept less than 7 hours per night on 7 nights per week, 26.7% (n=4) on 6 nights per week, 13.3% (n=2) on 5 nights per week, 13.3% (n=2) 4 nights per week, 26.7% (n=4) on 3 nights per week, 6.7% (n=1) on 2 nights per week, 13.3 (n=2) on one night per week, and 6.7% (n=1) on 0 nights per week.
Chapter 5

Conclusions

Significance

The purpose of this feasibility study was to acquire methodological and protocol insights for a subsequent larger study that will be fully-powered to assess executive function in adolescents with obesity and OSAS and examine the effects of sleep duration and physical activity on executive function. This feasibility study employed a one-week protocol inclusive of objective sleep duration and self-reported physical activity followed by executive function outcomes; a secondary purpose of the feasibility study was to describe and explore the relationship of sleep duration and physical activity in this high risk target population.

Adolescents with obesity and OSAS are at exceedingly high risk for negative health consequences inclusive of increased morbidity and mortality (Olshansky et al., 2005; Reilly & Kelly, 2011). Among the plethora of deleterious physical health outcomes, global cognition is also seriously impacted by obesity and OSAS (Beebe & Gozal, 2002; Reinert et al., 2013; Smith et al., 2011); a component of global cognition specifically addressed in the current study, executive function, provides an important foundation for learning and adaptation in multiple contexts. Executive function plays an important role when it comes to attention-regulation skills and problem solving in the context of goal-directed behavior. Because executive function has less to do with intellectual knowledge and is more relevant to how knowledge is purposefully used and practiced, executive function is an important focal point for interventions that address decision making. This is especially important as such decision making plays an important role in health maintenance behaviors, for example, CPAP use or weight loss. If this high-risk target population of adolescents with obesity and OSAS do in fact exhibit executive dysfunction,
application of the educational components of treatment and/or health maintenance behaviors related to any given treatment may need to be adapted. Further, this study contributes to the scant literature addressing sleep durations and physical activity engagement in obese adolescents with OSAS.

**Summary of Findings**

To gain methodological and protocol insights for a future study to assess executive function and potential mediators such as sleep duration and physical activity, the following aims were addressed:

- **Aim 1:** To determine the feasibility of recruiting and retaining a sample of obese adolescents (11-17 years of age) with and without-OSAS.

- **Aim 2:** To pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation.

- **Aim 3:** To explore executive function impairments as measured by the Global Executive Composite (i.e., overall summary score) and three subscales (i.e., Behavior Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index), within groups, compared to published normative data, and explore differences in executive function impairments between groups (obese adolescents with and without-OSAS).

- **Aim 4:** To describe differences in activity levels (frequency, intensity, time) and sleep duration (major sleep bout total sleep time), measured by 1-week actigraphy (objective measure of rest/activity and sleep) and self-report, between obese adolescents with and without OSAS and explore the relationship between activity levels and sleep duration with executive function (Global Executive Composite scores).
The major findings resulting from this study are presented by aim:

- **Aim 1:**
  
  - Face-to-face recruitment techniques were more successful than mailed invitation letters; almost all adolescents who were approached on night of PSG agreed to enroll in the study.
  
  - Once participants enrolled in the study, almost all completed the protocol.
  
  - Identifying and enrolling obese adolescents without-OSAS was not feasible with the study recruitment methods employed.
  
  - Many adolescents scheduled for overnight PSG’s have a preexisting ADD or ADHD diagnosis.

- **Aim 2:**
  
  - Complete data rates were higher for the paper diaries than the wrist worn actigraphy.
  
  - Adolescents were willing to participate in future similar studies, indicating that they did not perceive participation in a 1-week protocol as too burdensome despite having to complete daily study-associated tasks.
  
  - Valuable insights for future study protocol design were gained from the end of study survey. Insights include:
    
    - Adolescents expressed interest in reviewing their sleep and activity information
    
    - Text message reminders were helpful
    
    - High tolerability of paper instrumentation
    
    - “Better looking” devices were valued/desired
Aim 3:
- Adolescents with obesity and OSAS had impaired executive function at clinically significant levels.
- Though there are not statistically significant differences between self-reported and parent-reported executive function, clinically meaningful differences were identified.
- Adolescents with obesity and OSAS had significantly worse executive function than a normative sample.

Aim 4:
- Participants did not meet the national recommended guidelines for sleep duration or physical activity.
- Sleep duration or time spent in moderate-to-vigorous intensity activity did not have an influence on executive function.

Discussion

Aim 1: To determine the feasibility of recruiting and retaining a sample of obese adolescents (11-17 years of age) with and without-OSAS.

Little research is published on the combined effects of obesity and OSAS in adolescents; therefore, it is essential to determine the feasibility of conducting research with this target population. Overall, the study recruitment and enrollment plan was successful, with more favorable responses for research participation when face-to-face recruitment techniques were used than when mailed invitation letters were used. This suggests that researchers can potentially enrich enrollment by interfacing with adolescents at the point of care. This also requires that
researchers garner access to clinical research sites and establish partnerships with clinical stakeholders to support face-to-face recruitment.

Invited adolescents were interested in participating in the research and if fully eligible, almost all consented participants completed the protocol. This brought forth an interesting dynamic while recruiting and enrolling adolescents for research. Enrollment and retention was a concern at the study outset, as there is a need for interest from the adolescent as well as approval to participate from the parent/legal guardian for both legal and personal reasons. Adolescents who chose to enroll in this one-week study were required to return for a second research visit. Further, they needed to coordinate transportation with their guardian for either one (if enrolled on night of PSG) or two visits (if recruited using mailed invitation letter). Face-to-face recruitment enrollment rates may have been higher than invitation letters for this very reason, as adolescents and their guardian(s) were already present at the sleep center and able to complete research visit 1. Those who received mailed invitation letters may have perceived greater burden for participation in that they would need to make two separate visits (i.e., requiring more travel) if they did not have an upcoming clinic visit scheduled. A prior study that used web-based recruitment to acquire a sample of adolescent-parent dyads also identified difficulty in initial study enrollment (response rate, 29.4%; enrollment of 38.7%; Oh et al., 2017). Future research studies should aim to coordinate research visits with clinical care to avoid excessive participant burden, such as transportation, by considering different ways to design a protocol that allows for rigorous data collection procedure and protocol while minimizing participant burden.

An obese, without-OSAS adolescent group was intended in the current study in order to examine differences in executive function outcomes. Low feasibility for including such participants in the current study was identified. It is possible that almost all obese adolescents
that underwent an overnight PSG had an increased likelihood for OSAS due to seeking care for OSAS symptoms, or, due to a referral by another clinician for symptoms suggestive of OSAS. There was hope that recruiting from outside of a sleep lab (i.e., weight clinic) would increase the likelihood of recruiting adolescents without-OSAS; however, many weight clinic patients did not have prior PSG to confirm or exclude OSAS. It is therefore likely that different recruitment approaches are necessary to identify and enroll an obese, without-OSAS adolescent group.

The extant literature has supported community-based recruitment for obese, without-OSAS samples (Xanthopoulos et al., 2015). Though community-based recruitment may be advantageous, such approaches do not come without complexities. There are important and costly considerations with community-based recruitment, such that it would necessitate funding for research PSG’s or acquisition of home sleep testing equipment to rule out OSAS. Though screening questionnaires for OSAS are available for employ in child/adolescent populations, for example the OSA-18 (Franco, Rosenfeld, & Rao, 2000), teen STOP-Bang (Combs, Goodwin, Quan, Morgan, & Parthasarathy, 2015), and the Pediatric Sleep Questionnaire (Chervin, Hedger, Dillon, & Pituch, 2000), the accuracy (i.e., sensitivity/specificity) of such questionnaires is not adequate to ensure group criterion for non-OSAS is met. Definitive conclusions about the combined effects of OSAS and obesity on executive function outcomes require two definitive groups of adolescents (i.e., with and without-OSAS). Therefore, rigorous studies will necessitate extramural or intramural funding to support research PSG’s or home sleep testing to confirm the absence/presence of OSAS.

Another barrier between recruitment and enrollment was the strict, but necessary, exclusion criteria employed in the study. Many adolescents were ineligible to participate due to attention/behavioral diagnoses such as ADD, ADHD, ODD, or OCD. There is a strong
association between these behavioral disorders and impaired executive function (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006; Long, Hill, Luna, Verhulst, & Clark, 2015; Pietrrefesa & Evans, 2007; Snyder, Kaiser, Warren, & Heller, 2015; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005) and therefore, this study established exclusion criteria for attention/behavioral diagnoses. As this pilot study intends to support designing a subsequent study wherein the combined effect of OSAS and obesity on executive function will be examined, it was methodologically prudent to maintain strict exclusion criteria for confounding factors. This is, however, a difficult issue to navigate, as those with an attention/behavioral disorder are also likely to have OSAS (Hvolby, 2015) and/or obesity (Cortese & Tessari, 2017). In a recent published review, up to 95% of OSAS patients have attentional deficits, and of those with ADHD, approximately 20-30% have OSAS (Youssef, Ege, Angly, Strauss, & Marx, 2011). Further, the symptoms associated with OSAS can closely mimic those of ADHD (Blesch & Breese McCoy, 2016); for this reason, it has been suggested that sleep disorders should be ruled out prior to establishing a diagnosis, or beginning treatment, of ADHD (Hvolby, 2015). As these diagnoses are common in OSAS and obese adolescent populations, future studies may consider statistically controlling for the confounding effects of ADD/ADHD on executive function rather than establishing ADD/ADHD exclusion criteria. Sample size is, however, an important consideration when planning such analysis.

**Aim2:** To pilot test a protocol that incorporates a 1-week measurement period for physical activity and sleep to assess for complete data rates and participant acceptability of instrumentation.

This study had one-week, continuous measures (i.e., sleep diary and physical activity diary) as part of the protocol. Measures that require multiple days of data collection can increase
the risk for protocol non-compliance and missing or incomplete data, as the responsibility for data collection is shifted to the research participant to provide daily input (Fraley & Hudson, 2014). In an attempt to minimize these issues, daily text message reminders were sent to research participants in this study. This text-reminder approach was also successful in a one-year, longitudinal study requiring data collection at 6-months and 12-months with overwhelmingly positive retention rates (87-91%) (Davis, Demby, Jenner, Gregory, & Broussard, 2016). In the current study, participants indicated in response to the end of study survey that they valued daily text message reminders for diary completion. Future studies that incorporate a longitudinal data collection period, therefore, should use some type of text message reminder to cue participants for diary completion. In addition, shared insights from the current study participants suggest keeping the dairy somewhere “in sight” and asking the parent/guardian to follow-up with the adolescent participant regarding completion of the diaries are protocol opportunities to directly support compliance and data completion rates.

Complete data for wrist-worn actigraphy was plagued by instances of both device error and non-wear. According to Acebo, et al. (1999), up to 28% of one-week actigraphy data may be deemed incomplete due to illness, non-adherence, and/or device failure (Acebo et al., 1999). A review of studies using actigraphy in children (ages 2-18 years) found that the mean attrition rate was 11.5% (SD 10.1%), mean non-compliance rates were 22.7% (SD 16.4%) at baseline and 29.6% (SD 19.4%) at follow-up, and mean total study data missingness was 37.4% (Howie & Straker, 2016). The authors of this study claim that missingness is common in studies that use actigraphy in children and that researchers must plan for high levels of missingness when considering study design (Howie & Straker, 2016). Another study determined the more involved (i.e., complex) a protocol was, the risk/likelihood for less complete data was higher; in a study
using surveys and actigraphy, 85.6% in the survey-only group completed all four surveys compared to only 58.7% of those who were in the survey and actigraphy group (Oh et al., 2017). In addition to non-compliance with wearing the device, incomplete data or data loss can result from a lack of diary data necessary to identify artifact and or onset/offset of sleep (Acebo et al., 1999), when automated scoring may need overridden. Based on participant feedback, adolescents may benefit from being instructed to keep the device somewhere “in sight” when removing the device for hygiene or other reasons, asking parents to check on their adolescent’s wear of the device, and also informing participants that they may gradually get used to the feeling of having the device on their wrist.

Participants provided feedback on end of study surveys that they would prefer “better looking” devices. Given this feedback, it is possible that some non-wear periods may have been contributed to the fear of judgment by peers with having to wear the device during school hours, as social influences are predominant in the adolescent stage (American Psychological Association, 2002). Commercially available activity and sleep monitoring devices would draw less attention as such devices are commonplace in today’s environment; however, little is known about the accuracy of these devices. Validation studies of commercial devices that reportedly measure sleep and physical activity have recently gained the attention of researchers (Evenson, Goto, & Furberg, 2015; Ferguson, Rowlands, Olds, & Maher, 2015). One study examined nine research and commercial grade wearable devices for a 24-hour period; error rates among all devices ranged from 8.1–16.9% for sleep, 9.5–65.8% for sedentary behavior, 19.7–28.0% for light physical activity, 51.8–92% for moderate-to-vigorous physical activity, and 14.1–29.9% for steps (Rosenberger et al., 2016). Due to the novelty of research examining commercial grade devices, they were deemed not appropriate for use in a dissertation research study.
As this was a feasibility study, designed to provide insights for future study design, an end of study survey was constructed to evoke participant insights on the current study’s protocol, instrumentation, and gain participant feedback and suggestions to guide future decision making. Overall, participants were generally satisfied with their involvement in the current study and did not perceive it to be too burdensome. Participants stated they would be willing to enroll in future studies similar to this one, even if the protocol was longer in duration than one week. Longer data collection periods could contribute to a greater number of data collection points for more robust insights to adolescents’ typical sleep and physical activity; however, there is the accompanying risk of more incomplete data and missingness with a longer protocol period. Concerns that should be taken into consideration include: increased risks for incomplete data due to limited battery life of devices influenced by epoch settings (i.e., shorter epochs requiring more frequent data collection and limit battery life), risk of data loss due to device failure, and participant burnout/disinterest.

Adolescents claimed curiosity/interest in reviewing their sleep and physical activity output. As adolescents are developing more autonomy during this stage of life (American Psychological Association, 2002), their input and opinions should be considered in health-related decision making (Hein et al., 2015; Patton et al., 2016). Results of this study may suggest that adolescents are increasingly interested in self-management strategies. The development of self-management skills are critical to the health and well-being of the adolescent population as parental supervision is lower than in younger children; this is notably evident based on decreased parental supervision of bedtimes (Meijer, Reitz, & Dekovic, 2016; National Sleep Foundation, 2014). However, self-management in this population is also prone to additional obstacles, as parental lifestyle (i.e., diet and exercise) is influential on adolescent sleep and activity habits.
Some adolescents may be more disadvantaged due to inequality in the built environment, as low socioeconomic neighborhoods can confer safety risks for adolescents spending time outdoors, where opportunities for light exposure that influences sleep onset/offset and for physical activity occur (Ding et al., 2011; Ferdinand et al., 2012; Gordon-Larsen et al., 2006). Further, self-management skills may be compromised by short sleep durations experienced by this population, as those with insufficient sleep are more likely to have increases in high-calorie snacking and general food intake (Brondel et al., 2010; Chaput, 2016). Regardless, this study suggests that adolescents are potentially interested in self-management strategies and should be provided with opportunities to exercise self-management skills, even in the context of a research protocol.

**Aim 3:** To explore executive function impairments as measured by the Global Executive Composite (i.e., overall summary score) and three subscales (i.e., Behavior Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index), within groups, compared to published normative data, and explore differences in executive function impairments between groups (obese adolescents with and without-OSAS).

The association between pediatric sleep disordered breathing and executive function is significant (Mietchen, Bennett, Huff, Hedges, & Gale, 2016). In this study, obese adolescents with OSAS had significantly worse executive function, by both self-report and parent report, compared to a normative sample. The prevalence of clinically significant levels of executive dysfunction in this obese, OSAS sample are consistent with a prior study that used an earlier version of the same instrument to measure executive function; obese adolescents with OSAS had significantly worse executive function compared to both obese (p < 0.001) and lean (p< 0.001) controls (Xanthopoulou et al., 2015).
According to the clinical scoring criteria set by the BRIEF®2 guidelines (Gioia et al., 2015), up to 35% of the study participants had mild to clinically significant impairments across the indices for executive function. Based on the Global Executive Composite (GEC) (i.e., overall summary score), 20% of participants had scores considered to be mildly elevated based on self-report and 10% based on parent-report (i.e., GEC scores 60-64). Based on the score threshold for clinically abnormal scores (i.e., t-scores ≥ 65), 25% of participants (self-report) scored in the clinically abnormal range and 30% of participants (parent-report) scored in the clinically abnormal range. These findings are consistent with prior findings (Xanthopoulos et al., 2015). Xanthopoulos and colleagues (2015) found that 22.3% of obese OSAS adolescents had impaired executive function in the clinically abnormal range, based on parent-report, compared to 0% of the obese, non-OSAS group.

One new study examining the relationship between sleep disordered breathing and executive function has been published since the systematic review was conducted for this dissertation. Though this study does not meet the inclusion criteria of the systematic review, the study does provide some additional evidence for the association of weight status, potential presence of sleep disordered breathing, and executive function. In this recently published study, 37 overweight (i.e., ≥85th percentile) or obese (i.e., ≥95th percentile) adolescents (ages 12 to 17 years) and their caregivers completed the BRIEF (Gioia et al., 2000) (Mietchen et al., 2016). Presence of sleep disordered breathing was determined by the Pediatric Sleep Questionnaire (Chervin et al., 2000) and not PSG. There were significant correlations between sleep disordered breathing and executive function (r=0.75, p < 0.001) and significant differences observed between adolescents classified as at risk or not at risk for sleep disordered breathing based on BRIEF parent report (F (1, 35)= 3.73, p <0.01) but no significant differences based on self report
(F (1, 35)= 1.24, p > 0.05) (Mietchen et al., 2016). This study also showed that, based on parent report, 77.3% of the sample at high risk for sleep disordered breathing had scores in the clinically significant range compared to 27.8% of the minimal risk group (Mietchen et al., 2016). Similarly, a study that also assessed for potential presence of sleep disordered breathing using the Pediatric Sleep Questionnaire found that higher scores were associated with significantly worse executive function based on BRIEF parent and self-report (r= 0.49, p<0.01; r= 0.45, p <0.01, respectively; Lande et al., 2015).

It is important to note that while there were no statistically significant differences between self-report and parent-report mean t-scores in the current study, there were clinically significant differences. For example, based on the cut-point t-score of 65, the threshold considered clinically elevated/impaired, 25% of participants’ self-report scores were categorized as clinically abnormal whereas this prevalence was 30% based on parent-report. It should be noted that these differences are expected, as parent-report t-scores are typically higher on the GEC than self-report (Gioia et al., 2015). The self-report form was added after the development of the BRIEF parent and teacher report forms (Gioia et al., 2000) and the three were offered in the BRIEF® 2 (Gioia et al., 2015). The self-report form was designed to gain self-perspectives of the adolescent, providing a more comprehensive set of responses, as it can be compared to the parent and teacher forms (Gioia et al., 2015). The authors state that differences between raters may vary based on perspectives, and rather than viewing one set of ratings as correct, the differences can be informative and meaningful (Gioia et al., 2015). In extreme cases of disagreement between self-and parent-report scores, adolescents may display poor self-awareness, parents may have excessively negative views of the adolescent, stress may exist in
the parent-adolescent relationship, or there may be an oppositional stance on adolescents behalf (Gioia et al., 2015).

According to the systematic review conducted as part of this dissertation, there are mixed results for executive function impairments in those with obesity and OSAS; two studies support statistically significant differences between obese-OSAS subjects and controls (McNally et al., 2012; Xanthopoulos et al., 2015) while two other studies indicate no statistically significant differences between groups (Hannon et al., 2012; Tan et al., 2014). Because of the small sample sizes, a relatively limited set of cumulative evidence, varied instruments used to measure executive function, and inconsistent findings, it is difficult to draw definitive conclusions about the relationship between obesity and OSAS as it relates to executive function. Though this study failed to enroll obese adolescents without-OSAS (i.e., comparisons between those with and without-OSAS could not be established), the results do contribute to the relatively scant literature addressing the presence of executive function impairments in obese adolescents with OSAS.

**Aim 4: To describe differences in activity levels (frequency, intensity, time) and sleep duration (major sleep bout total sleep time), measured by 1-week actigraphy (objective measure of rest/activity and sleep) and self-report, between obese adolescents with and without OSAS and explore the relationship between activity levels and sleep duration with executive function (Global Executive Composite scores).**

Consistent with the published literature on physical activity and sleep duration in adolescents, study participants of the current study did not meet the national recommended guidelines for physical activity or sleep duration (Centers for Disease Control and Prevention, 2013; National Sleep Foundation, 2014). Many adolescents had restricted sleep, a prominent issue that is similarly portrayed in the extant literature (National Sleep Foundation, 2014);
restricted sleep places adolescents at high risk for negative health consequences (Becker et al., 2015; Hirshkowitz et al., 2015; Paruthi et al., 2016). Study participants achieved approximately 6.87 hours of sleep per night. In a 2014 U.S. poll, over half of 15-17 year olds report sleeping 7 hours or less per night (National Sleep Foundation, 2014). Further, it is likely that the curtailed sleep time experienced by participants in this study is a result of the various biological and psychosocial factors influencing adolescent sleep (Carskadon, 1993; Carskadon & Acebo, 2002; Crowley et al., 2014; Hale & Guan, 2015; Rofey et al., 2013), and not influenced by the presence of pediatric OSAS, as cortical arousals do not occur in response to obstructive apneas and result in sleep fragmentation as in adult OSAS (Goh et al., 2000). Restricted and inadequate sleep has detrimental health consequences such as mental and emotional dysfunction, including engaging in risky behaviors and reduced school performance (Lovato & Gradisar, 2014), and physical health consequences such as obesity (Fatima et al., 2015; Grandner et al., 2015; Meldrum & Restivo, 2014; Owens, 2014). Short sleep durations can increase or sustain obesity in adolescents (Padez et al., 2009; Taveras, Rifas-Shiman, Oken, Gunderson, & Gillman, 2008). As thoroughly discussed in chapters 1 and 2, curtailed sleep can also affect executive function. Previous studies have shown significant relationships between sleep and executive function in adolescents (Andersen et al., 2016). The current study does not confirm such findings, likely related to the small sample size and relatively homogenous sleep duration data.

Adolescents are especially vulnerable to sleep deprivation due to developmental changes in intrinsic sleep mechanisms, such as delayed circadian phases and psychosocial changes including social jet lag (Carskadon, 2008; Gradisar et al., 2011). It is also difficult to implement interventions aimed at increasing total sleep time in adolescents as many responsibilities may take precedence over sleep, such as after school activities, homework, jobs, socialization, etc.
Though difficult, it is vital to attempt to increase sleep time in this at risk population, especially as adolescents with obesity are at higher risk for shorter sleep durations than lean counterparts (Chaput, 2016; Moraleda-Cibrian & O'Brien, 2014a). Some schools have begun to recognize the importance of adequate sleep and delayed circadian phases experienced by adolescents, and have started to implement later start times to account for this (Minges & Redeker, 2016; Wolfson & Johnson, 2014; "Zzz's to A’s Resolution," 2009); implementation of such changes are yet limited (Barnes et al., 2016). Parental monitoring of bedtimes tend to increase total sleep time (National Sleep Foundation, 2014), however, there’s also potential that this may lead to more time in bed but also worse sleep quality due to longer sleep-onset latency (Brand, Hatzinger, Beck, & Holsboer-Trachsler, 2009). If consistent bedtimes become habitual, there is high potential for better sleep quality over time (Meijer et al., 2016). Though policy changes and interventions at the individual level have provided necessary first steps to promote sleep duration in adolescents, further self-management interventions and policy work must be prioritized.

Engagement in 60 minutes of moderate-to-vigorous activity is extremely low in obese and OSAS populations (Spruyt et al., 2010). The Youth Behavioral Risk Factor Survey indicates only 27% of high school students meet national recommendations (Centers for Disease Control and Prevention, 2013), despite the profound known health benefits (Warburton & Bredin, 2016). In this study, over a one-week period, only 27.8% of participants engaged in moderate-to-vigorous physical activity for at least 30 minutes on at least three days. Even fewer (16.9%) participated in 60 minutes per day for at least three days. These findings are relatively consistent with the 2014 U.S. Report Card on Physical Activity for Children and Youth, which found that approximately one-quarter of children and adolescents (ages 6 to 15 years) were at least moderately active for
60 min/day on at least 5 days per week (Dentro et al., 2014). In a global assessment of physical activity in adolescents, 80.3% of 13-15 year olds engaged in fewer than 60 minutes of moderate to vigorous intensity activity per day (Hallal et al., 2012). Further, overweight or obese youth also tend to over-report physical activity (McMurray et al., 2008). If this is true, the already limited duration of time (minutes) spent engaged in moderate-to-vigorous activity in the current study sample may be overestimated.

This study was not sufficiently powered to detect statistically significant relationships between moderate-to-vigorous activity, and separately, sleep duration, with executive function. No significant relationships emerged between moderate-to-vigorous physical activity, sleep duration, and executive function. Alternatively, it is possible that a relationship between activity levels and executive function does not exist, as a review of five studies failed to find a significant effect (d=0.14) of chronic exercise on executive function, though this was attributed to by the limited set of evidence (Verburgh et al., 2014). However, a meta-analysis of 19 studies examining the effects of acute exercise on executive function identified a moderate effect size (d=.52) and this relationship did not vary by age (Verburgh et al., 2014). Similarly, there is evidence of aerobic exercise interventions improving executive function within-subjects (Best, 2010; Davis et al., 2011; Hillman, Buck, Themanson, Pontifex, & Castelli, 2009). As the evidence to date is inconsistent, larger studies that prioritize this issue are needed.

Despite the strong link between obesity and OSAS, treatment remains problematic. CPAP compliance is poor in adolescents (Andersen et al., 2016; Sawyer et al., 2011; Simon et al., 2012) and there are high rates of persistent OSAS post-surgery in obese adolescents (Andersen et al., 2016; Z. Li et al., 2016; Tagaya et al., 2012). Lifestyle interventions such as weight loss have shown to be beneficial for OSAS (Marcus, Brooks, et al., 2012) but the sole effectiveness of this
approach has been somewhat limited (Alonso-Fernandez et al., 2006). Because increased physical activity and adequate sleep duration tend to have a protective effect on executive function (Andersen et al., 2016; Davis et al., 2011), these potential intervention opportunities should be explored. This may be of particular importance in an obese, OSAS population, who may be at even higher risk for impaired executive function in addition to other serious physical health consequences.

**Limitations**

There are a few study limitations that should be considered. First, an obese, without-OSAS group could not be feasibly recruited; therefore, analyses to compare the two groups could not be completed as originally proposed. This limitation significantly impacts the overall scientific validity of the study findings as some research questions could not be answered; yet, the decision to forgo persistent recruitment efforts of a non-OSAS, obese adolescent group was pragmatically necessary for study completion. Another limitation is the small sample size of the current study that precludes any generalizability of the study findings; however, this study was designed, intentionally, to address feasibility aims, not to detect statistical significance. The Previous Day Physical Activity Recall (PDPAR) instrument only provides activity data in 30-minute blocks which potentially under-estimates actual time spent engaged in a specific activity; this is particularly true when METs are a reported outcome metric as METs are based on time and the specific physical activity. Ideally, a concurrent objective measure of physical activity, such as waist accelerometry, would have been employed in the protocol to limit risks of under-estimating physical activity and derived METs outcomes. Because this was a pilot study with limited funding, objective measurement of physical activity by accelerometers was not feasible. Additionally, the PDPAR instrument allowed respondents to select “school” as an activity; this
activity characterization does not differentiate between public school, home school, or cyber school, which are likely to vary daily schedules with regard to “free-time” and energy expenditure. For example, a participant involved in cyber school may expend less energy than a participant who attends school in-person, as cyber school may involve more screen time (associated with lower energy expenditure) than walking between classes and taking stairs (Ainsworth et al., 2011). For the purposes of this study, this limitation likely did not affect the results, as MET values associated with both school types would be categorized as “low-light intensity” category. Similarly, “shopping” was listed as an activity on the diary. It is possible for “shopping” to be misinterpreted as online shopping, which has a lower MET value than walking through stores and carrying bags. Future researchers using this instrument should take these response categories into consideration and potentially adapt it to account for modern day activities that may be different than the instrument-designated activities. Lastly, it should be noted that part of the recruitment and enrollment took place over a holiday season, when adolescents’ schedules may not be representative of “typical” routine, including both sleep duration and physical activity.

**Implications**

Because this was a feasibility study, the majority of implications stemming from the results of this study are research-based. No policy implications can be proposed, and practice implications are minimal. Recent results from a 35 year follow-up of participants of the Bogalusa Heart Study found that being overweight or obese for 1 year, up to >8 years during childhood increased the risk of OSAS, defined by Berlin Questionnaire scores, by 0.96 to 1.52 times compared to those who were never overweight (Bazzano et al., 2016). One practice implication that can be highlighted from the current study is for providers to have an awareness of the high-
rates of OSAS observed in adolescents with obesity. Providers who care for adolescents who are overweight or obese should assess for OSAS symptoms and provide referrals for sleep evaluation for adolescents.

The majority of the implications derived from the results are research-based. Perhaps one of the most profound findings, contributing to an inability to meet portions of the proposed aims, is the necessity to employ community-based recruitment techniques in order to enroll obese adolescents without-OSAS. Of participants enrolled in the study, only three had OSAS excluded by PSG. This is potentially due to the presence of OSAS symptoms experienced by adolescents who are being referred to a sleep clinic, therefore, increasing the likelihood of a positive diagnosis. Suggested recruitment techniques that stem from the results of the current study include using recruitment flyers placed in public places frequented by adolescents, approaching local school districts to inquire about research collaboration and/or approval for study advertising, and social media advertisements. With the well-recognized profound use of technology and social media among adolescents (Yonker, Zan, Scirica, Jethwani, & Kinane, 2015), there are new opportunities to reach adolescent communities through advertisements on social media platforms such as Facebook (www.facebook.com) or Instagram (www.instagram.com). As technology has been successfully used to observe behavior, communicate health information, and recruit for research in the adolescent population (Yonker et al., 2015), technological approaches provide opportunity for not only recruitment, but also intervention and education.

As is evident from the complete data rates for this study, paper diary instruments were not problematic. In fact, complete data rates for the diaries were higher than wrist-worn actigraphy. Based on both the complete data rates and end of study survey responses,
participants did not perceive daily diaries to be burdensome. This is an important finding as actigraphy measures must be accompanied by some type of daily, concurrent log/diary to guide data scoring. With these findings, a future larger study can be confidently designed to include similar measures.

Based on participants’ willingness to engage in a study with a longer data collection period, a two to four week data collection period may be considered in future studies. This consideration must be cautiously approached though, as a longer data collection period may pose risks for higher incomplete data rates. Incomplete data risks must be cautiously considered in any study using actigraphy as a measure of sleep and/or physical activity. Specifically, the limited battery life of these devices influences epoch settings (i.e., shorter epochs require more frequent data sampling and thereby limit battery life) and therefore valid scoring procedures (Meltzer, Montgomery-Downs, et al., 2012); there is also risk of data loss due to device failure with longer data collection intervals. For these reasons, researchers should first consider what is the most rigorous data collection protocol based on the research questions being answered and should also take epoch settings and battery life into consideration when making decisions regarding device selection.

The end of study survey was designed for this feasibility study with the goal of gaining adolescent feedback to provide valuable insights for planning a future study. Research implications derived from the results of the end of study survey suggest that daily text message reminders are preferred by adolescents and a single daily reminder is sufficient to support complete data for daily diaries. Additionally, adolescents prefer electronic diaries to be available on an app (smartphone, computer, tablet, etc.). An electronic diary combined with an automated
alert/notification to complete diaries, may be valued by adolescents and should be considered in future studies.

Lastly, executive function was measured in this study. Researchers should consider whether a performance-based or rating scale-based measure of executive function is appropriate for their study. Because this feasibility study aimed to detect a more ecological assessment of executive function, based on every day, real-world aspects of executive function, a rating scale-based measure was chosen. Additionally, this instrument allowed for a comparison to a large, nationally stratified standardization sample, in lieu of a control group in this feasibility study. If a study is seeking to determine the effects of an intervention on executive function outcomes, a performance-based measure may be more appropriate for a pre-and post-intervention measure. However, there is uncertainty as to whether these two types of executive function measures actually reflect the same construct (Toplak, West, & Stanovich, 2013). A recent meta-analysis of 14 studies examining executive function in pediatric sleep disordered breathing concluded there is evidence of worsened executive function performance based on subjective ratings (i.e., questionnaires) but less evidence to support poorer executive function performance when using objective testing measures (Mietchen et al., 2016). Though results from studies using either type of measure are valuable (Toplak et al., 2013), varied measurement approaches across studies limits the comparison of results in the extant literature.

**Future Directions**

This area of scientific inquiry is significant and important, as there are exceedingly high rates of obesity and OSAS in the adolescent population (Ogden et al., 2014; Verhulst et al., 2008), contributing to both short and long-term detrimental health outcomes (Freedman et al., 2007; Olshansky et al., 2005). This feasibility study provided crucial insights for the
development and design of a future, larger, fully-powered two-cohort study inclusive of obese, OSAS and obese, non-OSAS adolescents. First, it is evident that face-to-face recruitment is a successful technique to enroll adolescents with obesity and OSAS from a sleep center, where PSG’s are already being conducted as a part of their clinical care. However, a future recruitment plan will need to be developed to enroll obese adolescents’ without-OSAS. This will require the need for community-based recruitment, requiring funding to support the conduct of research PSG’s or purchase/loan of home sleep testing equipment. Additionally, it was observed that many adolescents were ineligible to participate in the study due to an attention/behavioral diagnosis such as ADD or ADHD. Because these diagnoses are common in adolescents with obesity and OSAS, and are known to impair executive function (Long et al., 2015; Snyder et al., 2015; Willcutt et al., 2005), it may be important to include adolescents with an attention/behavioral diagnosis in a larger, fully powered study where an established attention/behavioral diagnosis can be controlled for in the analysis. A larger, subsequent study with funding should additionally aim to assess other neurocognitive measures, beyond executive function, to provide a broader understanding of cognitive function in this high risk population and determine if other significant cognitive impairments exist.

Feedback on instrumentation and study participation was also an important component of the feasibility study. Adolescents were overwhelmingly satisfied with their participation, with many claiming they would be willing to enroll in another similar research study, even for a longer period of time. Though the protocol was deemed acceptable by most adolescents, there are opportunities to further improve the current protocol. Paper instrumentation (i.e. diaries) was well-received based on feedback and complete data rates; however, an electronic form of the diary was desired by a majority of participants. As text-message reminders were deemed helpful
by participants, a future study should consider an electronic-based diary that is designed to include automated reminders to complete the daily diaries. Future research that allows for additional funding, should consider the purchase of more aesthetically pleasing devices, as this was desired by adolescents and may contribute to greater compliance and complete data rates. In recent studies (not inclusive of only adolescents), the Jawbone UP, a commercially available activity tracking device, has shown good agreement with PSG-measured total sleep time and wake after sleep onset. Further validation of commercial devices, including the Jawbone UP, are needed before advocating for their use in sleep research (de Zambotti, Baker, & Colrain, 2015).

Use of commercial grade devices is also of interest in the physical activity research field. Similar to sleep research, evidence of the validity of these devices for accurately measuring physical activity is preliminary (Evenson et al., 2015; Rosenberger et al., 2016). But an important component with regard to protocol adherence is that commercial devices have shown evidence of increased adherence, with one study reporting Fitbit devices were worn for 10 or more hours per day on 95% of intervention delivery days for a 16 week intervention (Cadmus-Bertram, Marcus, Patterson, Parker, & Morey, 2015). Both commercial and research devices have their pros and cons, such that research-grade devices often have greater accuracy and reliability but are far more expensive; whereas commercially available devices are cheaper and more aesthetically pleasing, yet are less supported in research due to their novelty and lack of evidence for validity/reliability. Moving forward, researchers interested in tracking sleep and physical activity will be faced with the decision of whether to use research-grade or commercially available devices.

In addition to feasibility, this study aimed to assess executive function in obese adolescents with OSAS. Though a comparison group was unable to be successfully recruited,
results indicate that adolescents with obesity and OSAS have significantly worse executive function than a normative comparison group. Even though the sample size was small, prevalence of executive function impairments were evident at rates similar to what is published in the small body of comparable, extant literature. This supports the notion that this area of scientific inquiry is worthy of further investigation. Also, this phenomenon is important to research further in order to determine if adolescents diagnosed with both obesity and OSAS are at higher risk for executive function impairments than adolescents experiencing either condition alone.

The overall outlook on health is poor for adolescents who experience both obesity and OSAS. This study additionally aimed to gain an understanding of this population’s sleep and physical activity habits, as they relate to the national recommendations set forth in the U.S. Participants of this study did not meet sleep or physical activity recommendations on the majority of days per week; sleep duration, and time spent engaged in moderate-to vigorous activity were alarmingly low. As previously discussed in chapter two, short sleep durations and inactivity are associated with poorer health. Further, adolescents with obesity and OSAS are at higher risk for negative health outcomes (Gozal, 2014; Vitelli et al., 2015) that are further compounded by habitual sleep duration curtailment and physical inactivity. As sleep and physical activity may have protective effects or even improve executive function in adolescents with obesity and OSAS, these two health habits (i.e., sleep duration and physical activity) may be important focal points for interventions to target health and wellness and reduce comorbidities in adolescents. However, additional barriers exist in the development of healthy lifestyle interventions in adolescents. For example, parental diet and physical activity habits have a strong influence on adolescents’ behavior, indicating the need for targeting both parents of children and adolescents (Davison & Birch, 2002; Krahnstoever Davison et al., 2005). Any future studies of
healthy lifestyle interventions, therefore, must be designed with careful consideration given to the type of intervention, target behavior, and multiple influences on behavior change uptake among adolescents.

**Conclusion**

Adolescents with obesity and OSAS are an understudied population with substantial short and long-term negative health consequences (Capdevila et al., 2008; Hargens et al., 2013; Marcus, Brooks, et al., 2012; Redline et al., 2007). As approximately 90% of obese adolescents are likely to become obese adults (American Psychological Association, 2002; Freedman et al., 2001; Freedman et al., 2005; Guo & Chumlea, 1999; Singh et al., 2008), strategies attempting to minimize poor health outcomes to be undeniably experienced by these adolescents are financially, ethically, and morally prudent. Additionally, this understudied population was addressed as a critical focus point in a statement issued by the American Thoracic Society, stating the need for better education and raising awareness with regard to the importance of early identification of high-risk OSAS groups due to the significant poor health implications of untreated-OSAS (Mukherjee et al., 2015). Scant literature exists on obese adolescents with OSAS, as the pediatric OSAS literature is often accompanied by a large age span with few studies focused strictly on adolescents (Andersen et al., 2016). This study contributes to the relatively scant literature by addressing executive function, sleep durations, and physical activity in this understudied population.

Obesity and OSAS have many shared negative health outcomes associated with both conditions, however, the strength and directionality of the relationship between obesity and OSAS remains unclear, as obesity contributes to the development of OSAS and untreated OSAS contributes to obesity (Hargens et al., 2013). In this study, adolescents with obesity and OSAS
had significantly worse executive function than a normative sample; a portion had executive function impairments at clinically significant levels, engaged in low levels of moderate-to-vigorous physical activity, and had short sleep durations.

In this study, adolescents with obesity and OSAS had (1) significantly worse executive function than a normative sample, (2) a portion had executive function impairments at clinically significant levels, (3) most engaged in low levels of moderate-to-vigorous physical activity, and (4) most had short sleep durations. Because physical activity and sleep have the potential to interact and influence each other, as well as profoundly impact obesity, OSAS, and executive function (Andersen et al., 2016; C. L. Davis et al., 2011), these health behaviors may be critical intervention opportunities for a population at exceedingly high risk for premature morbidity and mortality. Further, adolescence is a critical intervention period, as habits adopted early in life have increased potential to become lifelong habits. This study provided critical insights for decision making in the intended development of a future, larger, fully-powered two-cohort study that aims to define the relationship between obesity, OSAS, and executive function and fully explore how sleep duration and physical activity mediate the relationship between obesity, OSAS and executive; this intended research will provide imperative insights for targeting sleep and physical activity as foci for future intervention work.
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APPENDIX B

Informed Consent and Authorization to take part in Research

Signature of Person Giving Informed Consent and Authorization
Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative and have answered any questions he/she has about the research.

____________________________
Signature of person who explained this research
Date
Time
Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Parent(s)/Guardian for Child

By signing this consent form, you indicate that you permit your child to be in this research and agree to allow his/her information to be used and shared as described above.

___________________________
Signature of Parent/Guardian
Date
Time
Printed Name

ASSENT FOR RESEARCH

The research study has been explained to you. You have had a chance to ask questions to help you understand what will happen in this research. You Do Not have to be in the research study. If you agree to participate and later change your mind, you can tell the researchers, and the research will be stopped.

You have decided: (Initial one)

___ To take part in the research.

___ NOT to take part in the research.

___________________________
Signature of subject
Date
Printed Name
APPENDIX C

STUDY ELIGIBILITY QUESTIONNAIRE

DIRECTIONS: Please write in your answer or place an (X) in the box next to the options that best represent you. Please answer all questions to the best of your ability.

If conducted via phone, DIRECTIONS: “Now that the study has been explained to you and you have expressed interest in participating in the study, there are 6 short questions I must ask you prior to scheduling our first meeting at the clinic. Are you willing to answer these questions?” If yes, proceed with the following statement. “Thank you. Please answer all questions to the best of your ability”. At this time, questions and responses will be read aloud by the PI. If “no”, patient will be thanked for their time and interest to this point.

1. Age: ________ years old

2. Are you currently being treated for sleep apnea (other than your sleep study taking place tonight)?
   □ Yes
   □ No

3. Have you ever been diagnosed with any sleep-wake disorders, including: (check all that apply)
   □ Insomnia
   □ Restless legs syndrome
   □ Narcolepsy

4. Do you have a new or existing bodily injury or disability that hinders your ability to participate in physical activity or gym class?
   □ Yes
   □ No

5. Will you be doing anything out of your usual routine over the next week? Specifically, plans that may interfere with how much sleep or activity you normally get. For example: going on vacation, planned surgery, staying awake for extended periods of time for THON or similar school charities, etc.
   □ Yes
   □ No

6. Do you use any over the counter or non-prescription aids (>3 days/week) to help you sleep? For example: melatonin, Unisom SleepTabs, ZzzQuil, Benadryl, etc.
   □ Yes
   □ No

7. Have you ever been diagnosed with attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), or oppositional defiant disorder (ODD)?
   □ Yes
   □ No
APPENDIX D

CHARACTERISTICS QUESTIONNAIRE

DIRECTIONS: Place an (X) in the box next to the options that best represents you. Please answer all questions as of today.

1. Sex:
   □ Male
   □ Female

2. Race (select one or more that apply to you):
   □ White
   □ Black or African American
   □ Asian
   □ Native Hawaiian or Other Pacific Islander
   □ American Indian or Alaska Native

3. Ethnicity (select one that applies to you):
   □ Hispanic
   □ Non-Hispanic

4. What grade are you in? (Check one [or hand-write if other])
   □ 7th grade
   □ 8th grade
   □ 9th grade
   □ 10th grade
   □ 11th Grade
   □ 12th grade

6. Are you? (Check all that apply)
   □ Working part-time (school days)
   □ Working part-time (weekends)
   □ Involved in an organized sport (school sport, club sport, recreational sport)
   □ Involved in a school-based club
   □ Involved in a club outside of school hours
APPENDIX E

MODIFIED EPWORTH SLEEPINESS SCALE

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you.

Use the following scale to choose the most appropriate number for each situation:

- 0 no chance of dozing
- 1 slight chance of dozing
- 2 moderate chance of dozing
- 3 high chance of dozing

<table>
<thead>
<tr>
<th>Situation</th>
<th>Score (0-3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td></td>
</tr>
<tr>
<td>Watching TV</td>
<td></td>
</tr>
<tr>
<td>Sitting inactive in a public place (e.g., movie theater or a meeting)</td>
<td></td>
</tr>
<tr>
<td>As a passenger in a car for an hour without a break</td>
<td></td>
</tr>
<tr>
<td>Lying down to rest in the afternoon when circumstances permit</td>
<td></td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td></td>
</tr>
<tr>
<td>Sitting quietly after lunch</td>
<td></td>
</tr>
<tr>
<td>In a car, while stopped for a few minutes in traffic</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX F

The Behavior Rating Inventory of Executive Function, Second Edition (BRIEF®2)

Permissions prohibit copying of the instrument. In contacting PAR, Inc. the following sample document was provided for IRB purposes:

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PAR, Inc.
BRIEF-A

Behavior Rating Inventory of Executive Function—Adult Version

INFORMANT REPORT FORM

Robert M. Roth, PhD, Peter K. Isquith, PhD, and Gerard A. Gioia, PhD

Name of Rated Individual. .................................................. Gender □ Male □ Female Age ___
Your Name ................................................................. Today’s Date ___ / ___ / ___
Your relationship to him/her: □ Parent □ Spouse □ Sibling □ Friend □ Other ___
How well do you know him/her? □ Not well □ Moderately well □ Very well You have known him/her for ___ years.

During the past month, how often has each of the following behaviors been a problem?

<table>
<thead>
<tr>
<th>N = Never</th>
<th>S = Sometimes</th>
<th>O = Often</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Has angry outbursts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Makes careless errors when completing tasks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Is disorganized</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Has trouble concentrating on tasks (such as chores, reading, or work)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Taps fingers or bounces legs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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APPENDIX G

Consensus Sleep Diary

What is a Sleep Diary? A sleep diary is designed to gather information about your daily sleep pattern.

How often and when do I fill out the sleep diary? It is necessary for you to complete your sleep diary every day. Fill out question 1-9 within one hour of getting out of bed in the morning or as soon as possible after getting out of bed. Items 10 and 11 should be filled out before bed.

What should I do if I miss a day? If you forget to fill in the diary or are unable to finish it, leave the diary blank for that day.

What if something unusual affects my sleep or how I feel in the daytime? If your sleep or daytime functioning is affected by some unusual event (such as an illness, or an emergency) you may make brief notes on your diary.

What do the words “bed” and “day” mean on the diary? This diary can be used for people who are awake or asleep at unusual times. In the sleep diary, the word “day” is the time when you choose or are required to be awake. The term “bed” means the place where you usually sleep.

Will answering these questions about my sleep keep me awake? This is not usually a problem. You should not worry about giving exact times, and you should not watch the clock. Just give your best estimate.

Item Instructions

Use the guide below to clarify what is being asked for each item of the Sleep Diary. Date: Write the date of the morning you are filling out the diary.

1. What time did you get into bed? Write the time that you got into bed. This may not be the time that you began “trying” to fall asleep.

2. What time did you try to go to sleep? Record the time that you began “trying” to fall asleep.

3. How long did it take you to fall asleep? Beginning at the time you wrote in question 2, how long did it take you to fall asleep.

4. How many times did you wake up, not counting your final awakening? How many times did you wake up between the time you first fell asleep and your final awakening?

5. In total, how long did these awakenings last? What was the total time you were awake between the time you first fell asleep and your final awakening. For example, if you woke 3 times for 20 minutes, 35 minutes, and 15 minutes, add them all up (20+35+15= 70 min or 1 hr and 10 min).

6. What time was your final awakening? Record the last time you woke up in the morning.

7. What time did you get out of bed for the day? What time did you get out of bed with no further attempt at sleeping? This may be different from your final awakening time (e.g. you may have woken up at 6:35 a.m. but did not get out of bed to start your day until 7:20 a.m.)

8. How would you rate the quality of your sleep? “Sleep Quality” is your sense of whether your sleep was good or poor.

9. Comments If you have anything that you would like to say that is relevant to your sleep feel free to write it here.

10a. How many times did you nap or doze? A nap is a time you decided to sleep during the day, whether in bed or not in bed. “Dozing” is a time you may have nodded off for a few minutes, without meaning to, such as while watching TV. Count all the times you napped or dozed at any time from when you first got out of bed in the morning until you got into bed again at night.

10b. In total, how long did you nap or doze? Estimate the total amount of time you spent napping or dozing, in hours and minutes. For instance, if you napped twice, once for 30 minutes and once for 60 minutes, and dozed for 10 minutes, you would answer “1 hour 40 minutes.” If you did not nap or doze, write “N/A” (not applicable).

11a. How many caffeinated drinks (coffee, tea, soda, energy drinks) did you have? Enter the number of caffeinated drinks (coffee, tea, soda, energy drinks) you had where for coffee and tea, one drink = 6-8 oz; while for caffeinated soda one drink = 12 oz.

11b. What time was your last caffeinated drink? If you had a caffeinated drink, enter the time of day in hours and minutes of your last drink. If you did not have a caffeinated drink, write “N/A” (not applicable).
<table>
<thead>
<tr>
<th>Sample</th>
<th>Consensus Sleep Diary</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Today’s date: 11/1/16</td>
</tr>
<tr>
<td><strong>MORNING</strong></td>
<td></td>
</tr>
<tr>
<td>1. What time did you get into bed?</td>
<td>10:15 p.m.</td>
</tr>
<tr>
<td>2. What time did you try to go to sleep?</td>
<td>11:30 p.m.</td>
</tr>
<tr>
<td>3. How long did it take you to fall asleep?</td>
<td>55 min.</td>
</tr>
<tr>
<td>4. How many times did you wake up, not counting your final awakening?</td>
<td>3 times</td>
</tr>
<tr>
<td>5. In total, how long did these awakenings last?</td>
<td>1 hour 10 min.</td>
</tr>
<tr>
<td>6. What time was your final awakening?</td>
<td>6:35 a.m.</td>
</tr>
<tr>
<td>7. What time did you get out of bed for the day?</td>
<td>7:20 a.m.</td>
</tr>
</tbody>
</table>
| 8. How would you rate the quality of your sleep? | □ Very poor  
  □ Poor  
  □ Fair  
  □ Good  
  □ Very good |
| 9. Comments (if applicable)     | I have a cold                                               |
| **EVENING**                    |                                                             |
| 10a. How many times did you nap or doze? | 2 times                                                     |
| 10b. In total, how long did you nap or doze? | 1 hour 10 min.                                              |
| 11a. How many caffeinated drinks (coffee, tea, soda, energy drinks) did you have? | 2 drinks                                                    |
| 11b. What time was your last caffeinated drink? | 3:00 p.m.                                                   |
APPENDIX H

Previous Day Physical Activity Recall
Activities Scale

On the next page is a scale which records the main activities you did yesterday. Please be certain to write on the scale the day of the week that “yesterday” was.

1. For each time period write in the number(s) of the main activities you actually did in the boxes on the time scale.
2. Then rate how physically hard these activities were. Place an “X” on the rating scale to indicate if the activities for each time period were:

**Very light**- Slow breathing, little or no movement.

**Light**- Normal breathing, regular movement.

**Medium**- Increased breathing, moving quickly for short periods of time.

**Hard**- Heavy breathing, moving quickly for 20 minutes or more.

Please be as accurate as possible but fill out the scale quickly.
Activity Numbers

Eating
1. Meal
2. Snack
3. Cooking

Sleep/Bathing
4. Sleeping
5. Resting
6. Shower/bath

Transportation
7. Ride in car, bus
8. Travel by walking
9. Travel by bike

Work/School
10. Job (list)
11. Homework/paperwork
12. House chores (list)

Spare Time
13. Watch TV
14. Go to movies/concert
15. Listen to music
16. Talk on phone
17. Hang around
18. Shopping
19. Play video games
20. Other (list)

Physical Activities
21. Walk
22. Jog/run
23. Dance (for fun)
24. Aerobic dance
25. Swim (for fun)
26. Swim laps
27. Ride bicycle
28. Lift weights
29. Use skateboard
30. Play organized sports (school, club, town)
31. Did individual exercise
32. Did active game outside
33. Other (list)
<table>
<thead>
<tr>
<th>Time</th>
<th>Activity Numbers</th>
<th>Very Light</th>
<th>Light</th>
<th>Medium</th>
<th>Hard</th>
</tr>
</thead>
<tbody>
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<td>05:30</td>
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APPENDIX I

END OF STUDY SURVEY

You have now completed your participation in the study. Your feedback about your experience in the study will help us plan future studies.

DIRECTIONS: Please carefully read each question. Indicate your response to each question by placing an X in the box for your response.

1. Overall, are you satisfied with your involvement in this study?

<table>
<thead>
<tr>
<th>Very Dissatisfied</th>
<th>Somewhat Dissatisfied</th>
<th>Somewhat Satisfied</th>
<th>Very Satisfied</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

2. Would you participate in another study that used a daily diary?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
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</thead>
<tbody>
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<td></td>
</tr>
</tbody>
</table>

3. On days that you used the diary, how long do you estimate it took you to complete the diary each day?

<table>
<thead>
<tr>
<th>Less than 5 minutes</th>
<th>5-15 minutes</th>
<th>15-30 minutes</th>
<th>&gt;30 minutes</th>
</tr>
</thead>
<tbody>
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</tbody>
</table>

4. Did you have difficulty remembering to complete the diary on a daily basis?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

If YES, what did you do to help you remember to complete the diary each day?

___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
5. You received a text message every evening to remind you to fill out the diaries. Were these text messages:

<table>
<thead>
<tr>
<th>Too frequent</th>
<th>A good amount</th>
<th>Not enough</th>
</tr>
</thead>
</table>

How often would you like this reminder?

<table>
<thead>
<tr>
<th>Twice per day</th>
<th>Once per day</th>
<th>Every other day</th>
<th>Every 3rd day</th>
</tr>
</thead>
</table>

6. We sent text message reminders at 8 p.m. What time would you prefer to receive this message?

<table>
<thead>
<tr>
<th>Morning (6 a.m.-8 a.m.)</th>
<th>Late morning (9 a.m.-11 a.m.)</th>
<th>Afternoon (noon-3 p.m.)</th>
<th>Early evening (4 p.m.- 6 p.m.)</th>
<th>Evening (7 p.m.- 9 p.m.)</th>
<th>Late evening (10 p.m. – midnight)</th>
</tr>
</thead>
</table>

7. Would you prefer the diary to be available for your entries on an app (smartphone, tablet, computer, etc.)

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>

8. You wore a wrist-worn device for a 7-day period in this study. Did you remove the device at any time?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>
If YES, in what situations did you remove the device?
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________

If YES, did you put the device back on after removing the device for the above reasons?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

If YES, what helped you remember to put the device back on your wrist?
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________

9. Although this study asked you to wear the device and record a diary for 7-days, would you be willing to participate in the study that asked you to wear the same device and maintain a diary for a longer period of time?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
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</table>

If YES, how long a study period would be acceptable to you to wear a device and maintain a daily diary?

<table>
<thead>
<tr>
<th>2 weeks</th>
<th>3 weeks</th>
<th>4 weeks</th>
<th>&gt;4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
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</table>

10. In this study, we asked you to wear a wrist-worn device. Would you be willing to wear a small device at your waist for physical activity recording at the same time as wearing the wrist-worn device?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
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<tbody>
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</table>
11. Although this study did not include a time when you would receive/view your sleep and activity information, would this be of interest to you if you were to participate in a future, similar study? (i.e., the activity and sleep report)?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
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<tbody>
<tr>
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</table>

Why or why not?

_________________________________________________________________
_________________________________________________________________

12. Would you be willing to participate in another study similar to this one in the future?

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<thead>
<tr>
<th>YES</th>
<th>NO</th>
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</table>

13. Please provide any other feedback about your experience in the current study; this can be positive or negative feedback. Your honest feedback will help us plan future studies.

_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
VITA- Alexa Watach
College of Nursing- 90 Hope Drive, ASB 1300, Hershey, Pennsylvania 17033

EDUCATION
2017  **Doctor of Philosophy Candidate**
Pennsylvania State University, University Park, PA
2014  **Master of Science, Nursing**
Pennsylvania State University, University Park, PA
2012  **Bachelor of Science, Nursing**
Pennsylvania State University, University Park, PA

RESEARCH TRAINING:
- Research Assistant; Supervisor, Amy M. Sawyer, PhD, RN; American Lung Association Soci al Behavioral Award SB-417793 (Present)
- Research Training; Mentor, Jerilynn Radcliffe, PhD, ABPP; Behavior Rating Inventory of Ex ecutive Function (2016-present)
- Research Internship; Jennifer L. Kraschnewski, MD, MPH; PRO Wellness Center(2015-2016)
- Graduate Assistant;
  - Supervisor, Harleah G. Buck, PhD, RN, CHPN, FPCN; (2015-2016)
  - Supervisor, Amy M. Sawyer, PhD, RN; (2013-2015)
- Independent Study; Supervisor, Amy M. Sawyer, PhD, RN; CPAP Adherence in Pediatric OSAS (2014)

SELECTED PRESENTATIONS:

PROFESSIONAL EXPERIENCE
- Nurse, Perioperative Services (Adult & Pediatric Surgery), Hershey Medical Center, Hershey, PA

HONORS & AWARDS:
- Eight & Forty Pediatric Lung and Respiratory Disease Nursing Scholarship Award
- Beta Sigma Chapter, Sigma Theta Tau International
- PhD Doctoral Student Organization leader, Nursing
- Sigma Theta Tau International Honor Society
- President’s Freshman Award
- Virginia L. Mayers Memorial Scholarship

LICENSURE:
- Registered Nurse, Pennsylvania, 2012-Present

SELECTED PUBLICATIONS: