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Obstructive Sleep Apnea Syndrome and Neuropsychological Dysfunction:
Understanding the Impact of Obesity

A Dissertation

Presented to

the Faculty of the Morgridge College of Education

University of Denver

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

by

Chelsea A. Hilsendager

August 2014

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Abstract

Obesity is the largest risk factor for the development of obstructive sleep apnea syndrome (OSAS), which is a common sleep-related breathing disorder that is associated with cognitive dysfunction. A growing body of literature suggests that obesity is related to negative neuropsychological outcomes independent of other health problems known to impact cognitive functioning (e.g., type II diabetes, cardiovascular disease). The purpose of this study was to investigate the impact of obesity on the cognitive functioning of individuals with OSAS. Specifically, this study aimed to examine whether or not differences existed between obese and non-obese persons with OSAS on a battery of cognitive tests that assessed memory, attention, and executive functions both at baseline and over six months of continuous positive airway pressure (CPAP) treatment. This study utilized data from Project Breathe, which was a study conducted at National Jewish Health. It was hypothesized that obese participants with OSAS would demonstrate poorer baseline performance on tests of memory, attention, and executive functioning, and they would show lesser improvement in these cognitive domains over six months of CPAP treatment compared to non-obese participants. Analysis of covariance (ANCOVA) and repeated measures analysis of covariance (RM-ANCOVA) tests were used to analyze the data. Results indicate that obese and non-obese participants did not demonstrate differences in neurocognitive functioning at baseline or following six months of CPAP treatment after adjusting for age and hypertension. Several limitations, including how

obesity was measured, analyses used, and low statistical power may have contributed to the lack of significant findings in the predicted direction. Future research should focus on the following: larger sample sizes; using measures of obesity other than or in addition to body mass index (BMI); and examining the moderating impact of sex on neurocognitive functioning in this population.

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Chapter I: Introduction

Obesity and Obstructive Sleep Apnea Syndrome

Obesity is highly prevalent in the United States, and it is a growing health problem in other nations around the world (World Health Organization [WHO], 1998). Obesity results from the accumulation of excess body fat and is associated with myriad health problems and increased mortality (Olshansky et al., 2005). Obesity is one of the foremost risk factors for obstructive sleep apnea syndrome (OSAS), which is a common sleep-related breathing disorder characterized by repetitive episodes of upper airway collapse during sleep that cause breathing cessation and result in fragmented sleep and intermittent hypoxemia (American Academy of Sleep Medicine, 1999).

Obstructive Sleep Apnea Syndrome and Neuropsychological Impairment

OSAS is associated with several neuropsychological deficits, which are well documented in the literature. Those most frequently reported by OSAS patients and strongly acknowledged in the literature include problems with attention and vigilance (Bédard et al., 1991; Bédard et al., 1993; Findley et al., 1986; Ferini-Strambi et al., 2003; Greenberg et al., 1987; Munoz et al., 2000; Naegele et al., 1995; Redline et al., 1997). Some research suggests that impairments in attention/vigilance are related to apnea severity, specifically, the level of sleep fragmentation, as opposed to nocturnal hypoxemia (Bédard et al., 1991).

The literature also indicates that OSAS is associated with impairments in executive functions (Bédard et al., 1991; Greenberg et al., 1987; Kales et al., 1985; Lee et al., 1999; Naegele et al., 1995; Redline et al., 1997; Salorio et al., 2002). However, lack of consistency across studies in measures used to test executive functions obscure the specific aspects of executive functioning (e.g., working memory, cognitive flexibility, planning) that are impacted by OSAS. Investigators have argued that deficiencies in executive functions are related to nocturnal hypoxemia, as opposed to sleep fragmentation (Bédard et al., 1993; Ferini-Strambi et al., 2003; Valencia-Flores et al., 1996; Montplaisir et al., 1992).

The literature points to a relationship between OSAS and memory deficits (Bédard et al., 1991; Berry et al., 1986; Findley et al., 1986; Naegele et al., 1995; Kales et al., 1985); however, like executive functions, investigators have not reached consensus regarding the specific components of memory that are impacted due to divergent memory assessment methods across studies. The majority of studies have investigated the relationship between OSAS and impaired long-term visual and verbal memory (Bédard et al., 1991; Berry et al., 1986; Findley et al., 1986; Naegele et al., 1995; Kales et al., 1985). However, Kales et al. (1985) also found a relationship between OSAS and decrements in short-term visual and verbal memory. Investigators have attributed these memory deficits to both nocturnal hypoxemia (Findley et al., 1986) and sleep fragmentation (Kales et al., 1985; Bédard et al., 1991).

Several researchers have highlighted a clear relationship between OSAS and impaired fine motor coordination mediated by the brain (Bédard et al., 1991; Bédard et al., 1993; Greenberg et al., 1987). These investigators have observed associations

between fine motor coordination and nocturnal hypoxemia. Further, the literature suggests that impaired fine motor coordination due to OSAS may be irreversible, and thus, suggests an association between OSAS and permanent anoxic brain damage (Aloia et al., 2004).

Treatment

Oral appliances and surgical procedures are used to treat OSAS; however, the majority of patients do not receive adequate clinical benefit from these approaches. Considering the estimation that 70 % of persons with OSAS meet criteria for obesity (Malhotra & White, 2002), some investigators have analyzed the impact of weight loss as a treatment for OSAS. Veasey et al. (2006) found that a sufficient amount of weight loss through dietary modification can result in significant improvement in OSAS symptomatology among overweight and obese individuals. However, these investigators acknowledged that improvements in weight loss programs are warranted. Surprisingly, no studies in the extant literature have examined the impact of weight loss on the neuropsychological sequelae associated with OSAS.

Continuous-positive airway pressure (CPAP) is considered the most effective and preferred treatment for OSAS (Gay et al., 2006). The CPAP device contains a mask with a harness that fits over the head to hold the mask in place, as well as a flexible tube, and pump that provides continuous positive air pressure. The positive air pressure to the upper portion of the airway prevents it from collapsing during sleep, thus reducing or completely eliminating nocturnal respiratory disturbances. The decrease or absence of upper airway collapse results in minimized sleep fragmentation and nocturnal hypoxemia (American Thoracic Society, 1994). Unfortunately, despite the efficacy of CPAP

treatment, it is estimated that 25 - 50 % of individuals prescribed CPAP do not tolerate it (Zozula & Rosen, 2001).

Of the studies reviewed in Chapter II, there appears to be consensus among investigators regarding the impact of CPAP treatment on two cognitive constructs: attention/vigilance and motor coordination. The majority of studies suggest that attention/vigilance improves following CPAP treatment. Improvements in attention/vigilance have been observed in as little as 15 days of CPAP treatment (Ferini-Strambi et al., 2003). However, the literature indicates that fine motor coordination does not improve following CPAP treatment (Aloia et al., 2004; Bédard et al., 1993; Beebe et al., 2003). Investigators hypothesize that anoxic brain damage associated with repeated nocturnal hypoxic events might cause irreversible deficits in this domain of cognitive functioning (Aloia et al., 2004).

It is not clear if CPAP treatment improves memory deficits associated with OSAS. Borak et al. (1996) and Bédard et al. (1993) observed that CPAP treatment improved memory deficits after three and six months of CPAP treatment, respectively. However, Engleman et al. (1993; 1997) and Naegele et al. (1998) found that memory functioning did not improve after four weeks and six months of CPAP treatment, respectively.

Mixed results characterize the literature reviewed regarding the effectiveness of CPAP treatment in ameliorating executive functioning deficits in patients with OSAS. Some research suggests that executive functioning does not improve following CPAP treatment (Bédard et al., 1993; Ferini-Strambi et al., 2003; Valencia-Flores et al., 1996; Montplaisir et al., 1992). Investigators argue that executive functions may not respond to

treatment due to irreversible anoxic brain damage caused by repeated nocturnal hypoxemia. However, this hypothesis is not definitive, as some studies have demonstrated that executive functions do improve following CPAP treatment (Borak et al., 1996; Engleman et al., 1994; Engleman et al., 1997; Naegele et al., 1998). Further, the length of CPAP treatment necessary to improve executive functions is not clear. For instance, Bédard et al. (1993) found that six months of CPAP treatment did not improve executive functioning; however, Engleman et al. (1994, 1997) found improvements in certain aspects of executive functioning in as little as four weeks of CPAP treatment.

Obesity and Neuropsychological Functioning

A growing body of literature suggests that obesity is related to negative neurocognitive outcomes independent of other health problems (e.g., type II diabetes, OSAS, cardiovascular disease). Several researchers have identified relationships between obesity and attention deficits (Altfas, 2002; Elias et al., 2005; Cournot et al., 2006). However, some investigators have observed that these relationships are no longer significant when covariates, such as education, sex, and age were included in their models (Cournot et al., 2006; Elias et al., 2005). Further, Gunstad et al. (2010) observed a relationship between increased attentional performance and obesity. Therefore, despite some evidence that obesity is associated with attentional deficits, this relationship is not conclusive in the literature.

A number of investigators have observed relationships between obesity and executive dysfunction (Chelune et al., 1986; Gunstad et al., 2007; Gunstad et al., 2010; Waldstein & Katzel, 2006). The specific aspects of executive functioning that have been analyzed and appear to be affected include cognitive flexibility (Gunstad et al., 2010;

Chelune et al., 2007), verbal fluency, and planning (Gunstad et al., 2007). Further, there appears to be a relationship between obesity concomitant with high blood pressure and impaired response inhibition (Waldstein & Katzel, 2006). Overall, the research that has been done thus far concerning obesity and executive dysfunction points to a clear relationship.

Research suggests that there is also a relationship between obesity and memory impairments (Cournot et al., 2006; Elias et al., 2003; Elias et al., 2005; Gunstad et al., 2006; Gunstad et al., 2010). Elias and colleagues (2003, 2005) observed that obese men performed significantly more poorly on tests of verbal and visual memory compared to non-obese men even when controlling for age, education, occupation, cigarette smoking, and health conditions associated with obesity (e.g., type II diabetes). Notably, the relationship between obesity and memory deficits was not apparent in women. Additionally, Gunstad and colleagues (2007) found that obese individuals demonstrated significantly poorer verbal memory compared to non-obese individuals and later observed relationships between obesity and impairments in visual and verbal memory (Gunstad et al., 2010). By and large, the literature suggests that that obesity is an independent risk factor for memory decrements.

Along with the research analyzing relationships between obesity and impairments in different domains of cognitive functioning, several studies have demonstrated associations between obesity and dementia and Alzheimer's disease (Gustafson et al., 2003; Kivipelto et al., 2005; Razay et al., 2006), as well as compositional changes in the brain, characterized by atrophy and increased white matter lesions in older adults (Gustafson et al., 2004; Gustafson, Steen, & Skoog, 2004; Jagust et al., 2005; Ward et al.,

2005). Though there is evidence to suggest relationships between obesity and different aspects of neuropsychological impairment, the directional nature of these relationships has not been elucidated. Thus, it is unclear whether obesity is the result or cause of neuropsychological impairment. Additionally, it is not clear if the neuropsychological deficits associated with obesity improve following weight loss.

In addition to lack of clarity surrounding the directional relationship between obesity and cognitive dysfunction, the mechanisms underlying this relationship are also uncertain. Investigators have posited several potential explanations for this association. Dagenais et al. (2005) and Waldstein et al. (2006) suggested obesity causes vascular changes that prevent optimal blood flow to the brain, and thus, negatively impact cognitive performance. Others have pointed to the impact of obesity on glucose tolerance and insulin regulation, which are known to impair cognitive functioning (Convit et al., 2003; Teunissen et al., 2003). Additionally, some have argued that the increasing adipose tissue is associated with changes in certain proteins, such as leptin (Gunstad et al., 2008; Harvey, 2007; Wilson, Finch, & Harvey, 2002) and brain-derived neurotrophic factor (BDNF; Gunstad et al., 2008; Hariri et al., 2003) that may impact cognitive functioning.

Statement of Purpose, Hypotheses, and Relevance of the Study

Purpose of the Study. The extant literature suggests that both OSAS and obesity are related to deficits in neuropsychological functioning. There is evidence indicating that CPAP improves neurocognitive functioning in OSAS patients; however, the impact of obesity in the response to CPAP treatment has not been analyzed. Given that obesity is independently associated with impaired neurocognitive functioning, it is possible that the presence of obesity in OSAS patients could impact both the severity of impairment, as

well as their response to CPAP treatment. Further, no studies have examined differences in neuropsychological functioning between obese patients with OSAS and non-obese patients with OSAS or differences between these groups following CPAP treatment. Therefore, the purpose of this study is to elucidate the impact of obesity on the neuropsychological functioning of individuals with OSAS. Specifically, the purpose is to identify differences between obese and non-obese OSAS patients both at baseline and over six months of CPAP treatment.

Hypotheses. Based on the literature review presented in Chapter II, the following hypotheses were formulated:

Hypothesis I. Obese participants with OSAS will demonstrate poorer baseline attention compared to non-obese individuals with OSAS. Additionally, obese participants will show lesser improvement in attention over six months of CPAP treatment compared to non-obese participants. Attention will be assessed with the Trail Making Test Part A and a Psychomotor Vigilance Task.

Hypothesis II. Obese participants with OSAS will show poorer baseline executive functioning than non-obese individuals with OSAS. Further, they will display lesser improvement in executive functioning over six months of CPAP treatment compared to non-obese participants. Executive functions will be assessed with the Paced Auditory Serial Addition Test and the Trail Making Test Part B, which are measures of working memory and cognitive flexibility, respectively.

Hypothesis III. Obese participants with OSAS will demonstrate poorer baseline verbal memory than non-obese individuals with OSAS. In addition, obese participants will show lesser improvement in verbal memory over six months of CPAP treatment

compared to non-obese participants. Immediate and delayed verbal memory will be assessed with the Hopkins Verbal Learning Test.

Relevance of the Study. This study will fill a gap in the literature pertaining to the relationships between obesity, OSAS, and neuropsychological functioning both prior to and after CPAP treatment. The importance of clarifying these relationships ultimately lies in the treatment recommendations and interventions for obese individuals with OSAS. If obese patients with OSAS do not demonstrate the same improvements in neuropsychological functioning following CPAP treatment as non-obese patients with OSAS, additional interventions aimed at weight loss could be warranted for these individuals. Thus, this study has the potential to inform the treatment recommendations for obese OSAS patients, and could lead to greater efforts in the development of effective weight loss programs for this specific population. Ultimately, this study will enhance the existing knowledge regarding the impact of obesity on individuals with OSAS and could lead to enhanced treatment interventions, outcomes, and quality of life for obese individuals with OSAS.

Summary

Chapter I presented an introduction to the definitions of obesity and OSAS. Additionally, the neuropsychological deficits associated with obesity and OSAS were outlined, as well as the impact of CPAP treatment on neuropsychological functioning in individuals with OSAS. The purpose of the study and hypotheses were also outlined. Chapter II will present a thorough review of the literature pertaining to neuropsychological functioning in persons with OSAS and those who are obese.

Chapter II: Review of the Literature

Chapter II will present a review of the extant literature pertaining to the prevalence of obesity and the related health complications, with a salient focus on obstructive sleep apnea syndrome (OSAS). The prevalence and etiology of OSAS will be discussed, as well as common treatment interventions. Additionally, literature regarding the neuropsychological functioning of both persons with OSAS and individuals who are obese will be reviewed. The major sections of the literature review will cover the research pertinent to the present study, elucidating its relevance. Further, the literature review will highlight the research on which this study's hypotheses were predicated.

Obesity

Obesity is characterized by the accumulation of excess body fat that can impair health. Obesity is most often estimated using a formula that combines weight and height. Body mass index (BMI) is a calculation of weight in kilograms divided by height in meters squared. Though BMI is limited in that it does not distinguish fat mass from lean mass, it is the most frequently used formula to determine body fat in epidemiological studies (Kopelman, 2000). The WHO (1998) proposed a classification system for BMI with the definition of overweight as a BMI greater than or equal to 25 kg/m^2 , obesity as a BMI greater than or equal to 30 kg/m^2 , and morbid obesity as a BMI greater than or equal to 40 kg/m^2 . The decisive factor for defining obesity was based on the strong correlation

between BMI of 30 kg/m² and increased risk of death (Wadden, Brownell, & Foster, 2002).

Prevalence. The prevalence of obesity has increased substantially over the past four decades and is currently considered one of the foremost causes of preventable death in the United States (Mokdad et al., 2004). More than two thirds of adults in the United States are now classified as overweight or obese, which has led to predictions that obesity will cause the first decline in life expectancy in the past century (Olshansky et al., 2005). Obesity is not only increasing in prevalence throughout the United States, it is a growing problem in other industrialized and developing countries, and thus, has been deemed a “global epidemic” by the World Health Organization (WHO, 1998).

The etiology of obesity involves two primary factors: genes and environment. Genetic features are thought to account for 25 % - 40 % of the variance in BMI (Bouchard, 1990). The exact genes that contribute to obesity have not been determined; however, single-gene abnormalities have been found to result in obesity in laboratory animals and humans (Kopelman, 2000; Wadden, Brownell, & Foster, 2002).

Susceptibility genes appear to predispose certain individuals to develop obesity (Kopelman, 2000). For instance, the obese (ob) gene (Zhang et al., 1994) produces the hormone protein product leptin, which has demonstrated a key role in the regulation of food intake and body weight in laboratory mice. Researchers have genetically modified mice not to produce leptin, which results in obesity; however, this is reversed with the replacement of recombinant leptin (Campfield et al., 1995). Based on this research, it would be expected that obese individuals have a leptin deficiency, but this has not been observed. Rather, most obese persons have high leptin levels proportionate to their body

fat (Considine et al., 1996); thus, some researchers hypothesize that obese individuals have an insensitivity to leptin similar to the insulin insensitivity present in individuals with type II diabetes (Wadden et al., 2002).

Though susceptibility genes help explain why certain individuals become obese, environmental factors play a key role in the development of obesity and best explain its increasing prevalence over the past several decades (Wadden et al., 2002). Persons living in modernized countries are at greater risk of becoming obese compared to those living in lesser-developed societies. Two studies have demonstrated this phenomenon by following persons who migrated from underdeveloped to industrialized nations (Bhatnager et al., 1995; Ravussin et al., 1994). In both studies, the body weights of persons moving to modernized countries significantly increased compared to their relatives who remained in their native environment. This discrepancy is best explained by “toxic” environmental factors ubiquitous in developed countries, particularly the United States (Battle & Brownell, 1997). These toxic factors include the exposure to, and availability of energy-dense foods, coupled with an increasingly sedentary lifestyle.

Cultural dynamics also play an important role in the obesity epidemic. Obesity rates are associated with race, ethnicity, socioeconomic status (SES), and geographic location (Centers for Disease Control [CDC], 2011). Obesity is the most prevalent among non-Hispanic black Americans, followed by Hispanic Americans, then non-Hispanic white Americans (CDC, 2011). People of low income are disproportionately affected by obesity, especially women (Wadden, Brownell, & Foster, 2002). Research indicates that differences in SES contribute to discrepancies in the prevalence of obesity between white Americans and racial and ethnic minorities (Wadden, Brownell, & Foster, 2002), which

is not surprising considering the inextricable link between low SES and minority status. Additionally, obesity is more prevalent in the Midwest and the South (CDC, 2011).

Associated Health Complications. Elevated body fat results in significant changes in physiological functioning and risk for certain diseases that are related to the distribution of adipose tissue. For example, generalized obesity alters total blood volume and cardiac functioning, while increased adipose tissue around the rib cage changes respiratory functioning. Further, abdominal obesity plays a role in the development of type II diabetes and hypertension (Kopelman, 2000). Adams and colleagues (2006) found that the risk of mortality at midlife (i.e., 50 years) increases by 20 to 40 percent among overweight individuals and by at least two to three times among obese individuals. The risk of death associated with obesity is primarily a result of associated health complications, including type II diabetes, hypertension, cardiovascular disease, certain types of cancer, and sleep-disordered breathing (Pi-Sunyer, 1993).

Diabetes. Insulin sensitivity can be a consequence of obesity, independent of genetics. Katznel, Bugsby-Whitehead, and Goldberg (1993) demonstrated this in a study where 23 identical twins were discordant in terms of obesity. They found that the obese twins had higher fasting insulin levels and lower glucose tolerance than the normal weight twins. Hyperinsulinemia and insulin resistance create metabolic changes that can lead to type II diabetes, among other diseases (Pi-Sunyer, 1993). The positive correlation between BMI and the risk of developing type II diabetes is clearly illustrated by a study conducted in 1995 by Colditz and colleagues. These researchers demonstrated that women with a BMI of 35 kg/m^2 or more had a 93 times greater risk of developing diabetes than those with a BMI of less than 22 kg/m^2 . Though BMI is a strong predictor

of diabetes, abdominal obesity, measured by waist-to-hip ratio (WHR), may be a better predictor than BMI alone. Ohlson, Larsson, and Svardsudd (1985) followed a cohort of 54-year-old men for a period of 13.5 years and separated them into tertiles of BMI and WHR. They found that the men in the lowest tertile of WHR did not have an increased risk of developing diabetes, even when they were in the highest tertile of BMI.

Hypertension and Cardiovascular Disease. The risk of hypertension rises significantly with increasing BMI (Redon, 2001). Total blood volume in the body increases proportionate to body weight in order to meet the oxygen demands of lean and adipose tissue. Thus, obesity commonly augments the body's total blood volume, which requires increased cardiac output (i.e., the volume of blood expelled from the left ventricle of the heart in one minute) primarily through greater stroke volume (i.e., the volume of blood pumped from one ventricle of the heart with each beat; Poirer, 2006). The increase in stroke volume and cardiac output is associated with structural changes in the heart, including left ventricular dilation and hypertrophy (i.e., enlargement of muscle tissue that makes up the heart wall; Lauer, 1991), which is associated with congestive heart failure. In addition to the relationship between obesity, hypertension, and the associated changes in cardiac structure and function, the incidence of coronary heart disease is disproportionately high in obese individuals (Kopelman, 2000).

Cancer. Obesity is associated with increased risk of death from cancer. In a study of 750,000 people, men who were at least 40 % overweight were 55 % more likely to die from colorectal and prostate cancer than those at normal weight, and women who were at least 40 % overweight were 33 % more likely to die from endometrial, cervical, uterine, ovarian, gallbladder, and breast cancer than those at a normal weight (Garfinkel, 1985).

Further evidence for an association between obesity and risk of death from cancer in women was elucidated in an investigation conducted by Manson et al. (1995). They found that women with a BMI of at least 32 kg/m² were twice as likely to die from cancer than women with a BMI less than 19 kg/m².

Obstructive Sleep Apnea Syndrome

Obstructive sleep apnea syndrome (OSAS) is a common sleep-related breathing disorder characterized by repetitive episodes of upper airway collapse during sleep, which result in partial (hypopnea) and complete (apnea) occurrences of breathing cessation. Apnea and hypopnea events are generally stopped by arousals from sleep (AASM). The lack of airflow typically causes oxygen desaturation, and can lead to an increase in PaCO₂ in cases of extended events. Individuals presenting with OSAS frequently report excessive daytime sleepiness, cognitive performance problems, and decline in their overall quality of life (Engleman & Douglas, 2004), and it is hypothesized that these symptoms are related to repeated arousals from sleep and intermittent hypoxemia (American Academy of Sleep Medicine, 1999).

The signs and symptoms of OSAS include the following: excessive daytime sleepiness, choking or gasping during sleep, recurrent arousals from sleep, unrestful sleep, and cognitive problems. The essential diagnostic criterion for OSAS is an overnight sleep monitoring test that demonstrates an apnea-hypopnea index of five or more. Apneas are characterized by a cessation of airflow that lasts at least 10 seconds. Hypopneas are defined as a significant reduction in airflow (>50 %), or moderate reduction in airflow (<50 %) with evidence of oxygen desaturation (> 3 %) or arousal, and the event lasts at least 10 seconds. The level of OSAS severity is determined by two

factors: the intensity of the individual's daytime sleepiness and the results of the overnight laboratory monitoring, specifically the apnea hypopnea index (American Academy of Sleep Medicine, 1999).

Prevalence and Etiology. OSAS affects 2 % of middle-aged women and 4 % of middle-aged men in the United States (Young et al. 1993). Obesity is present in approximately 70 % of individuals with OSAS and is considered the most prominent, and only reversible risk factor. Though the underlying mechanisms of the association between obesity and OSAS are somewhat unclear, it is hypothesized that increased weight decreases the size of the upper airway, and thus, increases the propensity for apnea events. While obesity is the most common risk factor for OSAS, several other contributors have been identified, including male sex, being over the age of 65 years, post-menopausal status in women, African American race, and certain lifestyle choices (i.e., smoking and alcohol use; Malhotra & White, 2002).

Treatment. Oral appliances and surgical procedures are successful OSAS treatment options in some cases; however, the majority of patients do not receive sufficient clinical benefit from these approaches (Veasey et al., 2006). Continuous positive airway pressure (CPAP) is considered the most consistently effective and preferred treatment for OSAS (Gay et al., 2006). CPAP is comprised of a mask with a harness that fits over the head, a flexible tube, and a pump that provides continuous positive air pressure. The steady positive air pressure to the upper airway keeps it from collapsing during sleep, which typically reduces substantially or completely eliminates nocturnal respiratory disturbances, and thus, reduces sleep fragmentation and nocturnal hypoxemia (American Thoracic Society, 1994). Despite the effectiveness of CPAP

treatment, it is approximated that 25 - 50 % of persons with OSAS will refuse CPAP treatment or will not tolerate it (Zozula & Rosen, 2001).

In their review of alternative and/or supplemental approaches to treating OSAS, Veasey et al. (2006) found that a sufficient degree of weight loss, through dietary modification, can result in substantial improvement in overweight and obese persons with OSAS. Thus, they concluded that weight loss should be regularly recommended for the majority of overweight and obese patients with OSAS. However, they recognized that significant advances in dietary weight loss programs are necessary. Bariatric surgery can be an effective treatment option for some morbidly obese patients with OSAS; however, it can result in serious and potentially fatal complications (Veasey et al., 2006).

Obstructive Sleep Apnea and Neurocognitive Impairment

General Cognitive Functioning. General cognitive functioning can be conceptualized as a global entity comprised of abilities that span across multiple cognitive domains (Strauss, Sherman, & Spreen, 2006). Assessment of general cognitive functioning typically includes tests of general intelligence, or the intelligence quotient (IQ), which Wechsler (1944) defined as “the capacity to act purposefully, to think rationally, and to deal effectively with the environment” (p. 3). Comprehensive batteries assessing general intelligence are widely used; however, they can be time consuming. Thus, measures that estimate intelligence, as well as global cognitive screening measures, are also used to assess general cognitive functioning throughout the existing literature pertaining to OSAS and cognitive functioning.

The impact of OSAS on general intellectual functioning is not conclusive in the literature. Several studies have demonstrated that general intellectual functioning is

spared (Greenberg et al., 1987; Kales et al, 1985; Knight et al., 1987; Redline et al., 1997). However, others have identified relationships between OSAS and indicators of general intelligence (Bédard et al., 1991; Bédard 1993; Berry et al., 1990).

In a study conducted by Kales et al. (1984), the researchers found that 76 % of the 50 participants with severe sleep apnea showed cognitive impairment in one or more domain. However, they did not exhibit impaired overall intellectual functioning, as measured by the Wechsler Adult Intelligence Scale Revised (WAIS-R; Wechsler, 1981), compared to normative data. Moreover, in case-controlled studies completed by Greenberg, Watson, and Deptula (1987) and Redline et al. (1997) no differences were observed between persons with OSAS and matched controls on estimates of the WAIS-R (1981) Full-Scale Intelligence Quotient (FSIQ).

While there is some evidence that OSAS does not impact general intellectual functioning, a study conducted by Bédard et al. (1991) suggested otherwise. These investigators observed that participants with severe OSAS exhibited deficits on the WAIS-R FSIQ and Performance IQ compared to matched controls. Moreover, they observed that participants with severe OSAS demonstrated greater deficits on the FSIQ, Verbal IQ, and Performance IQ compared to participants with moderate OSAS. Additionally, reductions in general intellectual functioning were attributable to the severity of participants' hypoxemia, as opposed to daytime vigilance. Similar results were observed in a correlational study conducted by Berry et al. (1986). Results from this study indicated that severity of nocturnal hypoxemia was associated with Verbal and Performance IQ, such that increasing hypoxemia severity related to decreased performance on these measures.

In a subsequent study, Bédard et al. (1993) found no differences between patients with OSAS and matched controls on the WAIS-R FSIQ or Verbal IQ. However, they reported lower Performance IQ scores among the OSAS patients who were not treated with continuous positive airway pressure (CPAP) compared to those who were. Therefore, this study suggests that OSAS patients may not demonstrate global intellectual impairment compared to normal controls, but following CPAP treatment may show within-subjects improvement. This phenomenon is supported in the literature by other studies that have found improvements in general intellectual functioning following CPAP treatment (Engleman & Douglas, 1993; Engleman et al., 1994; Klonoff, 1987; Montplaisir, 1992).

Overall, the research regarding the relationship between OSAS and general intellectual functioning is mixed. There is some evidence to suggest that OSAS is associated with decrements in general intelligence; however, this has not been consistently observed. In the studies that have demonstrated associations between OSAS and general intelligence, apnea severity, specifically nocturnal hypoxemia, appears to be negatively correlated with intellectual ability. Further, despite the mixed data concerning between subjects differences in global intellectual functioning, there is some evidence supporting within-subjects improvements in this cognitive domain following CPAP treatment.

Attention. Attention consists of a complex network of elements with multiple underlying processes that allow persons to filter relevant and irrelevant information (Strauss, et al., 2006). The processes that underlie attention include sensory selection (e.g., filtering and focusing), response selection (e.g., response initiation and inhibition),

attentional capacity (e.g., arousal and effort), and sustained performance (e.g., vigilance and exhaustibility; Cohen, 1993). Further, attention can be conceptualized as consisting of distinct aspects, including selective attention, sustained attention, and divided attention. Attentional dysfunction can manifest as a variety of deficits in one or more of these components (Strauss et al., 2006).

Attentional functioning is the most commonly assessed cognitive domain in the study of OSAS, and it also appears to be the most consistently impacted in patients with OSAS (Aloia et al., 2004). In their meta-analysis of case-controlled and norm-referenced data, Beebe and colleagues (2003) determined that OSAS markedly impairs vigilance, showing a very large effect size (1.40) in case-controlled data. Several case-controlled studies have found deficits in attention/concentration (Bédard et al., 1991; Bédard et al., 1993; Findley et al., 1986; Greenberg et al., 1987; Naegele et al., 1995; Redline et al., 1997) and vigilance (Bédard et al., 1991; Bédard et al., 1993; Ferini-Strambi et al., 2003; Findley et al., 1986; Munoz et al., 2000; Redline et al., 1997) in patients with OSAS compared to normal controls. Bédard et al. (1991) analyzed the impact of OSAS severity on attention and vigilance, and observed that the level of OSAS severity may differentially impact vigilance performance. They found that patients with severe OSAS showed greater deficits in vigilance than those with moderate OSAS. Similarly, Naegele et al. (1995) showed that sleep fragmentation, as measured by the number of apnea episodes per hour of sleep, correlated with performance on tests of attention/concentration, but nocturnal hypoxemia did not.

Multiple case-controlled studies have demonstrated the impact of OSAS on attentional functioning; the effect of CPAP treatment on this cognitive domain is also

well documented in the literature. A number of studies have demonstrated that CPAP treatment improves attention/concentration (Bédard et al., 1993; Borak et al., 1996; Engleman et al., 1994; Naegele et al., 1998; Montplaisir et al., 1992; Valencia-Flores et al., 1996) and vigilance (Engleman et al., 1993; Ferini-Strambi et al., 2003; Munoz et al., 2000). The majority of these studies conducted follow-up assessments 6-to-12-months after collecting baseline data; however, some studies suggest that even short term CPAP treatment improves attentional functioning. Ferini-Strambi et al. (2003) conducted a study in which they evaluated the effectiveness of short-term and long-term CPAP treatment on cognitive functioning. They observed that after only 15 days of CPAP treatment, OSAS patients' vigilance improved. Moreover, in a placebo-controlled crossover study, Engleman et al. (1994) found that CPAP treatment improved vigilance and attention in a relatively short amount of time (4 weeks) compared to placebo.

Though research suggests short term CPAP treatment improves vigilance and attention, it may require more than one week of treatment to be effective, as evidenced by a study conducted by Bardwell et al. (2001). These researchers assessed the effect of one week of CPAP treatment on the cognitive functioning of persons with OSAS. They observed that one week of treatment improved overall cognitive functioning compared to placebo; however, benefits in specific cognitive domains, including attention/vigilance were not found. Thus, while CPAP treatment can improve vigilance in as little as 15 days, one week of CPAP treatment does not appear to be sufficient for improving attentional functioning in patients with OSAS.

CPAP treatment also failed to show improvements in attentional functioning in a study conducted by Monasterio et al. (2001). These researchers examined the

effectiveness of CPAP treatment compared to conservative treatment (i.e., sleep hygiene) in patients with mild OSAS. The CPAP group showed greater improvements in clinical symptoms of OSAS at 3 and 6-month follow-ups, but significant differences were not observed on measures of cognitive functioning, including attention/vigilance. These results differ from most other studies suggesting attention/vigilance improves following CPAP treatment. This discrepancy could be due to the fact that OSAS patients' baseline values for neurocognitive functioning were normal, as opposed to the majority of other studies in which impaired baseline values were observed.

Taken together, the literature suggests a clear relationship between OSAS and decrements in attention and vigilance. Additionally, some research has highlighted a relationship between apnea severity, specifically sleep fragmentation, and impaired attention and vigilance. CPAP treatment has consistently demonstrated efficacy in ameliorating attentional deficits and can be effective after a brief amount of time.

Executive Functions. Strauss et al. (2006) described executive functions as a set of complex processes mediated by the frontal lobes of the brain. Broadly, they allow persons to respond adaptively to their environment, particularly in novel situations. Executive dysfunction can manifest as a collection of problems in everyday life, such as difficulty with decision-making, problems following through and shifting plans, difficulty in circumstances involving different aspects of memory (e.g., remembering to carry out a goal-directed activity at a later time), and poor organizational ability, among others.

In their meta-analysis, Beebe et al. (2003) found that the domain of executive functioning is substantially impacted by OSAS. These investigators' analyses demonstrated moderate to large mean effect sizes (.53 in norm-referenced data and .73 in

control-referenced data) for this cognitive construct. While this meta-analysis suggests a clear relationship between OSAS and executive functioning, it is difficult to determine the specific meaning of this finding as the methods used to assess this domain vary considerably across studies (Décary et al., 2000). Aloia et al. (2004) acknowledged that several different tests are accepted as measures of executive functioning; however, each assesses a different component of the multiple functional systems within the frontal lobes of the brain. Therefore, although reviews and meta-analyses highlight the associations between OSAS and executive functioning (Aloia et al., 2004; Beebe et al., 2003), they do not elucidate the distinct “functions” affected within this cognitive domain.

In case-controlled studies conducted by Bédard et al. (1991) and Naegele et al. (1995), individuals with OSAS were characterized by deficits in various areas of executive functioning compared to normal controls. Naegele et al. (1995) found that OSAS patients demonstrated deficits on a modified Wisconsin Card Sorting Test (WCST; Nelson, 1976) and the Tower of “Toronto” (Saint-Cyr, Taylor, & Lang, 1988), which assess working memory and planning abilities, respectively. They also reported that errors on the modified WCST were related to the level of nocturnal hypoxemia. Bédard et al. (1991) reported significant differences between OSAS patients and normal controls on many different executive functioning assessments, including those that measure working memory, set shifting, and verbal fluency. They also observed that executive functioning deficits were attributable to the severity of nocturnal hypoxemia.

Among other studies that have addressed the construct of executive functioning, associations have been observed between OSAS and planning difficulties (Greenberg et al., 1987), verbal fluency (Salorio et al., 2002), and set shifting in the face of error (Lee et

al., 1999). Redline et al. (1997) reported that patients with mild OSAS performed significantly more poorly on tests of working memory than controls. However, working memory deficits were not observed in studies conducted by Lee et al. (1999) and Salorio et al. (2002). This inconsistency regarding deficits in working memory could be related to the fact that Redline et al. (1997) assessed working memory with the Digits Backwards Test from the WAIS-R, whereas, Lee et al. (1999) and Salorio et al. (2002) used the WCST.

It is unclear from the literature whether or not deficits in executive functioning improve following CPAP treatment. Some evidence suggests that while CPAP improves certain cognitive deficits associated with OSAS, executive functioning continues to be adversely impacted following treatment (Bédard et al., 1993; Ferini-Strambi et al., 2003; Valencia-Flores et al., 1996; Montplaisir et al., 1992). These investigators argued that the lack of treatment response in functions mediated by the frontal lobes of the brain may be the result of irreversible anoxic brain damage caused by nocturnal hypoxemia. However, this is not a conclusive argument in light of contradictory evidence: A number of studies have observed that executive functioning does improve following CPAP treatment (Borak et al., 1996; Engleman et al., 1994; Engleman et al., 1997; Naegele et al., 1998).

By and large, the literature suggests a relationship between OSAS and impaired executive functioning. However, given the variability across studies in the assessments used to analyze this relationship, the specific aspects of executive functioning that OSAS affects are unclear. There is some evidence to suggest that deficiencies in this cognitive domain are related to nocturnal hypoxemia, as opposed to sleep fragmentation. Several investigators have found that executive functions remain impaired following CPAP

treatment, which suggests that OSAS may cause irreversible anoxic brain damage. However, other researchers have observed that executive functions improve following CPAP treatment. Again, this lack of consistency could be the result of lack of standardization across studies in assessments used to analyze this cognitive domain.

Memory. Memory is a general term that refers to a complex set of processes in which individuals encode, store, and retrieve information. Models of memory typically divide the domain into long-term memory (LTM) and short-term memory (STM). LTM refers to the permanent or long-term storage of information, whereas STM refers to the brief (i.e., seconds), temporary storage of information. Current models of memory include working memory into the construct of STM. Working memory is a limited-capacity store that allows information to be temporarily held and manipulated. Memory dysfunction can occur following injuries or disorders of the brain that either directly impact regions of the brain involved in memory, or brain systems not directly related to memory, but associated with memory functioning (e.g., attention; Strauss et al., 2006).

Like executive functioning, the methods used to assess memory differ markedly across studies (Aloia et al., 2004). Beebe et al. (2003) determined that the impact of OSAS on memory functioning is inconsistent in the literature, and concluded that their mixed meta-analytic results were likely due to methodological problems (i.e., test selection) and inconsistency across studies regarding what specific aspects of memory were tested (i.e., initial learning, storage, retrieval, etc.) Though the literature may not be clear regarding the unique aspects of memory impacted by OSAS, in general, patients with OSAS perform more poorly on tests of memory compared to normal controls (Aloia et al., 2004).

Several studies have highlighted deficiencies in long-term memory (LTM) in persons with OSAS (Bédard et al., 1991; Berry et al., 1986; Findley et al., 1986; Naegele et al., 1995; Kales et al., 1985). These studies demonstrated that patients with OSAS have deficits in the delayed recall of visual and verbal information. Bédard et al. (1991) also found deficits in OSAS patients in both immediate and delayed recall on a measure of visuo-spatial constructional ability and visual memory. While Findley et al. (1986) found that poor performance on immediate recall of verbal and visual information was related to levels of nocturnal hypoxemia, others have observed that these memory deficiencies are related to daytime vigilance (Kales et al., 1985; Bédard et al., 1991).

The majority of studies have reported deficits in the delayed recall of visual and verbal information among patients with OSAS. However, Neagele et al. (1995) contended that the “forgetting curve” could not be accurately interpreted without first considering whether or not the initial learning of information differed between participants. Therefore, these investigators implemented procedures that allowed them to equalize the amount of learning across participants and assess the amount of forgetting per se. They found that OSAS patients do not have “forgetting disabilities,” but rather, that their LTM deficits are associated with learning impairment.

Though several studies have analyzed the impact of OSAS on LTM, fewer have assessed its affect on short-term memory (STM). Kales et al. (1985) found that 50 % of the 22 (total N = 50) participants with OSAS who completed the Wechsler Memory Scale (WMS; Wechsler, 1945) were impaired. Further, the investigators reported that of the entire sample that completed either the WMS, WAIS (Wechsler, 1955), or WAIS-R, 46 % of the participants demonstrated impaired STM and 32 % demonstrated impairments in

LTM. Naegele et al. (1995) reported poorer verbal and visual STM performance in patients with OSAS compared to normal controls. Moreover, through regression analyses, these investigators found that when patients were divided according to markers of severity of OSAS (i.e., number of apneas and hypopneas each hour during sleep and level of nocturnal hypoxemia), Digit Span and Visual Span predicted severity under the apnea-hypopnea index division, whereas only the Digit Span predicted severity under the hypoxemia division. Therefore, these results suggest that patients with severe OSAS perform poorly on the digit span, regardless of markers used to categorize their severity.

Borak et al. (1996) found that CPAP treatment improved visual, spatial, and recent verbal memory, as measured by the Benton Visual Retention Test (BVRT; Benton, 1968) and Rey Auditory Verbal Learning Test (RAVLT; Rey, 1958), respectively. These improvements were observed after only three months of CPAP treatment. Further, Bédard et al. (1991) reported improvements in immediate and delayed verbal memory after 6 months of CPAP treatment. Naegele et al. (1998) demonstrated that after 6 months of CPAP treatment, OSAS patients' learning disabilities improved; however, their short-term verbal and visual memory deficits remained unchanged. Engleman and Douglas (1993) and Engleman et al. (1997) also failed to observe differences in memory following 4 weeks of CPAP treatment, despite improvements in other areas of cognitive functioning. Naegele et al. (1998) suggested that the lack of improvement in short-term memory might be due to the accumulated pathogenic effect of sleep fragmentation and hypoxemia on the brain.

In a study conducted by Valencia-Flores et al. (1996) OSAS patients completed an alertness Multiple Sleep Latency Test and a brief neuropsychological assessment prior

to, and immediately following one night of CPAP treatment in a sleep lab. These investigators observed that performance on the RAVLT increased for participants with increased alertness, but decreased for those with decreased alertness. Thus, the authors concluded that some of the memory deficits associated with OSAS that are moderated by vigilance may be immediately reversible following CPAP treatment.

Taken together, the literature suggests that OSAS is related to memory decrements. However, it is not clear what specific aspects of memory are affected; this is likely a result of the divergent methods used across studies to assess this cognitive construct. The literature points to relationships between OSAS and impaired long-term visual and verbal memory, and there is some evidence to suggest that this relationship is due to learning impairment rather than forgetting disabilities. There also appears to be an association between OSAS and impaired short-term visual and verbal memory. The research is mixed regarding whether or not memory improves following CPAP treatment. Further, the relationship between impaired LTM and markers of apnea severity is not clear as it has been attributed to both nocturnal hypoxemia and sleep fragmentation in the literature.

Motor Functions. Many neurological disturbances involve impaired motor performance; therefore, tests of motor functioning are typically included in neuropsychological assessments (Strauss et al., 2006). Motor performance tests generally assess different aspects of handedness, including speed and dexterity. Deficits in motor ability can have a large impact on an individual's functional capacity, and can result in negative outcomes in the areas of employment and social functioning (Strauss et al., 2006).

Aloia et al. (2004) found that the majority of studies in their review that investigated the relationship between OSAS and motor functions reported impairments in persons with OSAS (Aloia et al., 2004). Based on their review, impairments in OSAS patients' motor functions appear to impact motor coordination, as opposed to motor speed. Similarly, in their meta-analysis, Beebe et al. (2003) reported that OSAS markedly impacted fine-motor coordination, but affected motor speed to a much lesser degree.

Several studies have used the Purdue Pegboard Test (Tiffin, 1968) to assess motor coordination in patients with OSAS (Bédard et al., 1991; Bédard et al., 1993; Greenberg et al., 1987). Greenberg et al. (1987) reported persons with OSAS performed significantly poorer on the Purdue Pegboard Test compared to normal controls. Additionally, they found that hypoxemia severity was correlated with deficits on the motor coordination task.

Bédard et al. (1991) reported similar results. In this study, the investigators compared normal controls to groups of patients with moderate and severe OSAS. The investigators reported statistically significant differences between all groups, such that moderate and severe OSAS patients performed poorer than normal controls, and severe OSAS patients performed poorer than moderate OSAS patients. Moreover, they reported that reductions in motor coordination were attributable to the severity of hypoxemia.

In their study of neuropsychological dysfunction in OSAS patients before and after CPAP treatment, Bédard et al. (1993) observed that motor coordination was impaired in OSAS patients at baseline compared to normal controls. Additionally, they reported that motor coordination continued to be impaired following CPAP treatment. These investigators argued that hypoxemia may result in irreversible anoxic brain

damage, which may contribute to the persistent deficits in this domain of functioning. Further, they contended that since the cognitive deficits found to be irreversible (e.g., motor coordination) are already apparent in patients with moderately severe OSAS (Bédard et al., 1991), individuals with this disorder need to be treated at an earlier stage of OSAS severity in order to avoid irreversible deficits in functioning.

Overall, the literature points to a relationship between OSAS and impaired motor coordination. Multiple investigators have observed associations between impaired motor coordination and nocturnal hypoxemia. Additionally, there is evidence to suggest that motor coordination decrements do not improve following CPAP treatment. Thus, it is possible that the enduring problems with motor coordination observed in OSAS patients are due to irreversible anoxic brain damage.

Neuropathological Mechanisms. Fragmented sleep and nocturnal hypoxemia contribute to the cognitive deficits observed in patients with OSAS; however, research suggests that these factors are differentially related to the neuropsychological sequelae associated with the disorder. While sleep fragmentation seems to be closely associated with attention (Bédard et al., 1991; Naegele et al., 1995) and memory (Bédard et al., 1991; Findley et al., 1986), nocturnal hypoxemia appears to be related to general intellectual functioning (Findley et al., 1986; Montplaisir et al., 1992), executive functioning (Montplaisir et al., 1992; Naegele et al., 1995), and motor coordination (Bédard et al., 1991; Bédard et al., 1993; Greenberg et al., 1987; Montplaisir et al., 1992).

Despite some evidence regarding the differential effects of sleep fragmentation and nocturnal hypoxemia on the cognitive deficits associated with OSAS, there is not a conclusive model among investigators regarding the pathogenesis of such deficiencies

(Aloia et al., 2004). However, changes in vascular function appear to be involved in the underlying processes. Lanfranchi and Somers (2001) argued that the hypoxemia experienced in OSAS results in increased vasodilatation and decreased vascular protective processes, which can eventually lead to changes in the structure and function of blood vessels. Indeed, others have observed relationships between OSAS severity and small vessel white matter disease (Aloia et al., 2001; Colrain et al., 2002), which is typically seen in persons with high blood pressure and type II diabetes. Though there is evidence to support the association between OSAS and aberrant vascular changes, it is unclear how those alterations impair specific domains of cognitive functioning.

Obesity and Neuropsychological Dysfunction

General Cognitive Functioning. Studies that have examined the impact of obesity on general intellectual functioning are largely nonexistent. Many investigators have used subtests from the WAIS (Wechsler, 1955) and WAIS-R (Wechsler, 1981) to measure different aspects of neurocognitive abilities in obese persons, but they have not examined their general intelligence specifically. However, there is one study in the extant literature that assessed this relationship. Chelune et al. (1986), investigated relationships between obesity and Full-Scale IQ scores on the WAIS (Wechsler, 1955). These researchers reported that their sample was of average intelligence, with scores distributed in a pattern similar to the general population. Thus, there is limited evidence to suggest that obesity is not related to deficits in general intelligence, but considering the overall lack of empirical inquiry, this relationship remains unclear.

Though the association between obesity and intelligence is uncertain, there is some evidence to suggest that obesity may be related to global cognitive impairment,

particularly in aging populations (Gunstad et al., 2010; Jeong et al.; 2005). Gunstad et al. (2009) analyzed global cognitive function with the Mini-Mental State Examination (MMSE; Folstein, 1975) and the Blessed Information-Memory-Concentration Test (IMC; Blessed, Tomlinson, & Roth, 1968) in their study of 1,703 individuals (aged 19 to 93 years) from the Baltimore Study of Aging. Using cross-sectional analyses, these investigators found that higher BMI was associated with poorer performance on both the MMSE and Blessed IMC, and higher waist-circumference (WC) and waist-to-hip ratio (WHR) were associated with poorer performance on the Blessed IMC. Their longitudinal analyses showed that BMI did not interact with age on either test of global cognitive functioning. However, WC and WHR did interact with age, and were related to poorer performance on the Blessed IMC over time. Joeng et al. (2005) reported similar results in their study of 467 individuals (ages 65 years and older). These researchers assessed global cognitive functioning using the Korean MMSE (K-MMSE; Kang, Na, & Hahn, 1997). Their results indicated abdominal obesity, as measured by WC, was strongly associated with poor cognition with increasing BMI.

Overall, the impact obesity has on general intellectual functioning is not clear due to the lack of research into this relationship. The extremely limited data available on this topic suggests that the two may not be correlated. There is, however, an increasing body of evidence that illuminates the relationship between obesity and global cognitive impairment in aging populations. Further, abdominal obesity appears to be a salient risk factor for global cognitive impairment in the elderly.

Attention. Research concerning the relationship between obesity and attention deficits has yielded mixed results. Altfas (2002) conducted a study in which the clinical

records of 215 patients seeking obesity treatment were reviewed. The author reported that 27.4 % of the sample had Attention Deficit Hyperactivity Disorder (ADHD), and 42.6 % of the extremely obese participants (i.e., those with a BMI greater than or equal to 40 kg/m²) had ADHD. The author argued that ADHD was highly prevalent among obese persons, especially those who met the criterion for morbid obesity. Though these results are compelling, the study had several methodological limitations. First, the results lack external validity, as 90 % of the sample consisted of middle-aged women. Second, the author based the diagnosis of ADHD on information in the patients' medical records, but not standardized interviews and cognitive testing. Finally, the author did not specify if he controlled for other psychiatric or medical conditions in the analyses that could have confounded the results.

Results from the Altfas (2002) study have not been replicated. On the contrary, some studies have reported no impairments in attention among obese persons. For example, Elias et al. (2003) used the Digit-Span Forward Subtest from the WAIS (Wechsler, 1955) to analyze this relationship, and found no associations between obesity and performance on this test with the following covariate set: age, education level, occupation, mean alcohol consumption, mean cigarette smoking, mean total cholesterol, and type II diabetes. Additionally, their multiple linear regression models combining obesity and hypertension yielded no significant effects for attention.

Elias et al. (2005) also used the Digit-Span Forward Subtest from the WAIS (Wechsler, 1955) to assess this domain of cognitive functioning among persons with obesity and/or type II diabetes. These researchers reported statistically significant, but weak, negative correlations for the performance of obese men and women on this test

with the covariates of age and cardiovascular risk factors. However, these associations were no longer significant for men or women when the covariates of education, occupation, and native language were included in the model.

In their prospective cohort study of 2,223 healthy individuals aged 32 to 62 years at baseline, Cournot et al. (2006) observed a relationship between obesity and attention. These investigators reported that at baseline women performed significantly more poorly on a selective attention test (adapted from the Sternberg test; Sternberg, 1975) as BMI increased when adjusting for age, educational level, diabetes, systolic blood pressure, and perceived health. However, this relationship was not observed in men. Additionally, they found that larger BMI changes in women were related to poorer performance on the selective attention test at follow-up. However, in their longitudinal analyses, after adjusting for age, region of residence, education level, baseline cognitive score, and medical or psychosocial confounders, the association between BMI and progression of attention deficit was no longer significant, and they did not observe any interaction between BMI and gender.

Gunstad et al. (2010) found divergent results in their study of obesity and cognitive functioning. These researchers assessed attention with the Trail Making Test-A (TMT-A; Reitan, 1992). In their cross-sectional analyses, higher BMI, WC, and WHR were associated with faster performance on the TMT-A. Further, their longitudinal analyses demonstrated that increasing obesity was associated with faster performance on the TMT-A as age increased. The investigators offered two potential explanations for these somewhat counterintuitive findings. First, the cognitive impact of intentional dieting could have impacted the performance of those participants at normal and low

weights. However, the researchers were not able to confirm this hypothesis, as data regarding participants' dieting status were not available. Second, the long-term affect of obesity on cognitive functioning may be partially determined by a person's weight across the lifespan.

In summary, several researchers have examined the relationship between obesity and attention, but results have varied significantly across studies. Though multiple studies have found significant relationships between BMI and attentional impairments, these relationships were not significant when covariates (e.g., education, sex, cardiovascular risk factors) were included in the models. One study found that obesity was related to increased attention with age; however, the underlying mechanisms for this relationship are uncertain. Thus, the affect of obesity on attentional functioning is unclear in the literature.

Executive Functions. Several studies have highlighted relationships between obesity and deficits in executive functioning. Gunstad et al. (2007) conducted a study that examined the executive functioning of 408 healthy individuals across the adult life span (20 to 82 years). After controlling for potential confounding variables, these investigators observed that overweight and obese persons (BMI greater than or equal to 25 kg/m²) demonstrated poorer performance on tests of executive functioning (i.e., verbal fluency and planning/rule learning) than normal weight individuals (BMI of 18.5 - 24.9 kg/m²). Gunstad et al. (2010) conducted a similar study in which they analyzed the relationships between obesity indices (i.e., BMI and WHR) and cognitive functioning in 1,703 persons from the Baltimore Longitudinal Study of Aging. Though cross-sectional analyses showed that no associations emerged for obesity indices and an executive functioning

task (i.e., cognitive flexibility), longitudinal analyses demonstrated that higher WHR was associated with poorer performance on the task as age increased. Thus, these results suggest that obesity produces detrimental effects on executive functioning as age increases.

Studies of neurocognitive functioning in morbidly obese persons provide additional evidence for the impact of obesity on executive functioning. Chelune et al. (1986) reported that 50 % of their sample (N = 44) of morbidly obese patients electing for bariatric surgery demonstrated impaired higher-level cognitive problem solving abilities. Additionally, they found that 21 % of patients showed impaired cognitive flexibility. However, they did not consider confounding health factors associated with obesity (i.e., type II diabetes, cardiovascular disease, OSAS) that could have concomitantly influenced patients' performance on these measures. In a more thorough study, Boeka and Lokken (2008) demonstrated that morbidly obese individuals seeking bariatric surgery exhibited impaired executive functioning on tests of planning, problem solving, and mental flexibility. Moreover, they did not find significant differences between morbidly obese patients with and without co-occurring health conditions. Taken together, results from these studies highlight the relationship between morbid obesity and executive functioning impairment.

Waldstein and Katzel (2006) assessed the interactive relationships between obesity indices, blood pressure (BP), and executive functioning performance. In their analyses of 90 healthy, middle-aged and older adults (54 - 81-years-old), they found that individuals with higher BMI and WHR and higher BP performed the most poorly on an executive functioning task that measured response inhibition. However, this relationship

was not observed on a mental flexibility test. These results suggest that the combination of greater WHR and BMI and higher BP has a detrimental effect on executive functioning, specifically, response inhibition.

Overall, the literature suggests a clear connection between obesity and executive functioning deficits. Further, this relationship has been observed after controlling for other potential risk factors (e.g., diabetes, hypertension, OSAS); thus, suggesting obesity is an independent risk factor for deficits in executive functions. The specific aspects of executive functioning affected appear to be verbal fluency, planning, problem solving, and mental flexibility. Some evidence suggests that WHR is associated with impaired executive functioning as age increases. Further, hypertension may moderate this relationship, such that increasing WHR and blood pressure result in poorer executive functioning performance.

Memory. The majority of studies that have analyzed the relationship between obesity and memory have observed impaired memory in obese persons (Cournot et al., 2006; Elias et al., 2003; Elias et al., 2005; Gunstad et al., 2006; Gunstad et al., 2010), specifically, in their visual and verbal memory abilities. Only one study in the extant literature found no relationship between obesity and impaired memory performance (Boeka & Lokken, 2008).

Elias et al. (2003) conducted a study in which they aimed to identify the independent effects of obesity and hypertension on cognitive functioning. These investigators included the Logical Memory (immediate and delayed recall), Visual Reproductions, and Paired Associates subtests from the WMS-III (Wechsler, 1997) in their assessment of memory. In this prospective study of 1,423 participants from the

Framingham Heart Study, the researchers found that obese men performed significantly more poorly than non-obese men on the Logical Memory and Visual Reproductions subtests when covariates (i.e., age, education, occupation, alcohol consumption, cigarette use, total cholesterol, type II diabetes) were included in the model. However, there were no significant obesity effects for women. In the combined hypertension and obesity model, hypertensive obese men showed significantly poorer performance on the Logical Memory and Visual Reproductions subtests than men who were either obese or hypertensive. Elias et al. (2005) carried out a similar study in which they examined both the independent effects of obesity on cognitive functioning, as well as the interactions between obesity and type II diabetes in the same cohort of individuals. In their analyses of the independent effects of obesity, these investigators found that obesity was associated with decrements in visual and verbal memory for both men and women (after adjusting for age). However, with the addition of the covariate set (i.e., hypertension, diabetes, BMI, total cholesterol, cigarette use, education, occupation, and English as a second language), the magnitude of these associations was reduced in men, and no longer significant in women.

Cournot et al. (2006) analyzed the relationship between BMI and cognitive functioning in a prospective study that followed 2,223 healthy individuals aged 32 to 62 years from 1996 to 2001. These investigators observed that BMI at baseline was associated with poorer performance on a word-list learning test (an adapted version of the Rey Auditory Verbal Learning Test [Rey, 1958]) in a linear fashion. Additionally, higher BMI at baseline was associated with significantly higher decline in word-list learning over time. The researchers did not observe any associations between change in BMI and

memory performance. Gunstad et al. (2006) also analyzed the relationships between obesity and performance on a word-list learning task. In their between- subjects analysis, they found that obese individuals demonstrated significantly poorer memory performance when comparing persons across adult lifespan (21 to 82 years) and in younger and middle-aged adults (21 to 50 years). The investigators did not find any interaction between BMI and age on the word-list learning test. However, they did not use an established measure in their assessment of memory performance, nor did they provide reliability and validity statistics for the specific measure that was used. Further, although the investigators reported there were no significant between-group differences for age, estimated IQ, education, anxiety, and depressive symptoms, they did not control for other potential confounding variables (i.e., cardiovascular risk factors, type II diabetes, OSAS) in their analyses. Thus, this study had some potentially significant methodological problems.

In a more methodologically sound study, Gunstad et al. (2010) assessed the relationships between different obesity indices (i.e., BMI, WHR, waist circumference [WC]) and cognitive functioning in 1,703 participants from the Baltimore Longitudinal Study of Aging. They used three measures to analyze memory, including the California Verbal Learning Test (CVLT; Delis, 1987), Prospective Memory Test, and the Benton Visual Retention Test (BVRT; Benton, 1946). In their longitudinal mixed-effects regression models with obesity index, age, sex, years of education, hypertension status, glucose intolerance or diabetes status, and anti-lipid medication used as covariates, they observed that BMI and WHR were related to significantly poorer performance on Prospective Memory, and WC and WHR were associated with significantly poorer

performance on the BVLТ. Additionally, they found a significant interaction between age and all of the obesity indices on the BVLТ, such that performance decreased over time as a function of obesity.

Unlike the aforementioned studies, Boeka and Lokken (2008) did not observe significantly poorer performance on the Logical Memory subtest of the WMS (Wechsler, 1993) and the California Verbal Learning Test- II (CVLT-II; Delis, 2000) among extremely obese individuals (mean BMI = 51.18 kg/m²) compared to normative data. Additionally, they used a series of one-way analysis of variance (ANOVA) tests to investigate relationships between cognitive performance and associated medical problems, including hypertension, type II diabetes, and OSAS. However, they did not find any significant differences with and without these self-reported conditions. Although these investigators examined differences between groups with co-morbid health problems, they did not specifically control for them in their analyses, which could have impacted the results. Moreover, the participants' medical diagnoses were self-reported, and not based on their medical records or examinations done by those involved in conducting the study.

Overall, the literature highlights obesity as a risk factor for visual and verbal memory deficits. Multiple studies have observed that this relationship is apparent even when adjusting for other variables that could impact the association (i.e., hypertension, diabetes, age, etc.). Thus, there is evidence to support the notion that obesity is an independent risk factor for memory deficits, and there is some evidence to suggest that these memory impairments may be more salient in men than women. Further, different

obesity indices may moderate the impact of obesity on memory performance, such that abdominal obesity magnifies the relationship.

Dementia and Alzheimer's Disease. Obesity increases the risk of vascular diseases, and there is mounting evidence connecting vascular diseases, such as hypertension, coronary heart disease, and diabetes mellitus to the development of dementia (Skoog et al., 1996). Considering these associations, several investigators have analyzed the relationships between overweight and obesity and the development of dementia and Alzheimer's Disease (AD). Results from these studies suggest that obesity is a risk factor for dementia and AD (Gustafson et al., 2004; Kivipelto et al., 2005; Razay et al., 2006).

Beydoun, Beydoun, and Wang (2008) conducted a review of the literature pertaining to the relationship between obesity and dementia. Their analysis of 10 studies yielded a significant U-shaped association between BMI and dementia, such that the risk for dementia increased for obese and underweight persons. They also determined that weight gain and high WC, or skin-fold thickness, increased the risk of dementia in the studies analyzed. These investigators concluded that there is a moderate relationship between obesity and the risks for dementia and AD.

Several longitudinal studies have investigated the relationship between body weight and dementia. Gustafson et al. (2003) conducted an 18-year follow-up study that tracked a cohort of 392 Swedish individuals aged 70 to 88 years at baseline. They observed that 93 participants developed dementia. Women who developed dementia between the ages of 79 and 88 years were overweight, and had higher average BMI at age 70, 75, and 79 years compared to non-demented women. Moreover, a higher degree of

overweight was reported in women who developed AD at 70, 75, and 79 years compared to non-demented women. Additionally, for every 1.0 increase in BMI at age 70 years, AD risk increased by 36 %. However, these relationships were not observed in men.

Kivipelto et al. (2005) conducted a study that expanded the findings from Gustafson et al. (2003) to a younger population and suggested obesity is a risk factor for the development of dementia in both men and women. Kivipelto et al.'s (2005) study consisted of analyzing survey data collected from the Cardiovascular Risk Factors, Aging, and Dementia (CAIDE) study. Their sample consisted of 1,449 participants aged 65 to 79 years who participated in follow-up at 21 years, on average. They found that obesity at midlife was associated with the risk of dementia and AD. Moreover, they reported that when hypertension and high total cholesterol level were added to the model, there was a 2-fold increase in the risk of dementia.

A study conducted by Stewart et al. (2005) suggests the relationship between obesity and dementia is also apparent in men. In this 32-year prospective study of 1,890 Japanese American men from the Honolulu-Asia Aging study, increasing BMI was associated with an increased risk for vascular dementia. However, this relationship was not true for AD. These investigators also observed that dementia-associated weight loss occurs prior to the onset of the disease and increases by the time of diagnosis. Razay et al.'s (2006) study examining the relationship between obesity and AD gleaned somewhat contradictory results. They found that the prevalence of obesity was significantly higher in a group of individuals, including men and women, diagnosed with AD compared to normal controls. Moreover, using logistic regression analyses, they observed that obesity was associated with an almost 10-fold increase in the risk of AD. They also observed this

association in underweight persons, with an 8-fold increase in the risk of AD. This study suggests that later-life obesity is associated with the development of AD.

Taken together, the research analyzing the relationship between obesity and dementia suggests that they are correlated. Multiple longitudinal studies have observed relationships between obesity and dementia and AD, such that increasing obesity is associated with increased risk for dementia and AD. Further, when obesity is combined with other risk factors, such as hypertension and high cholesterol, the risk for developing AD increases substantially. The literature also suggests that underweight persons may be at greater risk for developing dementia and AD than normal weight individuals.

Neuropathological Mechanisms. Though explanations regarding the underlying mechanisms relating to obesity and cognitive dysfunction remain unclear, several hypotheses have been posited. First, obesity causes vascular changes that necessitate increased blood flow throughout the body and may prevent optimal blood flow to the brain (Dagenais et al., 2005; Waldstein et al., 2006). An alternative explanation is that obesity can affect glucose tolerance and insulin regulation, and these factors are acknowledged to impair cognitive functioning (Convit et al., 2003; Teunissen et al., 2003). Another perspective is that adipose tissue contains cells that secrete proteins (e.g., leptin), and these proteins may negatively impact cognition when existent at high levels (Gunstad et al., 2008; Harvey, 2007; Wilson et al., 2002). Finally, research has demonstrated associations between BDNF and obesity, as well as memory performance, which suggest that BDNF may be involved in the underlying mechanisms linking obesity to cognitive dysfunction (Gunstad et al., 2008; Hariri et al., 2003).

Several studies have examined the relationship between obesity and structural changes in the brain that result from vascular and metabolic processes. These investigations provide insight into the underlying mechanisms involved in the relationship between obesity and dementia. Convit et al. (2003) found that reduced glucose tolerance was associated with hippocampal atrophy and poor memory performance in a sample of normal elderly individuals. Additionally, Jugust et al. (2005) observed a relationship between obesity and hippocampal atrophy, as well as white-matter hyperintensities. Gustafson et al. (2004) found relationships between overweight and obesity and white matter lesions in elderly women. Finally, Ward et al. (2005) observed an association between BMI and decreased global brain volume. Taken together, these studies provide evidence for the relationship between obesity and changes in brain structure that could affect cognitive functioning.

Summary

Chapter II presented a review of the literature regarding the medical complications associated with obesity, including diabetes, hypertension and cardiovascular disease, cancer, and OSAS. Additionally, an in-depth review of the literature regarding neurocognitive functioning in both obese individuals and those with OSAS was presented. Chapter III will outline the methods, which will include a discussion of the participants, inclusion and exclusion criteria, procedures, measures, and data analyses.

Chapter III: Methods

Participants

Three hundred participants were recruited to participate in a randomized clinical trial, referred to as Project Breathe (Aloia, 2012). Participants for Project Breathe were recruited from the Sleep Center at National Jewish Health (NJH) and were between the ages of 30 to 80 years. All participants were diagnosed with mild to severe OSAS and had no previous history of CPAP treatment. Of the 300 participants recruited for Project Breathe, 102 met the inclusion and exclusion criteria for the present study. Demographic characteristics of the final sample are outlined in Chapter IV.

Inclusion Criteria

The inclusion criteria for participants accepted into the Project Breathe were as follows: 1) 30 to 80-years-old; 2) diagnoses of OSAS based on initial polysomnography (PSG); 3) choice of CPAP as preferred method of treatment; and 4) considered by sleep physicians to be responders to CPAP. Participants were considered responders to CPAP if their apnea-hypopnea index (AHI) was less than 10, they did not snore, and they had an arousal index of less than 10 when titrated with the appropriate CPAP pressure in the sleep lab. An additional inclusion criterion was added for the present study: Participants who demonstrated adherence to CPAP, defined as an average nightly usage of four or more hours over six months of involvement in Project Breathe, were included.

Exclusion Criteria

The exclusion criteria for participants accepted into the Project Breathe were the following: 1) AHI < 15 on the PSG and no daytime functional symptoms or associated cardiovascular disease; 2) PSG confirmation of no OSA diagnosis; 3) diagnosis of a sleep disorder other than OSA that causes arousals from sleep; 4) past treatment of OSAS; 5) current substance abuse; 6) diagnosis of a serious medical condition; 7) significant global cognitive impairment on a brief screening (MMSE < 26/30); 8) history of or current diagnosis of a neurological illness; 9) history of or current diagnosis of a major psychiatric illness, except depression; 10) change in anti-depressant medications over the past three months.

Procedure

The Institutional Review Board at NJH approved Project Breathe. Project Breathe aimed to compare the efficacy of brief behavioral approaches to CPAP treatment on adherence and clinical outcomes. Further details regarding the behavioral interventions and their impact on CPAP adherence will be reported elsewhere as this information is not pertinent to the proposed study.

Research assistants at NJH recruited all study participants. Participants who agreed to be contacted regarding research studies, and who met the inclusion and exclusion criteria (determined by a sleep technician during his/her overnight sleep study at the Sleep Center at NJH), were phoned. They were told that the study was designed to identify methods to improve the response to CPAP treatment and that their use of CPAP would be monitored throughout their involvement in the study. Once participants were recruited, they were scheduled for a baseline assessment at NJH. Research assistants

coordinated with participants' physician and home healthcare company to secure a CPAP device for the participant. The research assistants programmed the CPAP machine with the participants' prescribed pressure, and handed off the CPAP to the patient at the baseline visit. Immediately following the baseline visit participants met with a representative at the home healthcare company who conducted a mask fitting and educated the patient on how to use the CPAP machine.

All participants received an Informed Consent Document, which introduced the purpose of the study, plan, and procedures. Research assistants provided participants with further details and clarification as needed, and made sure they understood the information entirely before signing the document. Participants were given a signed copy of the Informed Consent Document. After signing the document, participants completed the MMSE and the Alcohol Use Disorders Identification Test (AUDIT) to further determine their eligibility to participate in the study. Participants who scored less than 26 out of 30 on the MMSE and/or greater than or equal to 8 on the AUDIT were informed that they would not be able to participate, and they were paid \$25.00 for their time.

Participants completed baseline assessments, which included measures of cognitive functioning, mood, daytime sleepiness, sleep-related functional outcomes, and psychological constructs of behavior change principles. These assessments were repeated at 3, 6, and 12-month follow-up visits after the initiation of treatment. Participants were paid \$50.00 for each follow-up visit. Data from baseline, 3, and 6-month follow-ups were used in the present study.

Measures

A variety of reliable and valid measures were used in Project Breathe to assess cognitive functioning, mood, daytime sleepiness, sleep-related functional outcomes, and psychological constructs of behavior change principles. Those of interest in the present study were primarily related to neurocognitive functioning, but also included measures of anxiety and depressive symptoms as their presence can influence cognitive outcomes. All measures analyzed in the present study are described in detail below.

Demographics. Participants were asked to report their height, weight, age, sex, level of education (in years), ethnicity, employment status and household income, marital status, and whether or not they had any chronic health conditions (e.g., diabetes, hypertension). Participants' BMI and level of OSAS severity were obtained from the PSG report.

American National Adult Reading Test (AMNART; Grober, Sliwinski, & Korey 1991). The AMNART was intended to be used as a covariate in the present study. The AMNART is the American version of the Nelson Adult Reading Test (NART), which was developed in England by Nelson (1982) to approximate premorbid IQ in patients with dementia. The NART requires the reading of irregular words that cannot be pronounced correctly with the typical rules used to navigate spelling and sound (Grober, Sliwinski, & Korey, 1991). These irregular words are used in an effort to amplify the importance of previous familiarity with the words, and to decrease dependence on present ability to use rules to map spelling and sound. IQ estimates based on the reading of irregular words from the NART have been found to be better indicators of premorbid IQ in patients with dementia than estimates based on reading regular words (Nelson &

O'Connell, 1978). The British version includes words and spellings that might be unrecognizable to American English speakers; thus, Schwartz and Saffran (1987; cited in Grober, Sliwinski, & Korey, 1991) developed the American version.

The AMNART was standardized on 109 normal adults ages 40 to 89 years. Schwartz and Saffran (1987; cited in Grober, Sliwinski, & Korey, 1991) demonstrated that predicted IQ from the AMNART highly correlated with WAIS IQ measures when controlling for the impact of education: $r = .72$ for the Verbal Intelligence Quotient, $r = .51$ for the Performance Intelligence Quotient, and $r = .72$ for the FSIQ. These investigators also found that the predicted IQ of patients with AD was no different than the scores of normal controls; whereas, the current IQ of the patients with AD was consistently lower. In similar analyses, Grober and Sliwinski (1991) found that estimated premorbid IQ exceeded current IQ by at least 10 points in patients with dementia, but did not differ for non-demented participants. As the AMNART is a measure of premorbid IQ, these results highlight its construct validity: It would be expected that persons with dementia would perform poorer on a measure of current IQ (i.e., the WAIS) than a measure that assesses their IQ prior to the onset of dementia. The AMNART would not provide an accurate estimate of current intellectual functioning in individuals with dementia; however, its use as an estimate of current IQ in the present study is appropriate as participants were screened for, and excluded, if they met criteria for global cognitive impairment.

Hopkins Verbal Learning Test Revised (HVLT-R; Brandt & Benedict, 2001). The HVLT-R is a brief test of verbal learning and memory. The HVLT-R is a revised version of the HVLT, which was published by Brandt in 1991. The measure was

designed for use with moderately demented patients, particularly in situations that call for repeated neuropsychological evaluations. The measure is comprised of 12-item word lists, which consist of nouns that represent three semantic categories (e.g., musical instruments, spices, four-legged animals). It includes three learning trials, a delayed recall trial, and a yes/no delayed recognition trial.

The administration of the HVLT-R involves the examiner reading the word list aloud and asking the patient to verbally repeat the list of words in any order. The examiner reads the list of words three times, and the patient completes three free recall trials. The examiner records recall performance verbatim after each immediate recall. After a 20 to 25 minute delay, the patient completes one more free recall and a delayed recognition trial. For the recognition trial the participant is asked to identify target words by saying “yes” and non-target words by saying “no.”

The HVLT-R is scored by calculating the sum of correct free recall responses. Minor pronunciation mistakes are counted as correct and added to the total for each recall trial. In addition to the recall totals, including the delayed recall, three additional measures of learning and memory can be calculated. These consist of the Total Recall score (i.e., sum of learning trials 1 to 3), the Percent Retained after the delay (i.e., trial 4 recall divided by the best of trials 2 and 3 [$\times 100$]), and the Recognition Discrimination index (i.e., the number of true positives less the number of false positives). Raw scores are converted to T scores according to age-based tables.

The normative sample for the HVLT-R consisted of 1179 individuals who denied having neurological or psychiatric disorders (Brandt & Benedict, 2001). The mean age of the sample was 59 years ($SD = 18.62$), and ages ranged from 16 to 92 years. The sample

had 2 to 20 years of education, with a mean of 13.47 ($SD = 2.88$). The race and ethnicity of participants was not reported. The authors noted that the distributions for most age groups of the four primary scores (i.e., Total Recall, Delayed Recall, Percent Retention, and Recognition Discrimination Index) were all restricted in range, or significantly skewed. Additionally, there were ceiling effects for some variables, particularly for younger age groups.

In an assessment of 40 older adults who completed different forms of the test with an average time between tests of 6 weeks, Benedict et al. (1998) reported the following coefficients for the main HVLT-R variables: .74 for Total Recall; .66 for Delayed Recall; .39 for Percent Retention; and .40 for the Recognition Discrimination Index. The six alternate forms have demonstrated reliability for the recall trials (Benedict et al., 1998); however, they have shown differences in the false-positive responses on the Delayed Recognition trial. Specifically, Forms 1, 2, and 4 were more difficult on the Delayed Recognition trial than the other Forms. Due to these differences, Benedict et al. (1998) published adjusted norms for the Delayed Recognition trial between forms 1, 2, and 4 and forms 3, 5, and 6. Practice effects have been shown to be minimal: less than 1 point in Total Recall on the second testing (Barr, 2003).

The HVLT-R has demonstrated convergent validity with a similar measure (i.e., CVLT) in a sample of patients with AD (Lacritz, Cullum, & Weiner, 2001). Administration of the first test was performed in the morning and the second in the afternoon for each participant. The investigators found that Total Learning ($r = .36$), Delayed Recall ($r = .62$), Intrusion Errors ($r = .34$), and Recognition Hits ($r = .48$) were moderately correlated between tests. Several researchers have reported that the HVLT-R

is useful in screening for dementia (Hogervorst et al., 2002; Shapiro et al., 1999), and Carey et al. (2004) reported that the HVLT-R is effective in detecting neuropsychological deficits in individuals who have been diagnosed with HIV.

Paced Auditory Serial Addition Test (PASAT; Gronwell, 1977). The PASAT is a serial addition task used to measure working memory, divided attention, and information processing speed (Strauss et al., 2006). There are several different versions of the test available; the version used in this study is the auditory computerized version (Wingenfeld et al., 1999), which consists of four 50-item trials. The PASAT is appropriate to use with a wide range of ages, with norms available for ages 16 to 17 years depending on the version.

The test consists of a random auditory presentation of numbers from 1 to 9. The examinee is instructed to add pairs of consecutive numbers, such that each new number is added to the number that immediately preceded it. For instance, if the stimulus “2” followed by “9” is stated, the examinee would respond “11,” and if the next stimulus is “3,” the examinee would respond “14.” This pattern continues until the end of the trial, which consists of 50 numbers. The speed of the presented stimuli incrementally increases with each set of numbers; thus, decreasing the available response time for each trial.

The PASAT necessitates that the examinee maintains attention, uses working memory by performing mental calculations, and does this at an increasingly faster pace. It is considered a strong measure of divided attention, sustained attention, and working memory (Strauss et al., 2006). The PASAT has demonstrated very high internal consistency in adults ($r = .90$), and it has excellent test-retest reliability ($r > .90$) with

short retest intervals (i.e., 7 to 10 days; McCaffrey et al., 1995) and moderate test-retest reliabilities ($r = .73$) with longer intervals (Schachinger et al., 2003).

The PASAT demonstrates significant practice effects, regardless of the interval between tests. Reports of up to an 18 % increase in scores between first and second tests have been reported (Stuss et al., 1989). However, after the second presentation, practice effects appear to dissipate (Gronwall, 1977). The PASAT is moderately correlated with other measures of attention (O'Donnell et al., 1994) and IQ (Crawford et al., 1998), and highly correlated with tests of mathematical abilities (Crawford et al., 1998). The advantages associated with mathematic aptitude are likely related to reaction time, as individuals with stronger arithmetic skills are able to respond faster, thereby increasing the time interval between items, which allows them to rehearse the previous item (Chronicle & MacGregor, 1998). However, individuals with weaker mathematical skills take longer to respond, and thus, decrease their opportunity to rehearse the previous item (Chronicle & MacGregor, 1998).

Psychomotor Vigilance Task (PVT; Dinges & Powell, 1985). The PVT measures sustained attention and the ability to respond to stimuli in a timely manner. The PVT requires the subject to respond to a small red light stimulus by pressing the response button as soon as the stimulus appears. When the subject presses the response button, the stimulus displays the response time in milliseconds. The subject is instructed to press the button as soon as the stimulus appears, to keep their response time as low as possible, and not to press the button too soon. When the response button is pressed prematurely, the device shows a false start (FS) warning. (Dorian, Rogers, & Dinges, 2005).

The PVT has very minor learning effects (Dorian et al., 2005). Researchers have demonstrated that the sensitivity of the PVT is enhanced by using longer task durations (e.g., 20 minutes; Dinges & Weaver, 2003). As such, the task duration used in the present study was 20 minutes. Many studies have found that the PVT is a valid assessment of the neurocognitive effects of sleep loss on wakefulness as demonstrated in sustained attention, and this measure is commonly used in research related to the cognitive consequences of OSAS (Dorian et al., 2005).

Trail Making Test (TMT; Reitan, 1992). The TMT consists of two parts, A and B, which cumulatively test attention, speed, and mental flexibility. The TMT A entails connecting 25 encircled numbers in consecutive order that are randomly scattered on the page. The TMT B is similar; however, it also has encircled letters, and the examinee is required to alternate between numbers and letters in the proper order. Whereas the TMT A assesses attention, the TMT B is commonly used as a test of cognitive flexibility, as it requires divided attention and alternating sequencing (Strauss et al., 2006). The standard administration procedure involves practice trials for both parts A and B, and the entire test takes about 5 to 10 minutes to administer. Scoring is based on the time in seconds required to complete the task.

The TMT is appropriate to use with individuals ages 15 to 89 years. Performance on the TMT is impacted by age, with decreasing scores as age increases. However, these age-related differences are related to speed, as opposed to accuracy (Backman et al., 2004). Additionally, lower levels of education and lower IQ are associated with poorer performance on the TMT, with lower IQ being more strongly related to decreased performance (Steinberg et al., 2005).

The TMT has demonstrated adequate test-retest reliability for Part A ($r = .79$) and high test-retest reliability for Part B ($r = .89$) in a large sample of individuals aged 15 to 83 years (Dikmen et al., 1999). Practice effects are associated with short intervals between tests (Bornstein, Baker, & Douglas, 1987), but over longer intervals (4 to 24 months) practice effects diminish (Levine et al., 2004). The TMT B correlates moderately well with scores on other tests of processing speed (Royan et al., 2004) and cognitive flexibility (Kortte, Horner, & Windham, 2002).

Adherence. Adherence to CPAP was measured using electronic monitoring equipment. Participants received either a modem that attached directly to their CPAP device and automatically downloaded their usage data, or a microchip that could be removed, and the data were manually downloaded at follow-up visits. Adherence was measured as the amount of time the CPAP device was turned on and the amount of time the mask was properly positioned on the face and maintaining the appropriate prescribed pressure.

Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996). The BDI-II is a 21-item self-report measure of depressive symptoms. The BDI-II reflects the diagnostic criteria for Major Depressive Disorder outlined in the *Diagnostic and Statistical manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR; American Psychiatric Association, 2000). The BDI-II was adapted from an earlier version of the instrument and is one of the most widely used instruments for assessing the severity of depressive symptoms (Steer et al., 1999), which include the following: sadness, pessimism, past failure, loss of pleasure, guilty feelings, punishment feelings, self-dislike, self-criticalness, suicidal thoughts, crying, agitation, loss of interest,

indecisiveness, worthlessness, loss of energy, changes in sleeping, irritability, changes in appetite, concentration difficulty, tiredness or fatigue, and loss of interest in sex. Each item has a list of four statements that are organized in increasing severity regarding a particular symptom of depression, and participants choose one statement that matches their experience in the past two weeks. The BDI-II is appropriate to use with individuals ages 13 to 80 years.

The BDI-II has demonstrated very high internal consistency, with a Cronbach's alpha of .92 for clinical patients and .93 for non-clinical patients. The test-retest reliability with a one-week interval between tests was .93 in a sample of outpatients. Additionally, the BDI-II is highly correlated with its previous version ($r = .93$; Arnau et al., 2001).

Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). The HADS is a self-report measure that consists of anxiety and depression subscales, each of which contain seven items. The HADS was developed to identify anxiety and depression in general medical outpatient populations. The items comprising the HADS were selected to recognize anxiety and depression independent of somatic symptoms, as these are common in patient populations.

The HADS demonstrates good internal consistency, with Cronbach's alpha values of .83 and .74 for the anxiety and depression subscales, respectively (Pallant & Bailey, 2005). In an investigation of the HADS, Bjelland et al. (2002) found that the mean correlation coefficient between the anxiety and depression subscales was .56, which is quite high, and brings into question the dimensionality of the scale. Despite the high correlations between the subscales, the HADS has demonstrated high sensitivity and

adequate specificity in identifying anxiety and depression in patient populations (Pallant & Bailey, 2005).

Data Analysis

Prior to conducting the primary data analysis, participants were categorized as obese or non-obese according to the guidelines established by the WHO (1998), such that those with a BMI of less than 30 kg/m² were considered non-obese, and those with a BMI greater than or equal to 30 kg/m² were considered obese. Preliminary analyses were conducted to define the demographic characteristics of the sample, including age, sex, level of education (in years), ethnicity, employment status, household income, marital status, and the presence of chronic health conditions (e.g., diabetes, hypertension). Preliminary analyses were also performed to determine if differences in these demographic variables, as well as AMNART, BDI-II and HADS scores existed between obese and non-obese participants. Independent samples t-tests were used to analyze these differences.

Due to correlations among dependent variables in the present study, analyses were conducted using univariate, as opposed to multivariate methods. Though the disadvantage of this approach includes an inflation of Type I error, the correlations among dependent variables would significantly reduce statistical power in a multivariate design (Tabachnick & Fidell, 2007). Thus, analysis of covariance (ANCOVA) and repeated measures analysis of covariance (RM-ANCOVA) were the primary methods used for testing the hypotheses of the present study. ANCOVA is an extension of analysis of variance (ANOVA) in which main effects are interpreted after adjusting for one or more covariates. ANCOVA is commonly used to increase the sensitivity of the test of main

effects by accounting for the relationship between the dependent variable and covariate(s) (Tabachnick & Fidell, 2007). RM-ANCOVA is used for longitudinal studies in which the researcher is interested in the effects of treatment over time; both within-subjects and between-subjects differences can be analyzed (Dimitrov, 2009).

The ANCOVA assumptions were tested prior to conducting the analyses. These assumptions included the following: 1) normality of sampling distributions, 2) homogeneity of variance, 3) linearity, and 4) homogeneity of regression slopes. RM-ANCOVA has the additional assumption of sphericity, which was also tested prior to conducting the analyses.

Summary

Chapter III provided a description of the methodology used in the present study. Descriptions of the participants, inclusion and exclusion criteria, procedures, and measures were included. The preliminary and primary analyses that were used to test the hypotheses of this study were also discussed. Chapter IV includes the results of both the preliminary and primary data analyses.

Chapter IV: Results

Chapter IV will highlight the data screening methods used in the present study, including an analysis of missing data, and the process by which theoretically derived covariates were selected for the final models. This chapter will also summarize the methods used to check assumptions of ANCOVA and RM-ANCOVA and the results of these analyses. Finally, results of the preliminary and primary data analyses will be reported.

Data Screening

Missing Data. Missing data is a common problem in longitudinal data analysis; however, the pattern of missing data is more important than the quantity. Missing data are generally categorized according to the following characteristics: missing completely at random (MCAR), missing at random or ignorable non-response (MAR), and missing not at random or non-ignorable response (MNAR). The best scenario occurs when missing values are MCAR as this indicates that the pattern of missingness is unpredictable and not related to the independent or dependent variables. When variables are MAR, the pattern of missing values is predictable based on other variables, and in the case of MNAR, the missing values are related to the dependent variable (Tabachnick & Fidell, 2007).

The pattern of missing data was analyzed using the Missing Values Analysis (MVA) in SPSS 19.0. The following variables were selected for the MVA for baseline, 3,

and 6-month follow-up visits: PVT scores; HVLT Total Recall and Delayed Recall scores; TMT A scores; TMT B scores; and PASAT Total scores. The percentages of missing data for these variables across time points are displayed in Table 1. There were no missing values for the demographic variables of interest in this study; thus, these variables were not included in the MVA.

Table 1		
<i>Missing Data Percentages at Baseline, Three, and Six Month Follow-Ups</i>		
Variable	Time Point	Percentage
PVT	Baseline	13.9 %
PVT	3-month	9.6 %
PVT	6-month	16.5 %
HVLT Trial 1, 2, 3, and Delayed	Baseline	.9 %
HVLT Trial 1, 2, 3, and Delayed	3-month	1.7 %
HVLT Trial 1, 2, 3, and Delayed	6-month	10.4 %
TMT A and B	Baseline	0 %
TMT A and B	3-month	1.7 %
TMT A and B	6-month	10.4 %
PASAT Trials 1, 2, 3, and 4	Baseline	.9 %
PASAT Trials 1, 2, 3, and 4	3-month	1.7 %
PASAT Trials 1, 2, 3, and 4	6-month	10.4 %

Little's MCAR test demonstrated that missing values for all outcome variables were missing in a completely random pattern. Results from Little's MCAR test are outlined in Table 2.

Table 2			
<i>Results of Little's MCAR Test</i>			
Variable	<i>df</i>	χ^2	<i>p</i> value
PVT	9	14.908	.086
HVLT Total Recall	15	11.096	.746
HVLT Delayed Recall	5	3.658	.600
TMT A	3	3.048	.384
TMT B	3	.766	.858
PASAT Total	20	11.482	.933

Tabachnick and Fidell (2007) explained that a small number of data (i.e., 5 % or less) missing in a random pattern from a large dataset (i.e., $N \geq 100$) typically causes less serious problems, and virtually any method used for dealing with missing data yields similar results. Though values were missing at a higher rate than 5 % for the PVT and other variables at the third time point, the data were MCAR. The simplest and most pragmatic way of imputing missing values is through Expectation Maximization (EM); this approach is appropriate to use when missing values are MCAR. EM is an iterative procedure that involves using non-missing variables to impute missing values, and then checks to determine whether that value is the most likely. If the imputed value is not the most likely, a more likely value is re-imputed, and this process occurs until the most likely value is reached. This simple imputation technique can result in underestimated standard deviation and standard error due to the decrease in variation; thus, inferential results must be interpreted with caution (Tabachnick & Fidell, 2007).

Selection of Covariates

Based on the literature review, a large number of variables could impact participants' neuropsychological performance. Ideally, each of these potential sources of variability could have been adjusted for in the analyses; however, there are a number of

assumptions surrounding covariates that need to be assessed before including them in the models. First, covariates should be correlated with the dependent variable, but uncorrelated with each other. Second, the relationship between the covariate and the dependent variable should be the same for all combinations of factors; this assumption is referred to as homogeneity of regression slopes. Covariates need to be selected carefully, as including extraneous covariates can complicate the models and result in reduced statistical power (Tabachnick & Fidell, 2007).

The initial set of covariates was theoretically based and included the following variables: sex, age, baseline BDI score, presence of hypertension, and presence of diabetes. Statistically significant, though weak, negative correlations were observed between age and baseline BDI score $r(100) = -.213, p = .032$, as well as years of education and baseline BDI score $r(100) = -.264, p = .007$. Given the correlations between these variables, their correlations with the dependent variables were analyzed, and the variables most strongly correlated with the outcome variables were selected for inclusion in the models, as recommended by Tabachnick and Fidell (2007). Age and years of education demonstrated statistically significant correlations with dependent variables, whereas baseline BDI score did not. Based on this analysis, baseline BDI score was eliminated from the covariate set.

After analyzing correlations among covariates, as well as covariates and dependent variables, the remaining covariates (i.e., sex, age, years of education, presence of hypertension, and presence of diabetes) were further tested for the assumption of homogeneity of regression slopes to determine whether or not they were appropriate to include in the models. This assumption was tested using SPSS 19.0 by analyzing

interactions between the covariates and the independent variable (i.e., BMI: obese vs. non-obese). Sex demonstrated a statistically significant interaction with the independent variable $F(1, 98) = 6.054, p < .05, \eta_p^2 = .058$. Presence of diabetes also demonstrated a statistically significant interaction with the independent variable $F(1, 98) = 4.064, p < .05, \eta_p^2 = .040$. Thus, the null hypothesis of homogeneity of regression slopes was rejected and these were not appropriate covariates to include in the analyses. After evaluating the potential covariates, the following covariate set was appropriate to include in the analyses: age, years of education, and presence of hypertension.

Once age, years of education, and presence of hypertension were identified as appropriate covariates, it was necessary to test them for the additional assumption of linearity. ANCOVA is based on the assumption that there is a linear relationship between covariates and the dependent variables, and violations of this assumption reduce the power of the statistical test (Tabachnick & Fidell, 2007). This assumption was assessed using the test of linearity within the compare means function in SPSS 19.0. Age demonstrated a linear relationship with all outcome variables that were statistically significant at the $p < .01$ level. However, years of education and baseline HADS score did not demonstrate linear relationships with outcome variables. Tabachnick and Fidell (2007) noted that if covariates do not demonstrate linear relationships, the researcher could consider transforming the variables or removing them from the model. Given the difficulties associated with interpreting transformed variables, these covariates were removed from the models. Based on a thorough analysis of all potential covariates, age and presence of hypertension were determined to be appropriate for inclusion in the analyses.

Assumption Checking for ANCOVA

In addition to the homogeneity of regression slopes and linearity assumptions previously discussed, several other assumptions needed to be checked prior to conducting the ANCOVA, including the assumptions of normality, homogeneity of variance, and linearity (Tabachnick & Fidell, 2007).

Normality. According to Tabachnick and Fidell (2007), assessing continuous variables for normality is an important aspect of screening data for inferential goals. This is also an assumption of ANCOVA and RM-ANCOVA; thus, normality of continuous dependent variables and covariates was assessed by BMI group. Variables and covariates that were screened for normality included age, PVT scores, HVL Total Recall and Delayed Recall scores, TMT A score, TMT B score, and PASAT Total score. Tabachnick and Fidell (2007) recommend assessing normality for large sample sizes by analyzing skewness and kurtosis, as well as visually appraising the distributions. All variables were normally distributed with the exception of those outlined in Table 3.

Table 3				
<i>Normality of Continuous Dependent Variables and Covariates</i>				
Group	Variable	Time Point	Skewness	Kurtosis
Obese	HVLT Delayed Recall	6-month	-.1667	3.098
Non-Obese	HVLT Delayed Recall	6-month	-.1913	3.098
Obese	TMT A	3-month	1.278	3.408
Obese	TMT A	6-month	1.527	2.572
Non-Obese	TMT A	Baseline	1.059	1.227
Non-Obese	TMT A	3-month	1.508	2.775
Obese	PASAT	Baseline	-1.292	1.331
Obese	PASAT	3-month	-1.270	1.284
Obese	PASAT	6-month	-1.424	1.271
Non-Obese	PASAT	3-month	-1.189	.951
Non-Obese	PASAT	6-month	-1.181	.642

The kurtotic distribution of the HVLT Delayed Recall variable was somewhat expected as the maximum score is only 12. The negative skewness of this variable demonstrates that the majority of participants tended to get upwards of 10 points on the Delayed Recall Trial. The same is true of the PASAT Total score, with the majority of participants in both groups earning between 150 to 200 points out of a possible 200 points. The positively skewed and kurtotic distributions of the TMT A scores in the obese and non-obese groups again demonstrates that the majority of participants tended to take between 20 to 40 seconds to complete the task, with fewer participants exceeding that amount of time. Though some variables demonstrated deviations of normality, Dimitrov (2010) noted that ANCOVA is generally robust to violations of the assumption of normality.

Homogeneity of Variance. ANCOVA assumes that the variance of dependent variable values within each cell of the design provides a separate estimate of the same population variance. The homogeneity of variance assumption was tested in SPSS 19.0

using Levene's Test of Equality of Error Variances. This assumption was tested and met for both the ANCOVA and RM-ANCOVA designs as indicated by p values greater than .05. Tables 4 and 5 provide results for this test for both the ANCOVA and RM-ANCOVA.

Table 4		
<i>Levene's Test of Equality of Error Variances for ANCOVA</i>		
Dependent Variable	<i>F</i>	<i>p</i> value
PVT	1.097	.354
HVLT Total Recall	.522	.668
HVLT Delayed Recall	.370	.775
TMT A	1.937	.129
TMT B	1.204	.312
PASAT Total	1.800	.152

Table 5			
<i>Levene's Test of Equality of Error Variances for RM-ANCOVA</i>			
Dependent Variable	Time Point	<i>F</i>	<i>p</i> value
PVT	Baseline	1.097	.354
PVT	3-month	.616	.606
PVT	6-month	.511	.675
HVLT Total Recall	Baseline	.017	.997
HVLT Total Recall	3-month	.970	.413
HVLT Total Recall	6-month	.115	.951
HVLT Delayed Recall	Baseline	.370	.775
HVLT Delayed Recall	3-month	2.399	.072
HVLT Delayed Recall	6-month	.188	.905
TMT A	Baseline	1.937	.129
TMT A	3-month	2.399	.388
TMT A	6-month	.188	.195
TMT B	Baseline	1.204	.312
TMT B	3-month	1.717	.168
TMT B	6-month	.741	.530
PASAT	Baseline	1.800	.152
PASAT	3-month	.931	.429
PASAT	6-month	.792	.501

Assumption Checking for Repeated Measures ANCOVA

By checking the data for the assumptions of ANCOVA, the majority of the assumptions for RM-ANCOVA were also assessed. However, RM-ANCOVA carries the additional assumption of sphericity. When the assumption of sphericity is met, population variances of the differences for all levels of the repeated-measures factor are equal (Dimitrov, 2010). Sphericity was assessed in SPSS 19.0 using Mauchly's Test of Sphericity. This assumption is met when the *p* value of Mauchly's Test of Sphericity is greater than .05. Results from this test are outlined in Table 6.

Table 6			
<i>Mauchly's Test of Sphericity</i>			
Dependent Variable	<i>df</i>	χ^2	<i>p</i> value
PVT	2	2.736	.255
HVLT Total Recall	2	7.334	.026
HVLT Delayed Recall	2	8.971	.011
TMT A	2	.800	.670
TMT B	2	12.061	.002
PASAT	2	48.375	.000

Results from Mauchly's Test of Sphericity indicate that the following dependent variables did not meet the assumption: HVLT Total Recall, HVLT Delayed Recall, TMT B, and PASAT. SPSS 19.0 provides corrected *F* ratios (i.e., Greenhouse-Geisser, Huynh-Feldt, and Lower Bound) for interpretation when the assumption of sphericity is violated. Thus, the corrected *F* ratios were interpreted in cases of this assumption not being met. Girden (1992) recommended using the Greenhouse-Geisser estimate when epsilon (provided by SPSS 19.0) is less than .75 and the Huynh-Feldt estimate when epsilon is greater than .75. Based on epsilon values, the Greenhouse-Geisser *F* ratio was interpreted for the following variables: HVLT Total Recall, HVLT Delayed Recall, and TMT B. The Huynh-Feldt *F* ratio was interpreted for the PASAT.

Preliminary Analyses

Demographic Characteristics of the Sample. Among the 300 participants recruited for Project Breathe, 102 met the inclusion and exclusion criteria for the present study. Participants were 66 men and 36 women. The ethnic breakdown of the sample was as follows: 77 % white, 9 % black or African American, 3 % American Indian, 3 % Asian, 1 % Native Hawaiian, and 7 % identified as "Other." Ten percent of the sample

identified as Hispanic or Latino, and 90 % of the sample identified as not Hispanic nor Latino. The average BMI of the sample was 32.35 ($SD = 6.86$). The age range of the sample was 30 to 76 years, and the average age of participants was 54 years ($SD = 11.20$). Among participants, 1 % were underweight, 9 % normal weight, 33 % overweight, 44 % obese, and 13 % morbidly obese. On average, the sample completed 16 years of education ($SD = 2.84$). Twelve percent of the sample reported a diagnosis of type 2 diabetes, and 42 % reported having hypertension. Participants used their CPAP device for the duration of the six-month study for an average of 6.3 hours each night ($SD = 1.28$). Household income, employment status, and marital status frequencies are outlined in Table 7.

Table 7		
<i>Frequencies for Income, Employment Status, and Marital Status Among the Sample</i>		
Variable	Descriptor	Frequency
Household Income	< \$10,000	3 %
	\$10,000-14,000	3%
	\$15,000-24,999	4 %
	\$25,000-34,999	4 %
	\$35,000-49,000	12 %
	\$50,000-74,000	15%
	\$75,000-99,999	20%
	\$100,000 or more	39 %
	Employment Status	Working Full-Time
Working Part-Time		7 %
Unemployed – Looking		1 %
Unemployed – Not Looking		1 %
Homemaker		3 %
Student		0 %
Disabled		3 %
Retired		14 %
Other		2 %
Marital Status	Never Married	7 %
	Living with Partner	3 %
	Married	70 %
	Separated or Divorced	16 %
	Widowed	4 %

Psychosocial Differences Between Obese and Non-Obese Participants.

Preliminary analyses were conducted to determine if obese and non-obese participants differed on key psychosocial variables, including years of education, estimated intelligence (AMNART score), level of depressive symptoms (BDI-II score), and level of anxiety symptoms (HADS score). A series of independent samples t-tests were performed to identify any group differences in these domains. Given the number of independent samples t-tests being performed, the Bonferroni correction, expressed as $\alpha' = \alpha / k$, was used to minimize the likelihood of making a Type I error (Tabachnick & Fidell, 2007).

Therefore, the alpha level used to determine whether or not the independent samples t-tests were significant was $p < .01$. Table 8 provides a descriptive summary of the aforementioned variables by BMI group. A chi-square test was used to determine if there were significant differences in sex between BMI groups. The percentage of males and females did not differ by BMI group, $\chi^2(1, N = 102) = .409, p > .05$.

Table 8				
<i>Descriptive Statistics for Psychosocial Variables by BMI Group</i>				
Variable	Group	Mean Score	Standard Deviation	Sample Size
Age	Non-Obese	57.86	9.70	44
	Obese	51.81	11.62	58
Years of Education	Non-Obese	16.45	2.96	44
	Obese	15.02	2.59	58
AMNART	Non-Obese	33.70	10.829	44
	Obese	34.47	9.829	58
BDI-II	Non-Obese	10.45	8.30	44
	Obese	12.93	10.71	58
HADS	Non-Obese	20.37	3.03	44
	Obese	20.28	3.28	58

Results of the independent samples t-tests are outlined in Table 9. These results indicate that there was a statistically significant difference between obese ($M = 51.81, SD = 11.62$) and non-obese ($M = 57.86, SD = 9.70$) participants in age, $t(100) = 2.794, p < .01$, such that participants in the obese group were younger than those in the non-obese group. There were no statistically significant differences between BMI groups in years of education, AMNART, BDI-II, or HADS scores.

Table 9			
<i>Results for Independent Samples T-Tests Assessing Differences Between Groups on Psychosocial Variables</i>			
Variable	<i>df</i>	<i>t</i>	<i>p</i> value
Age	100	2.794	.005
Years of Education	100	2.608	.011
AMNART	100	-.372	.711
BDI-II	100	-1.271	.207
HADS	100	.141	.888

Results for Specific Hypotheses

Hypothesis I. Prior to running the ANCOVA, analyses were conducted to determine if differences in PVT and TMT A scores at baseline existed between obese and non-obese participants without adjusting for age and hypertension. Results of the preliminary ANOVA indicate that there was not a statistically significant main effect of BMI on PVT scores $F(1, 100) = .527, p > .05, \eta_p^2 = .005$. Further, there was not a statistically significant main effect of BMI on TMT A scores $F(1, 100) = .001, p > .05, \eta_p^2 = .000$.

ANCOVA's were performed to determine if differences existed between obese and non-obese participants on baseline PVT and TMT A scores. The independent variable was BMI (obese and non-obese), and the covariates were age and hypertension. Table 9 provides a descriptive summary of PVT and TMT A scores among BMI groups. After adjustment for covariates, no statistically significant main effect of BMI was found $F(1, 98) = 2.569, p = >.05, \eta_p^2 = .026$. An additional ANCOVA with the same independent variable and covariates was performed to determine if differences existed between obese and non-obese participants on baseline TMT A scores. Table 10 provides a descriptive summary of TMT A scores among BMI groups. After adjustment for

covariates, no statistically significant main effect of BMI was found $F(1, 98) = 1.061, p > .05, \eta_p^2 = .011$.

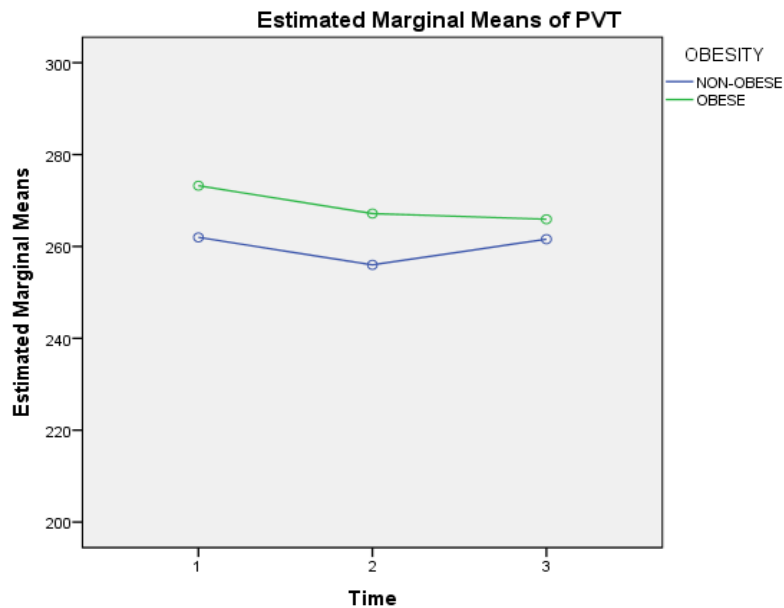
Table 10				
<i>Descriptive Statistics for PVT and TMT A by Group</i>				
Measure	Group	Mean	Standard Deviation	Sample Size
PVT	Non-Obese	265.81	35.464	44
	Obese	270.90	34.842	58
TMT A	Non-Obese	31.20	10.364	44
	Obese	31.28	11.472	58

Preliminary RM-ANOVA tests were conducted to determine if there were differences in PVT and TMT A scores by BMI group following CPAP treatment without adjusting for age and hypertension. Results from the RM-ANOVA indicate that there was not a statistically significant main effect for CPAP treatment over time on PVT scores without adjusting for age and hypertension $F(2, 200) = 2.220, p > .05, \eta_p^2 = .022$. Additionally, without adjusting for age and hypertension there was not a statistically significant interaction between BMI and CPAP treatment over time $F(2, 200) = .849, p > .05, \eta_p^2 = .008$. Finally, no statistically significant differences were found between obese and non-obese participants on PVT scores over time $F(1, 100) = .650, p > .05, \eta_p^2 = .002$. There was a statistically significant main effect for CPAP treatment over time on TMT A scores $F(2, 200) = 11.126, p < .001, \eta_p^2 = .100$, such that scores decreased over time, which indicates improved performance. There was not a statistically significant interaction between BMI and CPAP treatment over time $F(2, 200) = .358, p > .05, \eta_p^2 = .004$, and there were no statistically significant differences between obese and non-obese participants on the TMT A over time without adjusting for age and hypertension $F(1, 100) = .742, p > .05, \eta_p^2 = .001$.

RM-ANCOVA tests were conducted to determine if BMI impacted performance on PVT and TMT A scores following CPAP treatment after adjusting for age and hypertension. Covariates were age and presence of hypertension. Table 11 provides a descriptive summary of PVT scores among BMI groups. There was not a statistically significant main effect for CPAP treatment over time on PVT scores $F(2, 196) = .594, p = > .05, \eta_p^2 = .006$. Additionally, there was not a statistically significant interaction between BMI and CPAP treatment over time for PVT scores $F(2, 196) = 1.079, p > .05, \eta_p^2 = .011$, nor was there a statistically significant difference between obese and non-obese participants on PVT scores over time $F(1, 98) = 2.121, p > .05, \eta_p^2 = .021$. Figure 1 displays PVT scores over time by BMI group.

Table 11				
<i>Descriptive Statistics for PVT at Baseline, 3-Month, and 6-Month Follow-Up by Group</i>				
Measure	Group	Mean Score	Standard Deviation	Sample Size
Baseline PVT	Non-Obese	265.81	39.97	44
	Obese	270.90	34.84	58
3-Month PVT	Non-Obese	260.62	30.08	44
	Obese	265.12	34.93	58
6-Month PVT	Non-Obese	265.87	31.65	44
	Obese	264.81	35.66	58

Figure 1

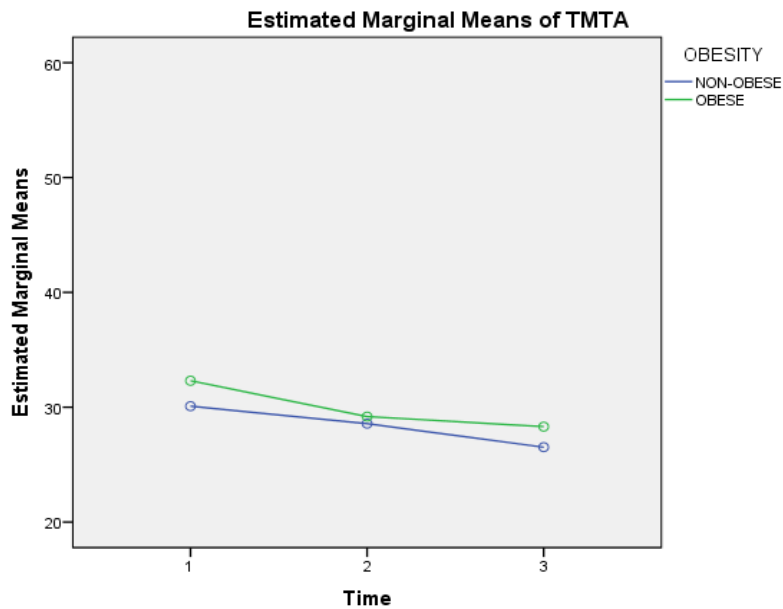


Covariates appearing in the model are evaluated at the following values: Age at time of study = 54.42

Table 12 provides a descriptive summary of TMT A scores among BMI groups. Results from the RM-ANCOVA indicate that after adjusting for age and hypertension there was not a statistically significant main effect for CPAP treatment over time on TMT A scores $F(2, 196) = 1.482, p > .05, \eta_p^2 = .015$. Further, there was not a statistically significant interaction between BMI and CPAP treatment over time for TMT A scores $F(2, 196) = .310, p > .05, \eta_p^2 = .003$, nor were there statistically significant differences between obese and non-obese participants on TMT A scores over time $F(1, 98) = .253, p > .05, \eta_p^2 = .003$. Figure 2 Displays TMT A scores over time by BMI group. Taken together, analyses surrounding TMT A scores indicate that there were statistically significant differences in performance following CPAP treatment, such that performance improved; however, these differences were no longer significant after adjusting for age and hypertension.

Table 12				
<i>Descriptive Statistics for TMT A at Baseline, 3-Month, and 6-Month Follow-Up by Group</i>				
Measure	Group	Mean Score	Standard Deviation	Sample Size
Baseline TMT A	Non-Obese	31.20	10.34	44
	Obese	31.28	11.48	58
3-Month TMT A	Non-Obese	29.57	11.02	44
	Obese	28.36	9.87	58
6-Month TMT A	Non-Obese	28.04	10.42	44
	Obese	27.24	10.96	58

Figure 2



Covariates appearing in the model are evaluated at the following values: Age at time of study = 54.42

Hypothesis II. Preliminary analyses were conducted to determine if differences in PASAT and TMT B scores at baseline existed between obese and non-obese participants without adjusting for age and hypertension. Results of the preliminary ANOVA indicate that there was not a statistically significant main effect of BMI on PASAT scores $F(1, 100) = .601, p > .05, \eta_p^2 = .006$. There was, however, a statistically

significant main effect of BMI on TMT B scores $F(1, 100) = 5.835, p < .05, \eta_p^2 = .055$, such that obese individuals tended to take less time to complete the task than non-obese individuals. Better performance on the TMT B is indicated by less time; thus, results of this analysis are not in the predicted direction.

ANCOVA's were performed to determine if obese and non-obese participants demonstrated differences on baseline PASAT and TMT B scores after adjusting for age and hypertension. Table 13 provides a descriptive summary of PASAT and TMT B scores among BMI groups. After adjustment for covariates, no statistically significant main effect of BMI was found $F(1, 98) = .033, p > .05, \eta_p^2 = .000$.

Table 13				
<i>Descriptive Statistics for PASAT and TMT B by Group</i>				
Measure	Group	Mean Score	Standard Deviation	Sample Size
PASAT	Non-Obese	134.67	44.47	44
	Obese	141.57	44.57	58
TMT B	Non-Obese	78.16	29.73	44
	Obese	64.38	22.51	58

An additional ANCOVA was performed to determine if differences existed between obese and non-obese participants on baseline TMT B scores after adjusting for age and hypertension. No statistically significant main effect of BMI was found $F(1, 98) = 2.520, p > .05, \eta_p^2 = .025$ after adjusting for age and hypertension. Thus, with the inclusion of covariates, differences in TMT B performance between BMI groups did not reach statistical significance.

RM-ANOVA tests were conducted to determine if differences existed in PASAT and TMT B scores between obese and non-obese participants following CPAP treatment without adjusting for age and hypertension. Results from the RM-ANOVA indicate that

there was a statistically significant main effect for CPAP treatment over time on PASAT scores $F(2, 200) = 31.308, p < .001, \eta_p^2 = .238$, such that scores improved over time. Additionally, without adjusting for age and hypertension there was not a statistically significant interaction between BMI and CPAP treatment over time $F(2, 200) = .285, p > .05, \eta_p^2 = .003$, nor were there statistically significant differences between BMI groups on PASAT scores following CPAP treatment $F(1, 100) = .265, p > .05, \eta_p^2 = .012$. There was a statistically significant main effect for CPAP treatment over time on TMT B scores $F(2, 200) = 7.200, p < .001, \eta_p^2 = .067$, such that scores improved over time. However, there was not a statistically significant interaction between BMI and CPAP treatment over time $F(2, 200) = 2.777, p > .05, \eta_p^2 = .027$, nor was there a statistically significant difference between obese and non-obese participants on the TMT B over time $F(1, 100) = 2.318, p > .05, \eta_p^2 = .023$ without adjusting for age and hypertension.

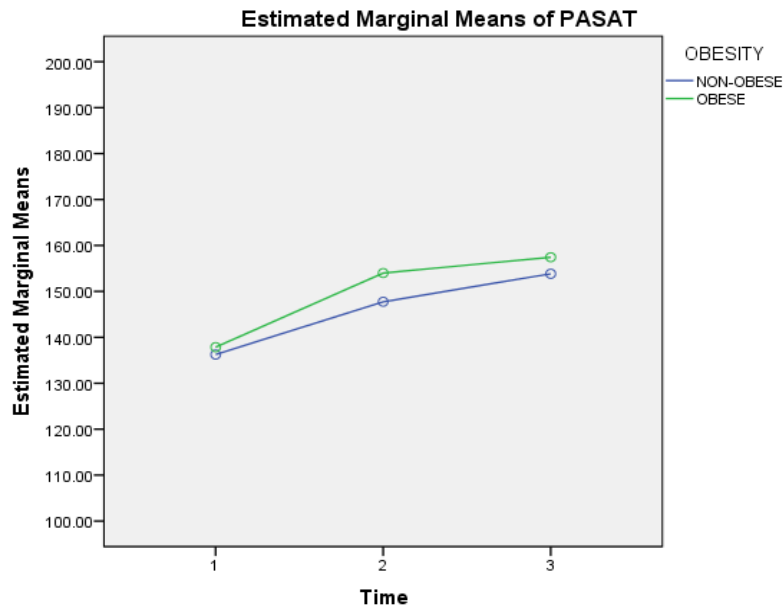
RM-ANCOVA tests were conducted to determine if BMI impacted performance on PASAT and TMT B scores following CPAP treatment after adjusting for age and hypertension. Table 14 provides a descriptive summary of PASAT scores among BMI groups. Results indicate that there was not a statistically significant main effect for CPAP treatment over time on PASAT scores $F(2, 196) = 1.032, p > .05, \eta_p^2 = .010$.

Additionally, there was not a statistically significant interaction between BMI and CPAP treatment over time for PASAT scores $F(2, 196) = .509, p > .05, \eta_p^2 = .005$, nor was there a statistically significant difference between obese and non-obese participants on PASAT scores over time $F(1, 98) = .238, p > .05, \eta_p^2 = .002$. Figure 3 demonstrates PASAT scores over time by BMI group. While there were statistically significant differences in PASAT scores following CPAP treatment, and a statistically significant

interaction between BMI and PASAT scores over time in the preliminary RM-ANOVA models, these differences were no longer statistically significant when age and hypertension were included as covariates.

Table 14				
<i>Descriptive Statistics for PASAT at Baseline, 3-Month, and 6-Month Follow-Up by Group</i>				
Measure	Group	Mean Score	Standard Deviation	Sample Size
Baseline PASAT	Non-Obese	134.67	44.47	44
	Obese	141.57	44.57	58
3-Month PASAT	Non-Obese	145.91	43.74	44
	Obese	156.25	34.47	58
6-Month PASAT	Non-Obese	151.12	42.71	44
	Obese	159.93	36.63	58

Figure 3

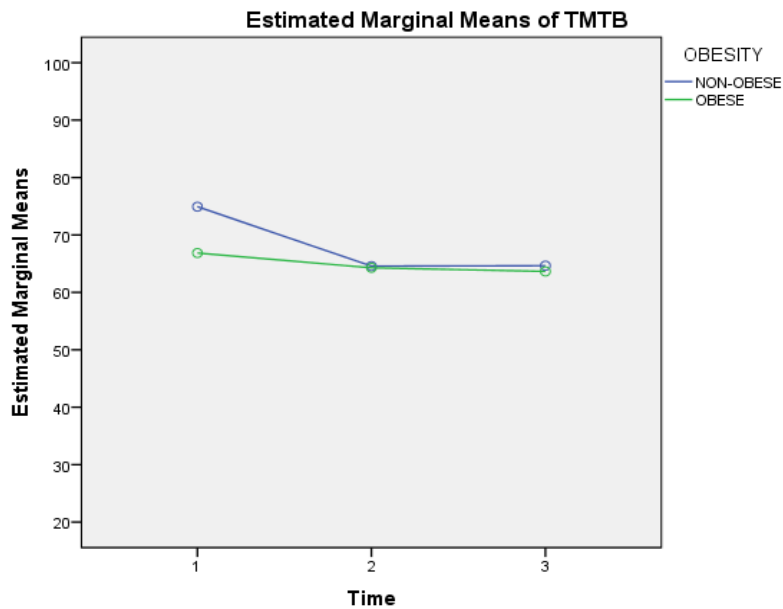


Covariates appearing in the model are evaluated at the following values: Age at time of study = 54.42

Table 15 provides a descriptive summary of TMT B scores among BMI groups. The RM-ANCOVA results indicate that there was not a statistically significant main effect for CPAP treatment over time on TMT B scores $F(2, 196) = 1.123, p > .05, \eta_p^2 = .011$. Additionally, there was not a statistically significant interaction between BMI and CPAP treatment over time for TMT B scores $F(2, 196) = 2.372, p > .05, \eta_p^2 = .024$, nor were there statistically significant differences between obese and non-obese participants on TMT B scores over time $F(1, 98) = .410, p > .05, \eta_p^2 = .004$. Figure 4 demonstrates TMT B scores over time by BMI group. Taken together, these results indicate that while preliminary models showed statistically significant differences in TMT B scores following CPAP treatment, these differences did not reach significance after adjusting for age and hypertension.

Table 15				
<i>Descriptive Statistics for TMT B at Baseline, 3-Month, and 6-Month Follow-Up by Group</i>				
Measure	Group	Mean Score	Standard Deviation	Sample Size
Baseline TMT B	Non-Obese	76.91	29.89	44
	Obese	64.38	22.51	58
3-Month TMT B	Non-Obese	66.16	22.46	44
	Obese	62.31	27.55	58
6-Month TMT B	Non-Obese	67.60	29.06	44
	Obese	61.44	29.79	58

Figure 4



Covariates appearing in the model are evaluated at the following values: Age at time of study = 54.42

Hypothesis III. Preliminary ANOVA's were conducted to determine if there were differences in HVLT Total and Delayed Recall scores between obese and non-obese participants without adjusting for age and hypertension. Results of the preliminary ANOVA's indicate that there was not a statistically significant main effect of BMI on HVLT Total Recall scores $F(1, 100) = .451, p > .05, \eta_p^2 = .004$. Additionally, there was

not a statistically significant main effect of BMI on HVLТ Delayed Recall scores without adjusting for age and hypertension $F(1, 100) = 2.891, p > .05, \eta_p^2 = .028$.

ANCOVA's were performed to determine if differences existed between obese and non-obese participants on baseline HVLТ Total Recall and Delayed Recall scores. Table 16 provides a descriptive summary of HVLТ Total Recall and HVLТ Delayed Recall scores among BMI groups. After adjustment by covariates, no statistically significant main effect of BMI was found $F(1, 98) = .010, p > .05, \eta_p^2 = .000$. An additional ANCOVA was performed to determine if differences existed between obese and non-obese participants on baseline HVLТ Delayed Recall scores. After adjustment by covariates, no statistically significant main effect of BMI was found $F(1, 98) = 1.303, p > .05, \eta_p^2 = .013$.

Table 16				
<i>Descriptive Statistics for HVLТ Total Recall and HVLТ Delayed Recall Scores by Group</i>				
Measure	Group	Mean Score	Standard Deviation	Sample Size
HVLТ Total	Non-Obese	25.61	4.64	44
	Obese	26.27	5.08	58
HVLТ Delayed	Non-Obese	8.73	2.58	44
	Obese	9.60	2.58	58

RM-ANOVA tests were conducted to determine if obese and non-obese participants displayed differences in HVLТ Total and Delayed Recall scores following CPAP treatment without adjusting for age and hypertension. Results from the RM-ANOVA indicate that there was a statistically significant main effect for CPAP treatment over time on HVLТ Total Recall scores $F(2, 200) = 36.225, p < .001, \eta_p^2 = .266$, such that scores increased over time indicating better performance. There was not a

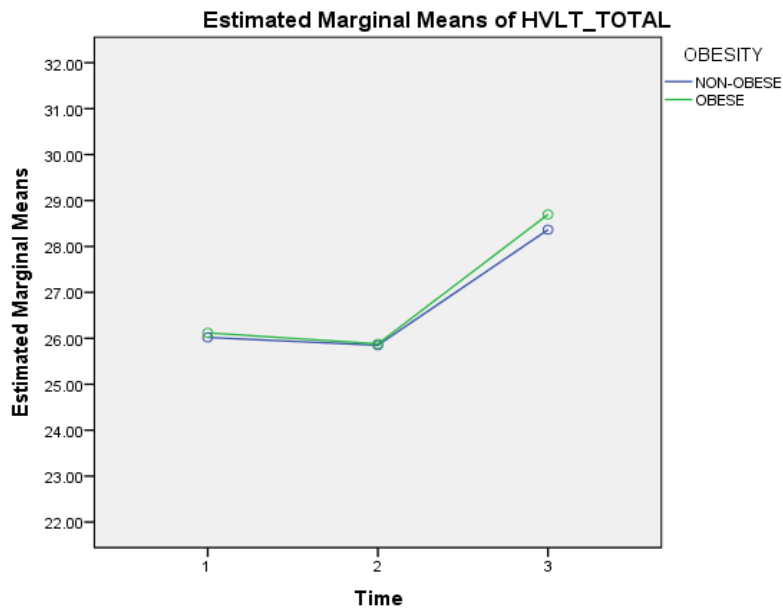
statistically significant interaction between BMI and CPAP treatment over time $F(2, 200) = .068, p > .05, \eta_p^2 = .001$. No statistically significant differences between obese and non-obese participants were found in HVL T Total Recall scores $F(1, 100) = .376, p > .05, \eta_p^2 = .008$. There was a statistically significant main effect for CPAP treatment over time on HVL T Delayed Recall scores $F(2, 200) = 9.621, p < .001, \eta_p^2 = .088$; however, there was not a statistically significant interaction between BMI and CPAP treatment over time on HVL T Delayed Recall scores $F(2, 200) = .790, p > .05, \eta_p^2 = .008$. Finally, there was not a statistically significant difference between obese and non-obese participants on HVL T Delayed Recall scores over time without adjusting for age and hypertension $F(1, 100) = 2.903, p > .05, \eta_p^2 = .028$.

RM-ANCOVA tests were conducted to determine if BMI impacted performance on HVL T Total Recall and HVL T Delayed Recall scores following CPAP treatment. Table 17 provides a descriptive summary of HVL T Total Recall scores among BMI groups. Results from the RM-ANCOVA indicate that there was not a statistically significant main effect for CPAP treatment over time on HVL T Total Recall scores $F(2, 196) = 1.219, p > .05, \eta_p^2 = .012$. There was not a statistically significant interaction between BMI and CPAP treatment over time for HVL T Total Recall scores $F(2, 196) = .100, p > .05, \eta_p^2 = .001$, and was there not a statistically significant difference between obese and non-obese participants on HVL T Total Recall scores over time $F(1, 98) = .028, p > .05, \eta_p^2 = .000$. Figure 5 demonstrates HVL T Total Recall scores over time by BMI group. Overall, there was a statistically significant difference in HVL T Total Recall scores following CPAP treatment, such that scores improved over time; however, these

differences did not reach significance when age and hypertension were included as covariates in the models.

Table 17				
<i>Descriptive Statistics for HVL T Total Recall at Baseline, 3-Month, and 6-Month Follow-Up by Group</i>				
Measure	Group	Mean Score	Standard Deviation	Sample Size
Baseline HVL T Total	Non-Obese	25.61	4.64	44
	Obese	26.27	5.08	58
3-Month HVL T Total	Non-Obese	25.34	4.45	44
	Obese	26.21	5.17	58
6-Month HVL T Total	Non-Obese	27.95	5.04	44
	Obese	28.83	5.04	58

Figure 5



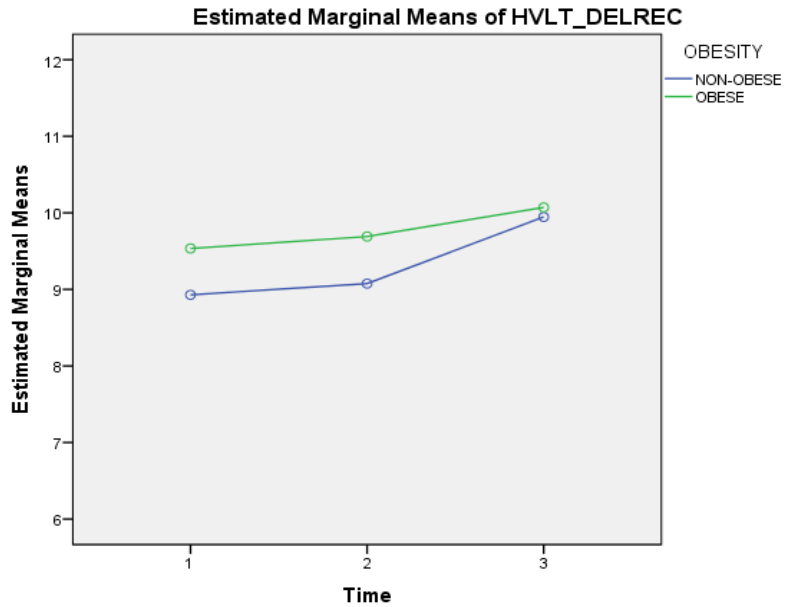
Covariates appearing in the model are evaluated at the following values: Age at time of study = 54.42

Table 18 provides a descriptive summary of HVL T Delayed Recall scores among BMI groups. RM-ANCOVA results indicate that there was not a statistically significant main effect for CPAP treatment over time on HVL T Delayed Recall scores $F(2, 196) =$

1.332, $p > .05$, $\eta_p^2 = .013$. Further, there was not a statistically significant interaction between BMI and CPAP treatment over time for HVLТ Delayed Recall scores $F(2, 196) = .993$, $p > .05$, $\eta_p^2 = .013$, nor were there statistically significant differences between obese and non-obese participants on HVLТ Delayed Recall scores over time $F(1, 98) = .996$, $p > .05$, $\eta_p^2 = .010$. Figure 6 demonstrates HVLТ Delayed Recall scores over time by BMI group. Considered with the preliminary analysis, results indicate that there were statistically significant differences in HVLТ Delayed Recall scores following CPAP treatment, such that performance improved over time; however, these differences did not reach significance after adjusting for age and hypertension.

Table 18				
<i>Descriptive Statistics for HVLТ Delayed Recall at Baseline, 3-Month, and 6-Month Follow-Up by Group</i>				
Measure	Group	Mean Score	Standard Deviation	Sample Size
Baseline HVLТ Delayed	Non-Obese	8.73	2.58	44
	Obese	9.60	2.58	58
3-Month HVLТ Delayed	Non-Obese	8.89	2.59	44
	Obese	9.79	2.19	58
6-Month HVLТ Delayed	Non-Obese	9.72	2.45	44
	Obese	10.20	2.44	58

Figure 6



Covariates appearing in the model are evaluated at the following values: Age at time of study = 54.42

Summary

Chapter IV presented the results of preliminary and primary data analyses for the present study. Differences between obese and non-obese participants in baseline cognitive performance and cognitive performance following six months of CPAP treatment were explored. Results, limitations of the present study, and future directions for research in this area will be discussed in Chapter V.

Chapter V: Discussion

Results

Preliminary Analyses. Preliminary analyses were conducted to determine if there were differences between obese and non-obese participants on key demographic variables. Obese and non-obese participants did not differ in terms of years of education, AMNART, BDI-II, and HADS scores. However, there was a statistically significant difference between the two groups in age, such that obese participants were younger. While obese and non-obese participants demonstrated differences in age, the ANCOVA models were adjusted for age, and thus, these differences did not impact the final analyses.

Hypothesis I. The first hypothesis predicted there would be differences between obese and non-obese participants on baseline PVT and TMT A scores, as well as differences between groups following six months of CPAP treatment, such that obese individuals would demonstrate poorer performance. Results indicate there were not statistically significant differences between obese and non-obese participants on PVT and TMT A scores at baseline. The same result was found after adjusting for age and hypertension. Finally, there were no statistically significant differences between obese and non-obese participants on PVT and TMT A scores over time. This result was the same before and after adjusting for age and hypertension.

There are several hypotheses related to the lack of statistically significant differences between obese and non-obese participants on measures of attention at baseline and following treatment, some of which relate to the study design and analyses and will be discussed in the following section. Another hypothesis relates to the construct of attention and the manner in which it was measured in the present study. Attention was measured using both the PVT, which is a measure of sustained attention and reaction time, as well as the TMT A, which measures immediate focus, sequencing, and to some extent, visual processing. No previous studies have analyzed the relationship between obesity and performance on the PVT specifically; therefore, comparisons between the results of this study and previous research regarding this measure are not possible. However, a study conducted by Gunstad et al. (2010) suggests that obesity does not impact performance on the TMT A, and that obese individuals may demonstrate better performance than their non-obese counterparts: These researchers found that increasing obesity was associated with better performance on the TMT A as age increased. The divergent results found in the present study and by Gunstad et al. (2010) suggest that the relationship between obesity and attention – particularly the aspects of attention measured by the TMT A – is unclear. Continued research in this area is warranted to clarify whether or not obesity negatively impacts attention.

Hypothesis II. Hypothesis Two predicted there would be differences between obese and non-obese participants on baseline PASAT and TMT B scores, in addition to differences between these groups following six months of CPAP treatment. It was predicted that obese individuals would demonstrate poorer performance at baseline and following six months of treatment compared to non-obese individuals. Results indicate

there were no statistically significant differences between obese and non-obese participants on PASAT scores. This result was the same after adjusting for age and hypertension. There were statistically significant differences between obese and non-obese participants on baseline TMT B scores, such that obese individuals performed better on this measure. However, these results did not reach significance after adjusting for age and hypertension. In addition, there were no between group differences on PASAT and TMT B scores over time both with and without adjusting for age and hypertension.

Overall, the results lead to a rejection of hypothesis two. In general, obese individuals demonstrated better performance on PASAT and TMT B scores; however, any statistically significant differences between groups were no longer significant after adjusting for age and hypertension. Therefore, since the non-obese group was older than the obese group, the differences between groups appear to be more attributable to age than BMI. Indeed, working memory abilities are particularly susceptible to decline with age (Strauss, Sherman, & Spreen, 2007). Nevertheless, the lack of differences between obese and non-obese participants on the PASAT and TMT B was unexpected.

The definition of obesity used in the present study could be related to this unpredicted finding. Obesity was defined solely by BMI, which is not an ideal measure, as it does not distinguish fat mass from lean mass, nor does it provide information regarding the distribution of fat. Other researchers have used measures of obesity including WHR and WC, as they provide information on upper body fat, which is highly correlated with the negative health consequences of obesity (Kopelman, 2000). Some evidence to support the hypothesis that differences may not have been detected between

obese and non-obese persons based on BMI is evident in the literature. For example, Gunstad et al. (2010) used two measures of obesity in their study, including BMI and WHR. They found that higher WHR was associated with poorer performance on an executive functioning task (i.e., cognitive flexibility), but the same was not true for higher BMI. Thus, it is possible that an alternative measure of obesity could have yielded different results in the present study. Unfortunately, this additional measure of obesity could not be attained for this project, but considering the limitations of using BMI as the only measure of obesity, future research should include supplemental measures such as WHR or WC.

Hypothesis III. Hypothesis Three predicted there would be differences between obese and non-obese participants on HVLT Total Recall and Delayed Recall scores at baseline and following six months of CPAP treatment, such that obese participants would demonstrate poorer performance. Results indicate there were no statistically significant differences between obese and non-obese participants on HVLT Total Recall or Delayed Recall scores at baseline. These results remained after adjusting for age and hypertension. Additionally, there were no statistically significant between group differences on HVLT Total Recall or Delayed Recall scores following CPAP treatment both with and without adjusting for hypertension.

Taken together, the results lead to a rejection of hypothesis three. The extant literature pertaining to obesity and memory deficits suggests there is a clear relationship between obesity and visual and verbal memory deficits; thus, an explanation for the lack of differences between BMI groups in the present study is not entirely clear. There is evidence to suggest that sex differences moderate the relationship between obesity and

memory impairments, and sex differences were not accounted for in the present study. It was hoped to include sex as a covariate in the final models, but this was not possible due to a significant interaction between obesity and sex, which violates an assumption of ANCOVA. An alternative method for analyzing the data could have been to include sex as a second factor in the models; however, this was beyond the purview of the present study. Nevertheless, the significant interaction between obesity and sex does suggest that there could be differences between obese and non-obese men and women, and this should be explored in future research. Another hypothesis for the lack of differences between obese and non-obese participants on verbal memory in the present study, again, concerns the way obesity was measured. There is evidence to suggest that memory impairments in obese persons may be more pronounced for individuals with abdominal obesity (Gunstad et al., 2010).

Secondary Findings. While the present study's hypotheses concerned differences in cognitive functioning between obese and non-obese participants at baseline and following treatment, the analyses provided secondary results surrounding the overall sample's cognitive functioning over time. Though these findings were of lesser importance in the present study, they were unexpected, and thus, warranted exploration. The secondary results indicate there was not a statistically significant within group difference on PVT scores following six months of CPAP treatment, both with and without adjusting for age and hypertension. There was a statistically significant within group difference on TMT A scores following CPAP treatment, such that scores improved over time; however, these differences did not reach statistical significance after adjusting for age and hypertension. Similarly, there were statistically significant within group

differences on PASAT, TMT B, HVL T Total Recall, and Delayed scores following six months of CPAP treatment, such that scores improved over time. However, these results did not reach significance after adjusting for age and hypertension.

The secondary findings are surprising given the research supporting the efficacy of CPAP treatment in mitigating many cognitive deficits associated with OSAS. One hypothesis for the lack of within group differences over time concerns the sample's baseline level of cognitive functioning. Participants' age and education adjusted mean scores across cognitive measures were in the Average Range. Thus, taken together the sample did not demonstrate the cognitive deficits typically associated with OSAS, and therefore, had less room to improve in their performance over time. Another possible explanation for these results is that the persons involved in the present study had certain protective factors (e.g., many years of education, higher than average household income, access to excellent healthcare) that mitigated the neurocognitive sequelae common among individuals with OSAS. Additionally, participants were recruited for the study immediately following their diagnosis of OSAS. While it is unclear how long participants had OSAS prior to being diagnosed, it is possible that they were diagnosed and treated early enough to prevent the deleterious cumulative effects of sleep fragmentation and oxygen deprivation on their cognitive functioning. Finally, only participants who were minimally compliant to the CPAP were included in the study. There could be important differences between individuals who adhered to treatment and those who did not such as education, motivation, and/or severity of OSAS, all of which could have impacted cognitive test performance.

Limitations

This study has several limitations. First, the majority of the sample was overweight to obese, with only 9 % of the sample falling in the normal weight BMI classification. Therefore, many individuals in the “non-obese” group were actually overweight, and thus, comparisons between groups might be more accurately described as obese vs. overweight. Unfortunately, due to the analyses used, BMI groups needed to be close to equivalent; therefore, it would not have been possible to use more discrete categories for BMI due to the fact that so few participants could be classified as normal weight. Analyses that do not require discrete categorizations of BMI, such as regression, might be more appropriate for future research in this area.

In addition to the problems with the categorization of BMI in the present study, the use of BMI as a measure of obesity, in and of itself, is problematic. BMI, though widely used to measure obesity, is not a highly sensitive measurement in that it does not differentiate between fat mass and lean mass, nor does it indicate the distribution of fat. Further, alternative measures such as WHR or WC, which measure abdominal obesity, have demonstrated greater sensitivity in detecting cognitive differences between obese and non-obese individuals. Thus, WHR and WC may be more appropriate measures of obesity for questions related to cognitive deficits in obese persons and should at least be used as a supplement to BMI in future research.

Another limitation of the present study pertains to the inclusion criteria. Only individuals who were minimally compliant to CPAP treatment were included in the study. This decision was made in order to eliminate potential confounding effects of limited CPAP use on longitudinal research questions. While it was necessary to control

for this variable, only including individuals who were minimally compliant with CPAP treatment significantly reduced the sample size. Additionally, as mentioned previously, individuals who adhered to CPAP treatment may have possessed unique traits that could have impacted cognitive test performance. Rather than only including individuals who were compliant with treatment, it may have been a better choice to statistically control for CPAP usage in the analyses.

In addition to the limitations surrounding the inclusion criteria, the generalizability of the sample is somewhat limited. The sample in the present study was highly educated, with a mean level of education that included four years of post-secondary study. Additionally, over half of the sample had a household income well above the median household income in the United States. Thus, the majority of the sample could afford and had access to the excellent healthcare offered at National Jewish Health, which is a highly regarded respiratory hospital and research center. Overall, there were some unique characteristics about the sample that do not generalize to the larger population of persons with OSAS, and these differences could have impacted the results.

The statistical analyses used in the present study are perhaps one of its largest limitations. It was originally proposed to use Multivariate Hierarchical Linear Modeling (MGLM). There would have been several advantages to using this approach, including accounting for the lack of independence that is inherent in hierarchically organized, longitudinal data. Further, this approach would have allowed for an analysis of growth trajectories and any differences that may have existed in growth over time between obese and non-obese participants. Snijders and Bosker (1999) highlighted several advantages of using MGLM, including the following: 1) it is possible to draw conclusions about the

correlations between the dependent variables; specifically, the degree to which the correlations depend on the individual and group levels; 2) the tests of specific effects for particular dependent variables are more powerful in multivariate analysis (i.e., the standard errors are reduced); 3) testing whether the impact of a predictor variable on a certain dependent variable is larger than the impact on another dependent variable when the data were observed on the same individual is only possible with multivariate analysis; and 4) if a researcher would like to perform a single test of the combined effect of a predictor variable on several dependent variables, multivariate analysis is compulsory. Though MGLM likely would have been a more sophisticated way to analyze the data, the complexities involved in this approach were beyond the scope of this project.

Although the analyses used in the present study were adequate for testing the hypotheses, they presented several problems due to strict assumptions. First, when using ANCOVA, datasets cannot have missing values. As a result of this assumption, missing values were replaced using EM. While this approach is acceptable, it is not ideal and can result in decreased variation and underestimated standard error. Alternative approaches, such as multilevel modeling, do not have this missing data requirement and may be a better option for longitudinal datasets with missing values. Second, ANCOVA has stringent requirements surrounding covariates, which resulted in the elimination of several potentially meaningful covariates in the models (e.g. sex, years of education, presence of diabetes, etc.). Third, as previously mentioned, ANCOVA requires relatively equivalent sample sizes within groups. As a result of this requirement, it was not possible to create several groups that included more than two categories of BMI (i.e., normal weight, overweight, obese, morbidly obese). Thus, the majority of the non-obese group

included individuals who were technically overweight. Being restricted to only having two BMI groups (i.e., obese and non-obese) reduced the naturally occurring variation in BMI as a continuous variable, which could have impacted the findings. Finally, due to correlations among some of the outcome variables, it was not possible to use a multivariate analysis of covariance (MANCOVA) or repeated measures multivariate analysis of covariance (RM-MANCOVA), and as a result, several ANCOVA and RM-ANCOVA models were used. Though MANCOVA and RM-MANCOVA were not appropriate analyses for this study, modeling several ANCOVA and RM-ANCOVA's may have inflated the Type I error rate (Tabachnick & Fidell, 2007).

Another problem related to the data analyses used in the present study involves the level of power and strength of effect sizes, both of which were very small across analyses. As power is the probability of correctly rejecting the null hypothesis when the alternative hypothesis is true, it is important to have adequate power in order to detect differences if they are indeed present (Tabachnick & Fidell, 2007). Given the extremely low statistical power of the analyses used in this study, the likelihood of making Type II errors was high. It is possible that differences did exist between obese and non-obese groups in different areas of cognitive functioning, but the analyses did not have enough power to detect them. Given that archival data was used, it was not possible to recruit a sample large enough to achieve adequate power.

Future Directions

While the hypotheses of the present study were not supported, there is much evidence to support the theory that obese individuals with OSAS demonstrate greater cognitive impairment than normal weight individuals with OSAS, and research in this

area should continue. Due to the inadequate power of the analyses used in the present study, a recommendation for future studies is to address differences in neurocognitive functioning between obese and non-obese individuals with OSAS using a larger sample size. A larger sample size would increase statistical power and reduce the likelihood of making a Type II error, thus increasing the possibility of detecting differences between obese and non-obese individuals if they do exist. In addition to a larger sample, future studies should recruit participants who are representative of the larger population of individuals with OSAS in order for the results to be generalizable.

Another recommendation for future research in this area is to use WHR or WC as a supplemental measure of obesity. BMI in and of itself is an inadequate measure of obesity, or at least abdominal obesity, which appears to be more closely related to the physical and neurocognitive problems associated with obesity. Having WHR or WC would allow for more nuanced analyses and conclusions regarding how the distribution of fat may contribute to different aspects of cognitive dysfunction.

Considering evidence in the literature pointing to sex differences in cognitive functioning between obese and non-obese individuals, as well the significant interaction found between obesity and sex when testing assumptions for the present study's analyses, it is recommended that future research analyze this relationship. It will be important to determine the extent to which sex moderates the relationship between obesity and cognitive dysfunction in the OSAS population, as this knowledge could lead to different gradations in treatment recommendations not only for obese and non-obese persons, but also for males and females.

Conclusions

The objective of this study was to examine differences in cognitive functioning between obese and non-obese individuals with OSAS. Specifically, this study aimed to identify differences between obese and non-obese patients with OSAS both at baseline and over six months of CPAP treatment. This study was the first of its kind and added to the literature concerning the relationships between obesity, OSAS, and neuropsychological functioning. Though this study did not find statistically significant differences in cognitive functioning between obese and non-obese persons with OSAS after controlling for age and hypertension, there were methodological limitations that could have precluded the detection of such differences. Considering the conflicting evidence suggesting obesity could negatively impact the cognitive functioning of individuals with OSAS, continued research in this area is warranted.

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