COGNITIVE DYSFUNCTION IN MIDDLE-AGED ADULTS VS. OLDER ADULTS WITH OBSTRUCTIVE SLEEP APNEA

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The presence of cognitive deficits in obstructive sleep apnea (OSA) is well-documented. Specifically, short- and long-term memory, attention/vigilance, and executive function (e.g. processing speed, mental flexibility, and problem solving) are affected. Cognitive deficits in aging occur in similar areas (i.e., memory and processing speed). Given that a greater percentage of older adults experience sleep-disordered breathing as compared to middle-aged adults, it is possible that OSA may account for some of the deficits typically attributed to aging. This study investigated this hypothesis by comparing middle-aged and older adults with and without OSA on computer-based measures of cognitive performance. No effect of OSA or an interaction between OSA and age on cognitive function was found; an effect of age on processing speed, distinguishing stimuli rapidly, attention, spatial ability/mental flexibility, and both working memory and short-term visual memory was found. This study also explored whether or not cognitive function may be improved in persons with OSA by re-assessing those participants one month after treatment. An effect of treatment on improvements on processing speed, distinguishing stimuli rapidly, mental flexibility, and short term memory was found. Overall, findings reflect the ability of treatment to improve cognitive function among OSA patients, regardless of lack of deficits when compared to those without OSA.

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INTRODUCTION

Obstructive sleep apnea (OSA) is a disorder involving frequent cessation of breathing during sleep, resulting in frequent sleep disruption and drops in oxygen levels. OSA is one of the most prevalent sleep disorders, affecting 22% of the general population (Hiestand, Britz, Goldman, & Phillips, 2006), with prevalence increasing with age (Carskadon & Dement, 1981). OSA is associated with a myriad of cognitive deficits including executive functions, memory, and attention, that many hypothesize result from OSA (Beebe, Groesz, Wells, Nichols, & McGee, 2003). There is considerable evidence that aging also relates to cognitive decline, but many hypothesize this relationship can largely be accounted for by increased medical problems, which also increase with age (Wahlin, McDonald, DeFrias, Nilsson, & Dixon, 2006). Given the evidence that cognitive decline is related to increased medical problems as we age, and OSA increases as we age, it is plausible that OSA may account for cognitive decline among many older adults. Continuous positive airway pressure (CPAP) may reverse this decline and provide for more comparable cognitive performance between middle-aged and older adults. The goal of this study was to evaluate the possibility that OSA causes the cognitive dysfunction commonly associated with aging, which may be reversed with treatment.

Adverse Cognitive Consequences of OSA

Numerous studies have been published over the last few decades that explore cognitive function in OSA. Impairments in attention/vigilance, memory, executive function, and fine motor coordination are typically observed (Decary, Rouleau, & Montplaisir, 2000; Aloia, Arnedt, Davis, Riggs, & Byrd, 2004).

A relatively recent meta-analysis provides a useful summation of the literature to date, comparing patients with OSA to controls in areas such as executive functioning, attention (aka,

vigilance), and memory (Beebe, Groesz, Wells, Nichols, & McGee, 2003). Patients with OSA performed worse on short- and long-term visual memory (d =.56 and d =.55, respectively), general visual ability (d =.68), attention (d = 1.4), motor coordination (d =1.21), and overall executive function (d =.73; e.g., mental flexibility, problem-solving, verbal fluency). Attention/vigilance and executive functioning are substantially affected by OSA, while results indicate that general intelligence and verbal ability remain unaffected. The relationship between OSA and visuomotor skills was too inconsistent to make any conclusions. The findings of the most seminal of these articles are reported in Table 1.

The most representative study was performed by Bedard, Montplaisir, Richer, Rouleau, & Malo (1991), who compared 10 patients with severe OSA, 10 patients with moderate OSA, and 10 healthy controls recruited through either a sleep disorders center or the general population. All patients were given a sleep study and an assessment battery consisting of a reaction time task, the Wechsler Adult Intelligence Scale-R (WAIS), subtests of the Wechsler Memory Scale (WMS), and measures of visual memory, verbal fluency, motor coordination, attention, and mental flexibility. Relatively few tests differentiated controls from moderate OSA patients, notably problem solving, motor coordination, and some aspects of memory. Patients with severe OSA differed from both controls and moderate OSA patients. Patients with severe OSA not only performed worse than controls in the same areas as those with moderate OSA (problem solving, motor coordination, and memory) but additionally performed worse than those with moderate OSA on verbal fluency, mental flexibility and psychomotor coordination. These findings suggest that greater severity of some aspect of OSA is associated with a greater number of deficits. No differences were found between moderate and severe patients on attention and memory, although both groups were impaired compared to normals. Most other studies described

in Table 1 have supported these results, with a positive linear relationship between OSA severity and increased executive dysfunction (Naegele et al., 1995; Roehrs, et al., 1995), but with similar levels of impairment in attention and verbal abilities, particularly verbal memory, among patients with varying OSA severity (Bedard, Montplaisir, Richer, Rouleau, & Malo, 1991).

While considerable evidence for impairments exists, the methodology of the individual studies included in both Table 1 and the meta-analysis described previously varied considerably in rigorousness, and all had a necessarily quasi-experimental nature, which compared some form of OSA or sleep disordered breathing to either a healthy control group or some other equally representative medical group. As opposed to having a true control group as in experimental research, use of these groups designated as "non-equivalent" albeit not randomly assigned or manipulated reduces ability to determine causation. Thus, no definitive statement that OSA directly causes cognitive dysfunction can be made. Also, a few studies used participants who had relatively mild sleep apnea, which understandably would have a milder, and perhaps undetectable, affect on cognitive function. This may make the findings of these studies somewhat questionable, although they do corroborate studies with more rigorous methodology. Overall, however, it is clear from the current literature that OSA and the resultant daytime consequences can have a severe negative impact on quality of life and functioning for patients.

Cause of Cognitive Dysfunction

There is some debate as to whether cognitive dysfunction in OSA patients results from reduced nocturnal oxygen saturation or sleep fragmentation/excessive daytime sleepiness. A recent literature review found that global cognitive functioning was more often associated with hypoxemia rather than fragmentation, while the converse was true for attention/vigilance and memory (Aloia, Arnedt, Davis, Riggs, & Byrd 2004). In general, then, it appears that low oxygen

saturation levels reduce executive function, while excessive daytime sleepiness reduces attention/vigilance and memory (Decary, Rouleau, & Montplaisir, 2000).

Cognitive Reserve

A theory on cognitive reserve states that some people have skills and experiences, such as inherent cognitive abilities and education typically acquired by young adulthood that enable them to better withstand progressive brain deterioration (Freund and Baltes, 2002). This may also be the case with the effect of OSA on cognitive abilities. For instance, a study of OSA patients and controls with either high or normal premorbid cognitive ability found high ability OSA patients and high ability controls performed similarly on various measures of executive function and attention, specifically visual and auditory reaction times, and selective and permanent attention (Alchanatis, Deligiorgis, Amfilochiou, Dionellis, & Orphanidou, 2005). However, normal ability OSA patients performed worse than normal ability controls on these measures. Thus, it appears that an OSA patient's "cognitive reserve," based on an estimate of cognitive ability prior to the onset of OSA, may act as a protective factor against subsequent cognitive performance deficits.

Of interest, some older persons appear to have a buffer against the potentially negative effects of aging on cognitive ability. One theory breaks the buffer concept into three components: selection, optimization, and compensation (SOC; Freund and Baltes, 2002). Selection refers to setting goals, either voluntarily or as a result of barriers to prior goals. Optimization refers to the acquisition of means to achieve of goals. Compensation refers to the use of alternate means when previously acquired means are no longer available. SOC-related behaviors are positively related to multiple successful indicators of aging, including satisfaction with aging and positive emotions (Freund and Baltes, 1998). While SOC composite scores do not

correlate with *g*, nor do measures of verbal intelligence (Freund and Baltes, 2002; Freund and Baltes, 1998), individual optimization scores do correlate with *g* ($r = .18$, $p < .001$; Freund and Baltes, 1998). Moreover, age negatively correlates with SOC after controlling for subjective health (Freund and Baltes, 1998). This suggests that cognitive ability to some extent relates to SOC behaviors, which may buffer against reductions in cognitive ability as persons age. At the same time, the process of aging itself may relate to decreased SOC behaviors such that older persons without higher levels of pre-morbid cognitive ability are more vulnerable to greater declines. Thus, SOC theory aligns well with cognitive reserve theory and may serve to explain more specifically mechanisms of cognitive reserve.

Effects of OSA on Cognitive Function in Older Adults

Several studies have been performed examining the effect of OSA on cognitive function among older adults, which parallel those results found in middle-aged adults (e.g., Berry et al., 1990; Yesavage, Bliwise, Guilleminault, Carskadon, & Dement, 1985). For instance, older adults with an average apnea-hypopnea index (AHI; i.e., number of full or partial cessations of breathing per hour) of 10 or more in one study had decreased delayed recall memory (Berry et al., 1990).

Three studies have examined the relationship between OSA and cognitive function of middle-aged and older adults within the same study, and found no between group differences, but these studies had several flaws (Hayward et al., 1992; Janssens, Pautex, Hilleret, & Michel, 2000; Phillips, Berry, Lipke-Molby, 1996; Yesavage, Bliwise, Guilleminault, Carskadon, & Dement, 1985). Namely, they often included persons below age 60 as "older adults," when many aging researchers define old age as above 65. Secondly, such studies tended to define OSA as the presence of an AHI of greater than or equal to five, when a cutoff of ten is what is used clinically

and in most prevalence studies of apnea (Janssens et al., 2000). For example, one study showed no differences in attention/vigilance at varying AHI cutoffs but defined older as 54 and up (Ingram et al., 1994). Another study concluded that no relationship between OSA and cognitive dysfunction exists among adults over 70; however, in this study the majority of persons had an AHI of 5 or less, which casts doubt on this conclusion (Hayward et al., 1992). Even with such a low AHI range, AHI still correlated with performance on tests of attention, mental flexibility, and problem solving (Hayward et al.). The one study that did the best job of comparing cognitive function of the different age groups found that, among patients with moderate sleep apnea, age did correlate with measures of abstract reasoning, vocabulary, processing speed, and mental flexibility, after controlling for depression, education, and sleepiness (mean age 69.5, SD 6.49) adults (Yesavage, Bliwise, Guilleminault, Carskadon, & Dement, 1985).

Adverse Cognitive Consequences of Aging

Declines in cognitive function are often assumed to be a de facto experience of aging. Indeed, a longitudinal study in the Seattle area over 35 years found changes in cognitive performance over time (Schaie, 1994). A pattern of moderate increases in verbal meaning, spatial orientation, inductive reasoning, number skills, and word fluency from young adulthood to early midlife was found. From that point onward, ability levels decreased, with scores lowest for number skills among adults in their late 80s. Other ability dimensions measured, inductive reasoning, spatial orientation, verbal ability, and verbal memory, similarly appear to increase through midlife, then return to or fall somewhat below young adulthood levels. Additionally, numeric ability remained stable through the mid-40s, then declined. Perceptual speed was the only composite ability to show a linear age related decline. Thus, older adults experienced the greatest cognitive decline in processing numbers and processing quickly, and somewhat lesser

declines in spatial orientation, verbal memory, and reasoning, particularly when compared to midlife. Decreases in functioning tended to occur around age 60, and more definitively by age 67. Overall cognitive ability, or *g*, did not, however, continually decline throughout the lifespan.

Other studies show the same trend for several cognitive abilities to increase throughout childhood and young adulthood, then decline sometime thereafter. Salthouse and Davis (2006) reported that age had a positive effect on crystallized abilities and a negative effect on spatial memory. In general, the single abilities of working memory, verbal memory, spatial memory, as well as speed and other fluid abilities showed the increasing-decreasing pattern, with declines beginning around age 30. Again, ability scores in late life after the decreases approximated those of younger persons (10-20 years old). Unlike the previous study, though, these findings come from cross-sectional data, which means that cohort differences potentially influenced results. .

Early work by Horn & Cattell (1967) also demonstrated an increase in crystallized abilities and a decrease in fluid abilities as age increased. While they did not find changes in processing speed or fluency abilities as Schaie (1994) did, the sample only went up to 61 years of age (Horn & Cattell). Given that Schaie's work notes decrements may occur later than 61, these early findings are not surprising. Indeed, a later longitudinal study called the Baltimore Longitudinal Study of Aging, which included adults up to 102 years of age, found that both scores on the WAIS vocabulary subtest and the Benton Visual Retention Test (BVRT), which measures ability to reproduce a geometric figure using working memory, showed greatest changes beginning in the 64-69 year age period (Giambra, Arenberg, Zonderman, Kawas, & Costa, 1995). While vocabulary scores representative of crystallized intelligence do eventually decline in the old-old likely as a function of age, age accounts for a much greater percentage of performance variability on measures of fluid ability than for crystallized ability (Giambra et al.).

Given the literature on aging, it appears that older adults experience cognitive changes. Abilities such as processing speed, numeric fluency, and other aspects of fluid intelligence decline as age increases. Memory also appears to decline; age has been shown to affect general memory performance over as little as three years (Zelinski, Gilewski, & Schaie, 1993). Evidence further suggests that practice effects and participant dropout have led to serious underestimation of age effects on cognitive performance (Rabbitt, Diggle, Smith, Holland, & McInnes, 2001). However, aging alone, as well as age-related decrements in performance on cognitive assessments, does not appear to sufficiently explain all changes in cognitive ability across the lifespan (Zelinski et al.).

Aging, Medical Problems, and Cognitive Decline

An interaction between age and medical issues may better explain changes in cognitive performance across the lifespan. A study of cognition in over 9,000 older women (mean age = 72) across 15 years found that only 9% maintained an optimal cognitive level, whereas 58% saw a minor decline and 33% saw a major decline (Barnes et al., 2007). Importantly, absence of a medical condition and better health ratings predicted maintenance of optimal cognitive function. Likewise, a longitudinal study of 386 persons ages 61 to 95 confirmed age related decrements in perceptual and verbal speed, reasoning, and working and episodic memory (Wahlin, McDonald, DeFrias, Nilsson, & Dixon, 2006). The authors concluded that poor health may reduce cognitive function so greatly that aging effects are not as readily apparent among this group. Additionally, health accounted for an average of 30% of the variance in age-related cognition.

Recent research among older adults (e.g. those 65 and over) on measures of sleep problems found that persons who endorsed more concerns related to sleep had poorer overall cognitive performance, abstract reasoning, mental flexibility and short term memory (Neves,

Buysse, Halligan, Houck, & Monk, 2009). Although this study did not assess or control for OSA, the authors described their research as preliminary, suggesting future studies should specifically target OSA.

Although some studies have shown that it is possible to reverse the cognitive deficits seen in aging (Hayslip & Maiden, 2005; Boron, Turiano, Willis, & Schaie, 2007), none have examined what would happen if an intervention eliminated the health problems associated with those same cognitive deficits. This type of study would help determine if a portion of the deficits that accrue with aging are, in fact, secondary to health problems (i.e., OSA in the current study).

Reversibility of Cognitive Dysfunction in OSA

Treatment of OSA may reverse the cognitive dysfunction observed with OSA. The gold standard of treatment for OSA is CPAP, which provides a steady stream of air into the patient's nasal and/or oral openings. Essentially, a blower unit moves the air to the patient via a hose held in place by some form of mask. Years of research have supported the beneficial effects of CPAP on the reduction of symptoms such as AHI and nocturnal awakenings, as well as on EDS. CPAP may also reverse some of the cognitive deficits found in middle-aged OSA patients when compared to patients who received either a sham CPAP or within groups design.

Studies of short duration show early improvement after initiation of CPAP. CPAP for as little as two nights can increase auditory verbal learning and visual retention for patients with significant sleepiness (Valencia-Flores, Bliwise, Guilleminault, Cilveti, & Clerk, 1996). Two nights can also increase attention scores among non-hypoxemic OSA patients, indicating that cognitive improvement with initial CPAP use relates more to reversal of sleepiness (Valencia-Flores et al.). For those already on CPAP, going off for one night did not lead to cognitive decline, but a trend for decreased vigilance was found (Kribbs et al., 1993).

After one week of CPAP treatment, scores across an entire neuropsychological battery, especially vigilance, were shown to improve among middle-aged adults (Bardwell, Ancoli-Israel, Berry, & Dimsale, 2001). After two weeks, reaction time, spatial learning, and constructional ability improve; these improvements remained after four months, but no further improvements were observed (Ferini-Strambi et al., 2003). In general, CPAP of short duration improves attention and some aspects of visuospatial processing. It is important to note that all of these studies were performed in individuals who were mostly middle-aged (i.e. mean age [46-57]).

Longer studies lasting multiple months do not show consistent improvements. A three month follow-up found that CPAP increases vigilance for OSA patients compared to controls, with further increases at 12 months (Munoz, Mayoralas, Barbe, Pericas, & Agusti, 2000). Another three-month study found CPAP improved visual/spatial learning and verbal learning for males, and that by 12 months these improvements remained, and speed of task completion improved (Borak, Cieslicki, Koziej, Matuszewski, & Zielinski, 1996). Around six months, CPAP increased Stroop scores, mental flexibility, and visual long-term, but not short-term memory (Naegele et al., 1998). In contrast, Bedard, Montplaisir, Malo, Richer, and Rouleau (1993) found that CPAP at six months improved short-term memory. Controls were age and gender matched to the ten male patients aged 35 to 65 who participated. Among patients with higher AHIs, CPAP may not affect IQ scores (Borak et al.). Thus, similar to short-term use, long-term CPAP can improve attention, mental flexibility and visuospatial function, but no consensus exists as to verbal and memory function. Again, most participants were middle-aged.

A series of studies by Engleman and colleagues compared CPAP treatment to an oral placebo with a total of four weeks on CPAP and concluded CPAP has more beneficial effects among those with a low AHI. Among a range of AHIs in middle-aged adults, CPAP improved

measures of vigilance, mental flexibility, and coding speed, and reduced the degree of overall cognitive deficit compared to placebo, although CPAP did not affect verbal fluency (Engleman, Martin, Deary, & Douglas, 1994). Specifically in persons with mild apnea (AHI <15), CPAP improved mental flexibility, and in a larger sample also improved coding speed and working memory (Engleman, Martin, Deary, & Douglas, 1997; Engleman et al., 1999). For persons with an AHI of 15 or higher, CPAP had no significant effect when compared to placebo, although in several areas, including vigilance, working memory, and visuospatial ability, differences favored CPAP (Engleman et al., 1998). Additionally, while analyses were not run, it appears that CPAP improved scores compared to baseline as well (Engleman et al., 1998). While these studies document a statistically significant benefit of CPAP only for those with mild OSA, CPAP may provide potentially clinically significant benefits to OSA patients of all severities.

CPAP may preferentially affect older adults than younger adults, in that they may have additional room for cognitive improvement. Yet only one study has explored CPAP in older adults (with a mild-moderate AHI of 10 or more). Patients were tested before and after three months of CPAP treatment (Aloia et al., 2003). Patients with six plus hours of CPAP use nightly had increased psychomotor skills, visuospatial memory and complex attention, and decreased reaction time compared to those who used CPAP for less than six hours nightly. Unfortunately, the *N* for this study was small at 12, and results may have been compromised as half the participants completed a behavioral intervention as part of another concurrent study. Additionally, this study defined older as above 55; as a result, no known study to date has addressed CPAP for cognitive symptoms in adults 65 and up.

Statement of the Problem

Areas affected in OSA include executive functions, specifically problem solving, mental flexibility, and processing speed. Aspects of memory, such as visual memory and possibly working and short term memory, as well as attention, are also affected. Interestingly, cognitive deficits in older adults compared to middle aged adults include problem solving/reasoning, processing speed, and spatial orientation; aspects of memory are also impaired. Thus, there is an overlap between cognitive deficits in both OSA and older adults. To date, no published study has directly compared this overlap or compared the effect of treatment of this medical condition on these areas of cognitive function between middle-aged and older adults. This study addressed both of these issues and filled a significant gap in the current literatures on both OSA and aging: the specific inclusion of adults 65 and over.

Statement of the Hypotheses

Experiment I: It was hypothesized that at baseline, older adults would perform worse on cognitive measures than middle-aged adults, that OSA patients would perform worse than normals, and that age group and OSA status would interact such that older persons with OSA would have the worst cognitive performance. Experiment II: In the OSA group, it was hypothesized that both age groups would show improvement in cognitive performance after one month of CPAP treatment, but that older adults would show greater improvements than middle-aged adults, such that there would be no differences between older and middle-aged adults on cognitive performance after one month of CPAP therapy.

For both hypotheses, based on previous research (Beebe, Groesz, Wells, Nichols, & McGee, 2003), it was expected that significant deficits and improvements in terms of cognitive function would be evident on measures of attention, short-term memory, processing speed,

problem solving and mental flexibility. In the spirit of cognitive reserve theory, it was hypothesized that persons with lower baseline cognitive function would improve more than persons with higher baseline cognitive function.

EXPERIMENT 1

Methods

Participants

This study recruited participants for four groups: older adults (ages 65+) with and without Obstructive Sleep Apnea (OSA), and middle-aged adults (35-55) with and without OSA. A power analysis using the effect sizes determined by Beebe, Groesz, Wells, Nichols, & McGee (2003) suggested that for comparisons of executive function to have power of .80 with an alpha level set at .05, 62 participants would be needed for a two-tailed analysis. For comparisons of attention with the same power and alpha level, only 20 participants would be needed. Thus, the goal was to recruit at least 15 participants for each condition, with a total of at least 60 participants. IRB approval for the study and all materials used were obtained prior to data collection, and informed consent was obtained prior to participation in the study; participants were advised of the possible benefits and potential risks/discomfort, were told about the study and their right to withdraw, and given contact information for the primary investigator as well as a copy of the informed consent sheet.

Materials

Independent Variables

The independent variables included age group (either older adult ≥ 65 years old vs. middle-aged = 40-60 years old), and OSA status (presence vs. absence). The operational definition of OSA is described in more detail in the procedures section.

Covariates

Covariates were measured using a self-report survey. Depression and anxiety measures were included in the survey as covariates based on prevalence rates up to 63% and up to 70%,

respectively, among persons with OSA (Saunamaki & Jehkonen, 2007), combined with awareness of the potential affects of depression and anxiety on cognitive function (Sternberg & Jarvik, 1976; Eysenck, Derakshan, Santos, & Calvo, 2007). Sleepiness can similarly effect performance (Dolan & Rosenthal, 2007) and so a measure of both subjective daytime and nighttime sleepiness was included. In light of both cognitive reserve theory and Baltes' SOC theory, both measures of premorbid function and of the components of SOC were also included as covariates. In addition, a screener for cognitive impairment was used to preclude persons with dementia from participating, which could artificially lower group mean scores on cognitive assessments and confound determination of between-group differences, although no potential participants obtained scores indicative of possible dementia or cognitive impairment.

Depression. The Geriatric Depression Scale short form (GDS-15) consists of 15 yes/no items of the original 30 items that had the highest correlations with symptoms of depression (Sheikh & Yesavage, 1986). The GDS-15 was found to correlate .84 with the full version (Sheikh & Yesavage). Among depressed older adults, the correlation has been found to be higher at .90 (Lesher & Berryhill, 1994). The GDS-15 has differentiated depressed from non-depressed older adults among several samples (Friedman, Heisel, & Delevan, 2005; Lesher & Berryhill). The best cutoff for the short-form to indicate depression is 7, where sensitivity is 83% and specificity is 73% (Lesher & Berryhill). Among a sample of 960 community dwelling cognitively intact older adults (65+) who reported some functional impairment, which is associated with late-life depression, Cronbach's alpha was .75 (Friedman, Heisel, & Delevan). The GDS was not developed for use in dementia patients and therefore has lower sensitivity and specificity among this population (Camicioli & Wild, 2006).

Anxiety. The anxiety measures included the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988) and the Health Anxiety Questionnaire (HAQ; Lucock & Morley, 1996). The BAI was created from a pool of three earlier anxiety instruments, after which principal factor analyses reduced the total number of items to 21. Items are rated on a 0 to 3 point Likert-type scale. The BAI has an alpha coefficient of .92, item total correlations that range from .30 to .71, and discriminant validity as determined by low correlations with measures of depression (Beck et al., 1998). The HAQ looks at several aspects of health including health worries and health interference with life, and has an alpha coefficient of .92, and test-retest reliability after six weeks of $r = .87$ (Lucock & Morley, 1996). A between-groups ANOVA among nurses, a lay group, and psychological and medical patient groups found significant differences between the groups, demonstrating discriminant validity for this scale.

Sleepiness/fatigue. The survey also included the Excessive Daytime Sleepiness and Nocturnal Sleepiness subscales of the Sleep-Wake Activity Inventory (SWAI-EDS and SWAI-NS), which has been validated against objective measures of sleepiness (Rosenthal, Roehrs, & Roth, 1993). The SWAI-EDS has a fairly strong internal consistency reliability of .89, while the SWAI-NS has only a moderate alpha of .69. The items of the subscales are rated on a Likert-type scale from 1 (always) to 9 (never) and consist of nine and three items, with total possible scores of 81 and 27, respectively. The subscales are reverse scored such that higher scores indicate less sleepiness. A study of 100 consecutive patients being evaluated for OSA showed that a SWAI-EDS score of ≤ 50 has a sensitivity of 77% and a specificity of 56% in detecting patients with a multiple sleep latency test score of ≤ 5 minutes (the MSLT is the gold standard of objective sleepiness measurement; Guido, Rosenthal, Bishop, Roehrs, Michaelson, Syron, &Roth, 1995). The Fatigue Severity Scale (FSS), a 9-item unidimensional measure of fatigue in the past week,

will also be included (Krupp, LaRocca, Muir-Nash & Steinberg, 1989). The items are rated on a Likert-type scale from 1 (strongly disagree) to 7 (strongly agree) based on the experiences of the previous week, with a total possible score of 63. The FSS has an internal consistency of .88, and has strong evidence of test-retest reliability. Importantly, the FSS has been shown not to correlate with daytime sleepiness (Lichstein, Means, Noe & Aguillard, 1997).

Educational level. In order to obtain a proxy for premorbid cognitive function, educational level was assessed several ways. First, participants were asked in an open-ended format how many years of education they have completed. Second, participants were asked to select their highest degree completed, from high school diploma to a doctoral-level degree. In the context of cognitive reserve theory, use of educational level as a measure of premorbid ability was found to enable detection of differential disease progression among a group of older Alzheimer's patients, where greater educational level was associated with greater physical neurological damage in the absence of worse clinical symptomology (Alexander et al., 1997).

Use of selection, optimization, and compensation strategies (SOC). The developers of SOC theory designed a measure of use of SOC-consonant strategies, called the SOC Questionnaire short form (Freund & Baltes, 1998). It has twelve items in a forced choice format, with two choices labeled "A" and "B," where once choice represents an SOC related strategy and the other represents a non-SOC related strategy; the items are divided among the three components of SOC. One month test-retest reliability for the three subscales ranged from .56 to .75. The full 36-item SOC questionnaire has internal consistency reliability for the subscales ranging from .67 to .78, depending on sample (Freund & Baltes, 2000). Factor analysis of the full form also confirmed the three-factor structure to be an acceptable fit among several samples, with a goodness-of-fit index of .96 (Freund & Baltes, 2000).

Mini mental status examination. The Mini Mental Status Examination (MMSE; Folstein, Folstein & McHugh, 1975) was developed to assess for cognitive impairment in older persons and is frequently used to screen for dementia. The MMSE is administered by an examiner. Scores total up to 30 points, with items ostensibly assessing orientation, attention, and reading comprehension (Camiciolo & Wild, 2006). Although Folstein and colleagues (2001) have recommended a cutoff of equal to or less than 27, numerous authors prefer a cutoff of below 24 which has been determined to be psychometrically 'adequate', more so in the context of confidence intervals (Lopez, Charter, Mostafavi, Nibut, & Smith, 2005). It has demonstrated good convergent validity, and test-retest and interrater reliability (Camiciolo & Wild). Cronbach's alphas range from .54 to .96 (Tombaugh & McIntyre, 1992). Although the MMSE has difficulty detecting dementia in the early stages, and may fail to detect cognitive impairment in persons with cerebrovascular disease and Parkinson's as it does not assess executive function (Camiciolo & Wild), and although specificity is only 56%, sensitivity is still an acceptable 79% (Hogan & Ebly, 2000).

Dependent Variables

ANAM. The Automated Neuropsychological Assessment Metrics (ANAM) is a computer-based neuropsychological battery developed as a "direct outgrowth of more than 20 years of Department of Defense computer-based test development" (Kane & Kay, 1992), designed for repeated assessments over time. The ANAM is composed of tests both newly developed by the Department of Defense and existing commonly used assessment measures. There were originally fourteen cognitive subtests: simple/two-choice reaction time, Sternberg memory search tasks, running memory continuous performance, mathematical processing, digit set comparison, logical reasoning, Tower of Hanoi, Stroop color/word interference, code substitution, both comparison

and recall, spatial processing, matching to sample, tapping, and an orientation test (Kay & Starbuck, 1997), although administrators can select which tests to include in a customizable battery. It measures constructs such as attention, aspects of memory including working and short term, processing speed, verbal ability, numerical ability, visuospatial ability, problem solving and mental flexibility (Schlegal & Gilliland, 2006). The ANAM provides detailed instructions for each test, computer-generated individual results reports, and has availability of practice tests.

The tests of the ANAM have identified cognitive dysfunction resulting from a variety of medical conditions such as Alzheimer's dementia and acquired brain injury with 86-96% accuracy (Kane, Roebuck-Spencer, Short, Kabat, & Wilken, 2007). The ANAM's measures of attention are correlated with the Trails A (r = .65), a widely used traditional measure of attention (Gilliland, 2008). The ANAM's measures of working memory are correlated with that Paced Auditory Serial Addition Test (PASAT; r = .78), a widely used traditional measure of that construct (Gilliland). A combination of at least the Sternberg memory test, a simple reaction time task, math processing, and a matching task on the ANAM has been determined to assess similar constructs as the use of the Stroop, Trails B, PASAT, and the Hopkins Verbal Learning Test (Bleiberg, Kane, Reeves, Garmoe, & Halpern, 2000). Importantly, the latter measures assess the areas of cognition addressed by this study's hypothesis: attention/inhibition, cognitive flexibility, processing speed, and verbal immediate and delayed recall memory. Other subtests that were included (see Table 2) measured differentiation between two stimuli, spatial pattern comparison ability, and logical relations. Note the highest correlations of ANAM subtests with external measures have been via the throughput scores (Gilliland).

Because the ANAM has been historically used in a variety of populations, Cronbach's alpha figures are not yet available among a relevant normative population. To ensure that

subtests utilized have acceptable psychometric properties, internal consistency reliability analyses were run on all the subtests of the ANAM administered. This information is reported in the results section.

Gf/Gc sampler

The Gf/Gc sampler (Horn, 1975) is a pen-and-paper measure composed of subtests that measure both fluid and crystallized intelligence. Answers are either multiple choice or fill-in-the-blank. For this study, four subtests were used: letter series (in which participants write in the next letter that fits in the sequence of a given letter series) and letter sets (where participants cross out the set of letters that do not match with four other sets), both of which tap into fluid intelligence, and common analogies, which taps into fluid and to some extent crystallized intelligence and abstruse analogies, which taps into crystallized and to some extent fluid intelligence; the latter two subtests are vocabulary-based. Relative to Gf measures, Gc measures on the sampler have been found to account for a greater proportion of variance in cognitive performance on non-novel tasks, and Gf to account for a greater proportion of variance in performance than Gc on novel tasks, with increased age (Hayslip & Sterns, 1979). The Gf/Gc sampler has also been found to detect differences between older and middle-aged adults' fluid and crystallized abilities (Hayslip & Sterns).

Design and Procedure

Potential participants with OSA were patients presenting at a local sleep medicine clinic, Sleep Medicine Associates of Texas, with a chief complaint of apnea symptoms such as snoring, apnea episodes, and excessive daytime sleepiness. Patients were seen in clinical consultation with a physician board certified in sleep medicine and scheduled for an in-laboratory overnight diagnostic polysomnography if warranted. At the end of the consultation, provided that they met

inclusion and exclusion criteria, patients were informed about the availability of the study and invited to participate. If patients agreed, at that time they were given a written description of the study and completed the informed consent form. In order to allow potential OSA patients to complete the battery during the typical process of initial consultation at the sleep clinic and scheduled sleep study, initial diagnosis was sometimes based only on clinical consultation and physical examination. However, data from patients who did not subsequently evidence OSA (defined as an AHI greater than or equal to 5 by minimum polysomnographic standards, note that 10 was suggested by Janssens et al., 2000) on their sleep study would have been excluded, although all had an AHI of over 5; of the two who evidenced an AHI below 10, both had an AHI above 10 when in rapid-eye movement sleep and a low oxygen saturation of 87-88%.

Patients with apnea completed the questionnaires described above and the ANAM immediately after initial consultation at the sleep clinic, if they agreed to participate in the study. The survey and ANAM were administered by the experimenter or a trained administrator who was either another student in the psychology department or a medical assistant at the sleep medicine clinic. Because the clinic is open between the hours of 8:00 a.m. and 5:00 p.m., administration occurred during the day.

Prospective participants without OSA were recruited through students in psychology (and possibly other) classes at the University of North Texas in Denton. Students will be offered extra credit if they or a friend or someone in their family participates in the study. If they agreed, participants were screened for apnea symptoms by the administrator who administered the questionnaires and the ANAM at the psychology clinic on campus during daytime hours. For participants living in the area but unable to come to campus, the study was administered, including the ANAM, at the participant's location.

In order to orient participants to use of the computer for computer-assisted testing, a brief demo version of the ANAM without data collection was completed by participants for two to three times prior to full administration with data collection. Each practice demo administration took approximately five to ten minutes to complete. Further, in order to experimentally control for potential order effects, administration of the demo and full versions of the ANAM were randomly counterbalanced with administration of the survey.

The sleep medicine clinic has two locations, one in Dallas and one in Plano, neither of which are near the Denton campus. As a result, multiple computers were occasionally necessary to gather data (e.g. a participant in Dallas and a participant in Denton are available concurrently), so the same model computer was used to administer the ANAM.

Analyses

Chi-square tests-of-independence and analyses of variance (ANOVAs) were run to determine if there are any significant between group differences on demographics that may affect cognitive performance and would have needed to be controlled for statistically in subsequent analyses. The independent variables were group membership (i.e., older and middle-aged adults, with and without apnea) and the Dependent variables were demographics, level of education, highest degree obtained, measures of depression/anxiety, health-related anxiety, fatigue, nocturnal sleepiness, daytime sleepiness, SOC, and mMSE score.

Next, two-way multivariate analyses of variance (MANOVAs) were run with age group (middle-aged vs. older), presence of OSA (no vs. yes), and their interaction as independent variables, and cognitive performance variables (including throughput, reaction time, and accuracy scores) as dependent variables. Multivariate analyses of covariance (MANCOVAs) were also run with hypothesized covariates. Post-hoc testing derived from the MANOVAs used

the LSD method to determine significant differences, and scores were reported as marginal means to account for the other factors in the model. Where post-hoc testing from the MANOVA does not specify the nature of the effect, follow-up ANOVAs and correlational analyses with Pearson's *r* were run.

Cognitive performance variables consist primarily of the throughput scores of the ANAM subtests, which are the overall scores incorporating both response time and percent correct. Additional analyses were run on the throughput components (i.e., response time and percent correct), and scores on the Gf/Gc sampler. Although speed and accuracy scores were analyzed to support throughput findings, the developers of the ANAM recommend primarily interpreting the throughput scores, because previous research have repeatedly demonstrated a negative skew on accuracy scores, where the majority of test takers score quite high on the ANAM batteries (Gilliland, 2008).

EXPERIMENT II

Methods

Participants

Participants consisted of the obstructive sleep apnea (OSA) patients from Experiment I. Given the goal of obtaining 30 OSA patients divided into two groups of approximately 15 participants in Experiment I, and taking into account potential attrition, the goal was to obtain an overall sample of 20 divided into approximately 10 follow-up data sets per group in Experiment II.

Materials

CPAP

Patients received a CPAP device as determined by individual preference and insurance requirements. CPAP pressure settings were determined during a titration sleep study. CPAP devices can track measures of adherence to treatment, including total hours of use and number of nights used, as well as measures of treatment effectiveness, such as snoring severity and number of airway closures and/or partial closures. Patients who use CPAP differentially may see differential improvement (Rosenthal, Dolan, & Taylor, 2006), consequently adherence differences were evaluated to determine if adherence would be included as a covariate.

ANAM

Participants completed the same tests of the ANAM as at baseline.

Design and Procedure

OSA patients whose diagnosis was confirmed by polysomnography, were titrated on CPAP, completed approximately one month of treatment, and returned for an in-office visit at one-month follow-up were asked to again complete the ANAM, at that time. If available,

compliance data from the CPAP machine was downloaded at that visit by a trained physician's medical assistant. Because OSA patients at Sleep Medicine Associates of Texas typically return for a follow-up visit after one month, and have compliance data downloaded, Experiment II was intended to only impose the ANAM on participants. Although the possibility of a follow-up survey was considered in the study design, time constraints on the part of patients and the medical assistants after the follow-up visit with the physician precluded this aspect.

Analyses

Patients whose sleep parameters were not significantly reduced, as determined by the CPAP device, would have been excluded such that only treated OSA patients are part of the study; note that all participant evidenced a decline in AHI of more than five.

Repeated measures multivariate analyses of variance (MANOVAs) were run with time (pre-treatment vs. post-treatment) and age group (middle-aged vs. older) as independent variables and cognitive performance variables as dependent variables.

RESULTS

Experiment I

Exclusions

Visual examinations of boxplots were conducted on all Independent variables, covariates, and Dependent variables to screen for repeat outliers. One participant was excluded from the middle-aged group because he reported taking an unusually high amount of medications, endorsed higher depression, and had reduced ANAM scores compared to the rest of his peers, indicating co-morbid conditions potentially affecting cognition. Two others were excluded for large amounts of incomplete data (e.g., the entire survey portion and half of the ANAM, respectively).

Participants

Data was collected from May 2008-February 2009. A total of 60 persons participated in the study, with 16 in the middle-aged normal group, 15 in the older normal group, 17 in the middle-aged obstructive sleep apnea (OSA) group, and 12 in the older OSA group (this group ended up being much more difficult to recruit than previously expected). Demographics of the different groups can be found in Table 3.

A series of parametric and non-parametric tests (e.g the Mann-Whitney U) were run on major demographic variables that were not hypothesized covariates in order to determine if there were any groups differences that might affect results on the primary dependent variables of interest (i.e., ANAM scores). As can be seen in Table 3, there were no statistical differences between the four groups in terms of gender, study administration order, income category, or highest degree obtained or on AHI between the different age groups with OSA.

Not surprisingly, participants with OSA had higher BMIs, F (1, 46) = 8.7, p <.01, and reported more medical conditions, F (1,56) = 4.0, p =.05, than those without. Similarly, older adults reported more medical conditions than the middle-aged, F (1,56) = 6.9, p =.01. There were no interactions between age and OSA status on these variables.

There were also significant differences between the age groups, and OSA groups, on number of medications taken with older adults, F (1,56) = 26.2, p <.001, and people with OSA, F (1, 55) = 7.1, p =.01, reporting the use more medications than the middle-aged group and those without apnea, respectively. There was also an interaction between age and OSA status, F (1,56) = 5.4, p =.02, where the middle-aged normal group took significantly fewer medications all other groups, and the middle-aged OSA group took fewer medications than the older OSA adults (all ps < .05). Of note, medications taken can include multivitamins, over the counter medications, and herbal supplements.

Covariate Analyses

Next, ANOVAs were run with age (middle or older) and OSA status (normal vs. OSA), and their interaction, as the independent variables, and potential confounds (i.e., Geriatric Depression Scale (GDS), Beck Anxiety Inventory (BAI), Sleep-Wake Activity Inventory Excessive Daytime Sleepiness subscale (SWAI-EDS), Fatigue Severity Scale (FSS)) as dependent variables to determine if differences between groups existed.

As can be seen in Table 3, the OSA group as a whole had higher GDS, F (1, 56) = 10.2, p <.01, BAI, F (1, 56) = 7.8, p < .01, SWAI-EDS, F (1, 56) = 15.2, p < .001, and FSS, F (1, 56) = 12.4, p <.001, scores than the normal group. There were no main effects of age and no interactions.

Additionally, older adults had lower scores on the Mini-Mental Status Examination (mMSE) than the middle-aged group, F (1, 55) = 12.3, p =.001. However, no mMSE score was below 24, the most widely used cutoff for dementia. There was no main effect of OSA status and no interaction. Older adults thus had significantly lower mMSE scores indicating reduced cognitive function, but these differences may be of questionable clinical significance, particularly as the mMSE has no age-adjusted norms as do many cognitive assessments.

There were no significant differences in terms of years of education, health-related anxiety, sleepiness at night, and scores on the Selection Optimization Compensation (SOC) questionnaire or its subscales Selection, Loss-Based choices, Optimization, or Compensation. Note for no analysis did retrospectively assessed power exceed .40, and for many power was below .10. Preliminary analyses of all potential covariates (e.g. all those variables with significant between-group differences) demonstrated that only GDS, BAI, and FSS scores were likely related to ANAM reaction time scores. Thus, only these variables were included in analyses of covariance.

Internal Consistency Reliability of ANAM Subtests

Internal consistency analyses, or measures of Cronbach's alpha, were run for each subtest of the ANAM as alpha has not previously been reported for this assessment. Because each subtest score is calculated by the computer as the "throughput," there are no individual items to analyze; for this reason, the internal consistency analyses were run using the response time in milliseconds and the percent correct for each subtest, as these two items compose the throughput score. See Table 4 for results. Alphas were minimal or even negative, which likely reflects a lack of relationship between speed and accuracy in some cases or a tradeoff between speed and accuracy in others.

Primary Analyses

ANAM Response Time

First, a MANOVA was run with age (middle or older) and OSA status (OSA vs normal), and their interaction, as independent variables and response time in milliseconds on the subtests of the ANAM as the dependent variables. The only significant result was a main effect of age, Wilks' Lambda = .40, F (10, 47) = 3.8, p =.001. There was no effect of presence of OSA and no interaction between age and OSA status. Follow-up univariate analyses showed middle-aged adults had faster speeds than older adults on every subtest except Mathematical Processing (see Table 5 and Figure 1 for reaction time scores by age group).

ANAM Accuracy

Next, a MANOVA was run with age and OSA status, and their interaction, as independent variables and accuracy (measured as percentage correct) on the subtests of the ANAM as the Dependent variables. There was again only a main effect of age, Wilks' Lambda = .55, F (10, 47) = 3.8, p =.001. There was no effect of OSA status and no interaction between age and OSA status. Follow-up univariate analyses showed middle-aged adults overall being more accurate on Code Substitution Delayed and Running Memory than older adults (Table 6 and Figures 2-4 for percent correct by age group and representative significant results from Running Memory and non-significant results from Logical Relations).

ANAM Throughput

A MANOVA was then run with age and OSA status, and their interaction, as Independent variables and throughput score on the subtests of the ANAM as the Dependent variables. Note that throughput score is a combination of accuracy and speed, with higher scores reflecting better cognitive function. There was again a main effect of age, Wilks' Lambda = .36,

(F (10, 47) = 8.3, p <.001, but no main effect of OSA status and no interaction between age and OSA status. Follow-up univariate analyses showed middle-aged participants had higher throughput scores than older participants on every subtest except Mathematical Processing (Table 7 and Figure 5).

Gf/Gc Sampler Scores

Finally, a MANOVA was run with age and OSA status, and their interaction, as independent variables and the four subtests of the Gf/Gc sampler (fluid and crystallized measures) as the dependent variables. There was again a main effect of age, Wilks' Lambda = .81, F (4,48) = 2.9, p=.03), but no main effect of OSA status and no interaction between age and OSA status. Follow-up univariate tests did not reveal any between group differences between the middle-aged and older adults on Gf or Gc measures (Table 8).

Analyses with Covariates

Next, separate MANCOVAs were run with age and OSA status and their interaction as Independent variables, GDS, BAI, and FSS scores as covariates (see Tables 9-11), and response time, accuracy, and throughput scores as the dependent variable, in an attempt to ensure those covariates were not confounding our analyses. The results from the above primary analyses continued to be significant.

A MANCOVA was also run with age and OSA status and their interaction as independent variables, number of medications and FSS scores as covariates (see Table 12), and Gf/Gc scores as the dependent variables. Again, no change was seen in results.

Experiment II

Participants

A total of 17 participants with OSA were available for follow-up in Experiment II; 9 middle-aged participants with OSA and 8 older participants with OSA. Of the original Experiment I sample of middle-aged patients (n = 17), 2 did not return for follow-up, 1 declined to participate in follow-up, 5 completed follow-up but were lost due to a computer malfunction. Thus, of the 17 initial middle-aged participants, 82.4% agreed to participate in follow-up and 52.9% had data available, and out of the 15 actually available for follow-up, 93.3% agreed to participate and 60% had data available, for a total of 9 middle-aged patients in Experiment II.

Among the original older patients (n = 12), 2 did not return for follow-up, 2 decided not to implement CPAP treatment, and 7 had follow-up data available for analysis. Thus, out of the initial 12 participants in Experiment I, 75% agreed to participate in follow-up and had data available, and out of the 10 actually available for follow-up, 80% agreed to participate and had data available, for a total of 8 older patients in Experiment II.

As can be seen in Table 13, groups did not differ on demographic variables, including BMI and gender (although given small cell sizes this should be interpreted with caution). Older adults almost took significantly more medications, F (1,15) = -2.0, p =. 056. Groups did not differ on sleep study or post-treatment CPAP variables, including diagnostic AHI, length of follow-up treatment period, total hours used, and average hours of use on nights the machine was used, and no differences on AHI during the follow-up treatment period. Groups differed on GDS, t (1,15) = 2.3, p= .03, and FSS, t (1,15) = 2.1, p =.05, scores, although differences on GDS scores were not clinically meaningful. Older adults also had a significantly lower mMSE score, t (1,15) = 2.4, p = .04.

Comparisons Between Follow-Up Participants and Those Who Did Not Follow-Up

Table 14 shows differences between groups based on Independent t-tests evaluating potential differences on baseline measures between those participants with OSA who completed approximately one moth of treatment and returned for follow-up, and those who were lost to follow-up. The only similar significant differences for middle-aged and older adults between those who did and did not follow-up were on the analogies questions of the Gf/Gc sampler. As this measure was not included as an IV and was not re-assessed at follow-up, this difference does not affect external validity of the analyses below.

Primary Analyses

Between groups (middle-aged vs. older adults) repeated measures (i.e., baseline vs. follow-up) MANOVAs were run, with response time, accuracy, and throughput score on each subtest of the ANAM as dependent variables.

ANAM Response Time

As can be seen in Table 15, there was a trend for a faster response times from pre- to post-treatment across age groups (within subjects) , Wilks' Lambda = .12, F (5,10) = 3.7, p =.08, but not between age groups, Wilks' Lambda = .27, F (5,10) = 1.4, p =.38, and there was no interaction, Wilks' Lambda = .17, F (5,10) = 2.4, p =.28. See Figure 6 for response times pre- to post-treatment.

Follow-up univariate analyses were run within subjects for exploratory purposes and showed that when scores were collapsed across groups, participants improved from pre-treatment to post-treatment on reaction time scores for the Two Choice, F (1,15) = 10.9, p <.01, Logical Relations, F (1,15) = 5.6, p = .03, and Mathematical Processing, F (1,15) = 4.4, p = .05, tasks.

ANAM Accuracy

As can be seen in Table 15, there were significant accuracy effects between age groups, Wilks' Lambda = .08, F (5,10) = 5.7, p=.03, but not within groups (pre- to post-treatment), Wilks' Lambda = .37, F (5,10) = .84, p=.62, nor was there an interaction, Wilks' Lambda = .47, F (5,10) = .57, p=.79. See Figure 7 for percent correct pre- to post-treatment.

Follow-up univariate analyses on the between groups effect showed that when scores were collapsed across time points (i.e., pre- and post-treatment), middle-aged adults performed significantly better than older adults on Code Substitution Delayed, F (1,14) = 7.8, p = .01, only.

Follow-up simple effects tests of potential interactions were run for exploratory purposes given the age effect, but showed no interactions.

ANAM Throughput

As can be seen in Table 15, throughput scores improved significantly from pre- to post-treatment across age groups (within subjects), Wilks' Lambda = .05, F (5, 10) = 8.7, p =.01, but did not differ not between age groups, Wilks' Lambda = .18, F (5,10) = 2.3, p =.19, and no there was no interaction, Wilks' Lambda = .4, F (5,10) = .74, p =.68. See Figure 8 for throughput scores pre- to post-treatment.

Follow-up univariate analyses on the within subjects effect showed that when scores were collapsed across groups, participants' throughput scores improved from pre-treatment to post-treatment on Logical Relations, F (1,15) = 5.2, p = .04, and Memory Search, F (1,14) = 5.4, p = .04.

Follow-up simple effects tests of potential interactions were run for exploratory purposes given the treatment effect and showed an interaction such that older adults saw no change in Code Substitution scores from pre- to post-treatment, but middle-aged adults' scores improved, F

(1,15) = 7.7, p = .01 (see Figure 9). Note this finding may have been spurious and capitalized on experiment-wise error.

DISCUSSION

Experiment I

In this study, in both primary analyses and secondary analyses controlling for potential confounds, middle-aged adults performed better than older adults on nearly every subtest of the ANAM excluding Mathematical Processing. In contrast, in no analysis was presence or absence of obstructive sleep apnea (OSA) found to have an effect on any measure of cognitive function. This suggests that a diagnosis of OSA does not affect cognitive performance. Instead, the effects of aging on cognitive function are so powerful that they overshadow any potential influence of OSA, where a middle-aged adult would be expected to perform better on measures of cognitive function than any older adult, even if that middle-aged adult has an OSA diagnosis.

The differences that were found reflect age differences on processing speed, distinguishing stimuli rapidly, attention, spatial ability/mental flexibility, and both working memory and short-term visual memory. Middle-aged adults attend to, retrieve, and process stimuli from memory more rapidly than older adults, and are more accurate in contexts that require attending to information and holding that information mentally for a brief time period. They are not, however, more accurate in any other area despite (or perhaps due to) their increased speed of responding.

Note that throughput scores are composed of the reaction time component and the accuracy component, although not evenly so. As a result, it is somewhat difficult to interpret these results, because results from the throughput scores appear to be perfectly in line with the results from the reaction time component of these subtests, but not the accuracy component. When evaluating accuracy subtest scores separately from speed, the only age differences were found on the Code Substitution and Running Memory subtests, which measure attention and

working memory. The similarities between findings on the throughput score and on the reaction time component but not the accuracy component suggest that the better performance on subtests among middle-aged adults results from a shorter latency before response to stimuli. Both groups obtain a similar percent correct, but the middle aged adults come to a correct answer much faster. It is likely that in order to maintain their accuracy, older adults sacrifice time, as opposed to responding more rapidly but potentially less accurately. This tradeoff of reaction time in order to maintain accuracy may translate into real-life concerns for older adults, for example while driving, making on-the-spot decisions, multi-tasking, and any activity requiring attention and immediate response. The negative skewness of accuracy scores as reported by researchers who normed the ANAM (Gilliland, 2008) indicates that people in general, regardless of age, may prioritize accuracy over reaction time. Thus, any improvement in cognitive function among older adults in the areas assessed in this study (processing speed, distinguishing stimuli rapidly, attention, spatial ability/flexibility, and working and short-term visual memory) would therefore need to occur via increased reaction time with maintained accuracy.

As mentioned previously, reaction time and throughput scores indicated middle-aged adults performed better on every subtest except Mathematical Processing. Since mathematical processing likely incorporates a component of crystallized intelligence as acquired in education, it is not surprising that there were no differences here, since groups were equivalent in terms of education.

Unfortunately, not all of the constructs often assessed in previous research (e.g. verbal memory, inductive reasoning, and spatial orientation, etc) are measured by the ANAM. Constructs that were measured, such as processing speed and working memory, compare to previous aging research in that they clearly differ between age groups; as definitive declines in

these areas of cognitive function occur between 60-67 (Schaie, 1994), the average ages of 68 and 76 for the two older adults groups facilitated detection of these differences.

The current findings are discrepant from previous research in the lack of a direct effect of OSA on cognitive function. Previous reviews and meta-analyses have determined an apparent effect of OSA, most notably on attention, and then on measures of working memory and mental flexibility (executive function), and lastly on measures of short term visual memory (Beebe, Groesz, Wells, Nichols, & McGee, 2003; Aloia, Arnedt, Davis, Riggs, & Byrd 2004). However, this effect is not always clear and previous studies have offered mixed and occasionally conflicting data (Beebe et al) with the result that researchers have concluded "no strong and consistent relationship" between nocturnal hypoxia and number of arousals as measures of OSA and cognitive function (Aloia et al.). Indeed, multiple early studies determined no relationship between "overall neuropsychological status" and nocturnal hypoxemia (Greenberg, Watson, & Deptula, 1987) and no effect of number of arousals on cognitive function (Berry, Webb, Block, Bauer, & Switzer, 1986; Block, Berry, & Webb, 1986; Findley, Barth, Powers, Wilhoit, Boyd, & Suratt, 1986). Even studies of patients with a mild level of hypoxemia or number of arousals show deficits in attention/vigilance, working memory, and other neuropsychological measures such that physiological markers of greater OSA severity do not appear to effect OSA in a proportional manner, which has led to the suggestion that unclear mediators exist in the relationship between OSA and cognitive function (Redline, Strauss, Adams, Winters, Roebuck, Spry, Rosenberg, et al., 1997).

Researchers have suggested that sleepiness may primarily mediate the relationship between OSA and cognitive function, especially attention, as OSA patients have been found to have deficits in cognitive function and studies on sleep deprivation show somewhat similar

deficits in cognitive function (Verstraeten, Clydts, Pevernagie, & Hoffmann, 2004). Ironically, the meta-analysis cited by Verstraeten and colleagues in support of their conclusion clearly notes that sleep deprivation impairs mood to a greater extent than it directly impairs cognitive function itself (Pilcher & Huffcutt, 1996). In fact, in one study measures of attention and reaction time among OSA patients as measured by computer demonstrated no effect of hypoxemia, arousals, or subjective sleepiness such that authors concluded "patients may differ in their vulnerability to neurobehavioral impairment from sleep-disordered breathing via mechanisms that are only loosely associated with objective indices of disease severity or subjective measures of patients' sleepiness" (Findley, Suratt, & Dinges, 1999). Certainly, a mediator would likely contribute to the variability in findings over the past two decades, but sleepiness does not appear to consistently act as that mediator. Similarly, the current study did not find an effect of subjective sleepiness on any measure of cognitive function, regardless of whether or not the participant had OSA.

It was interesting that mood and anxiety were related to some of the measures of cognitive function in this study. Participants with higher levels of anxiety and more depressed mood performed slightly worse on a complex measure of reaction time (e.g. involving distracting stimuli). Reduced mood was also related worse reaction times across Code Substitution, which measures attention, and a simple reaction time measure (e.g. with only one stimulus). There appears to be, then, some relationship between mood and anxiety, and decreased attention and reaction time. Similarly, increased fatigue was also related to percentage correct on Code Substitution and to a lesser extent on Running Memory, which is striking given that these very subtests were also affected by older age, although there was no relationship between fatigue and age.

Of particular salience to the current findings, however, is the lack of report on potential covariates in previous research. None of the studies assessing cognitive function in OSA patients as compared to normal controls has either included self-report psychological measures in analyses or reported on them with the exception of sleepiness. Thus, as conclusions about this study's failure to find a direct effect on OSA may reflect the contribution of mood, anxiety, and fatigue, findings might have compared more directly if previous studies had assessed these constructs. One study did control for persons who obtained scores consistent with clinically significant depression and/or anxiety (Cheshire, Engleman, Deary, Shapiro & Douglas, 1992); findings demonstrated a potential mediator effect of mood/anxiety on both attention and change in estimated IQ from premorbid function with OSA. It is impossible to guess as to how earlier analyses that did not include mood, anxiety, or fatigue might have differed, with the result that direct comparison of results between the existing literature and the current study lacks credence. Perhaps the most relevant comparison relates to the consensus that some relationship between OSA and cognitive function exists, although the nature of that relationship has yet to be clarified fully.

Unfortunately, use of the Gf/Gc sampler in this study did not further clarify differences in cognitive function between age groups despite a main effect of age on these scores. Results did suggest a potential effect of younger age on fluid measures, however, which fits with both the study's finding of an age affect on constructs considered fluid in nature, and the findings of Schaie's (1994) longitudinal research documenting a decrease in fluid intelligence measures from midlife to older adulthood.

Although this baseline cross-sectional study found an effect of age on cognitive function (e.g. on processing speed, distinguishing stimuli rapidly, attention, spatial ability/mental

flexibility, and both working memory and short-term visual memory), it did not determine a direct effect of OSA on cognitive function, nor a direct interaction between presence of OSA and age as hypothesized.

Experiment II

Unlike Experiment I, Experiment II showed that when scores were averaged over pre-post-treatment, middle-aged adults did not perform better on the majority of measures in terms of reaction time and throughput scores, although middle-aged adults did perform better on accuracy scores, specifically Code Substitution Delayed scores, which measure working memory. In combination with the age differences found in Experiment I at baseline, the lack of an overall age effect here suggests that with treatment, older adults with OSA are capable of performing cognitively at a similar level to middle aged adults with OSA, in particular regarding processing speed.

Furthermore, when data were collapsed across age groups, all patients showed a trend for significant improvement on reaction times (i.e., Two-Choice Reaction Time, Logical Relations, and Mathematical Processing), and did demonstrate an effect on throughput scores (i.e., Logical Relations and Memory Search), but not on accuracy. These findings demonstrate a treatment effect in terms of reaction time on the ability to distinguish two stimuli rapidly, mental flexibility with spatial information, and short term memory, respectively. Similar findings among throughput scores but not on accuracy scores also supports the impact of treatment on enhancing processing speed. Given the negative skew observed by the ANAM's developers on accuracy, as well as in this study, the lack of improvement on accuracy among both age groups may reflect a ceiling effect, although a longer treatment period would be of benefit in making such a conclusion. Interestingly, treatment also improved reaction time on Mathematical Processing,

which measures acquired math ability. These findings suggest that not only does treatment with CPAP improve measures of fluid intelligence as expected, it may also to some extent improve some aspects of crystallized intelligence. That is, beyond the potential to improve areas of cognitive function impacted by age and by mood and anxiety as previously reported, CPAP may also facilitate retrieval of previously learned information. Ostensibly, benefits come from the increased nocturnal oxygen saturation levels, but participants with OSA, on average, did not have abnormally low levels of oxygen saturation at baseline. Thus, benefits from CPAP may be found even in persons without significant hypoxia. Interestingly, these improvements were found despite no direct statistical effect of OSA at baseline, which supports the use of CPAP treatment. The use of brief administrations pre-treatment to reduce practice effects provide further support to the apparent benefit derived from CPAP.

Previous research on treatment of OSA with CPAP indicates that while CPAP may not always demonstrate superior benefit as compared to a placebo (Engleman, Martin, Kingshott, Mackay, Deary, & Douglas, 1998), it often does demonstrate improved attention, mental flexibility, working memory, and processing speed after approximately one month (Engleman, Martin, Deary, & Douglas, 1997; Engleman, Kingshott, Wraith, Mackay, Deary, & Douglas, 1999; Engleman, Martin, Deary, & Douglas, 1994). As compared to baseline, after half a month to a month of treatment, CPAP has been shown to improve attention, and mental flexibility (Ferini-Strambi, Baietto, Gioia, Castaldi, Castronobo, Zucconi, et al., 2003). Thus, current findings of improved mental flexibility with spatial information, short term memory, and processing speed, as well as attention among middle-aged adults with OSA, fit with previous results. Other findings on the effect of CPAP could not be compared to this study as they

evaluated CPAP after a longer treatment period (e.g. 3-12 months) or with measures not used in this study, including verbal fluency and verbal memory.

Medical conditions among older adults appear to exacerbate declines in working memory and processing speed in particular (Wahlin, McDonald, DeFrias, Nilsson, & Dixon, 2006), with the implication that treatment may reverse such declines, although no directly comparable study has targeted the effect of OSA treatment on adults 65 and over. One study did measure change in cognitive function among adults 55 and older after three months on CPAP (Aloia, Ilniczky, Di Dio, Perlis, Greenblatt, & Giles, 2003); that study found an improvement in attention and processing speed. In this light, the current study's findings of improvement in short term memory and aspects of executive function including processing speed and mental flexibility among both older and middle-aged adults with OSA after CPAP treatment are consistent with the literature. However, treatment of OSA in this study did not reverse apparent reductions in cognitive function in older adults to the extent that they saw greater improvement in function as compared to middle-aged adults, which is inconsistent with the implications of previous literature.

There was a potential interaction on throughput scores for age and treatment on Code Substitution (note that this interaction was found via exploratory follow-up analyses). Code Substitution measures attention, which is most frequently cited as impaired in OSA patients (Beebe, Groesz, Wells, Nichols, & McGee, 2003; Aloia, Arnedt, Davis, Riggs, & Byrd 2004). As indicated by throughput score, while older OSA patients saw no improvement in attention, despite having found a significant effect of older age on lower attention in Experiment I, middle-aged OSA patients did evidence an increase in attention. This interaction suggests that, even if only for attention, CPAP treatment is beneficial for middle-aged OSA patients despite no direct

effect of OSA on attention and despite their younger age (and presumably less impaired cognitive function), both in terms of reaction time and accuracy. As attention is critical for activities of daily living such as shopping, driving, and completing tasks, the effects of treatment for middle-aged OSA patients on attention could further confirm the effectiveness and importance of CPAP among this population. However, this conclusion should be considered tentative due to the potential experiment-wise error that may have arisen from this exploratory analysis.

Although no direct effect of OSA was found on even attention in Experiment I, the significant effects of treatment in Experiment II suggest that OSA patients have room for improvement in cognitive function (e.g. on perception, mental flexibility, processing speed, and short term memory) above and beyond any effect of age. These improvements should offer noticeable benefit to patients in their ability to function in daily life.

Strengths and Limitations

There are multiple aspects of this study, which if addressed might have considerably strengthened these findings. Most importantly, the largest of these limitations is the lack of power on many of the analyses. Because power is the ability of the analysis to detect significant differences if they exist, given a high level of power a lack of significance is likely an accurate finding; however, given a low level of power, a lack of significance may lead to a Type II error. As such, the relatively reduced power in this study, which ranged from .34 to .60 for potential effects of OSA presence, may have precluded the ability to definitively determine an effect of OSA. Power is a combination of several aspects, including the sample size of the study and the degree of difference between groups. This means that between-group differences may simply not have indicated that OSA actually does affect cognitive function, or it may mean that there were

not enough participants in this study. Certainly group sample sizes ranging from 12 to 17 can not be considered large or even medium, so a small sample size likely contributed at least in part to the reduced power in this study. Yet a visual inspection of mean scores suggests with a larger sample sizes an effect of OSA might become apparent; for example, on simple reaction time throughput scores those without OSA obtained a 184.7 and those with a 168. High variability in scores appears to explain the lack of an effect, another area in which a larger sample size might have helped.

Other issues related to the participants include difficulties obtaining complete datasets and difficulties obtaining participants. Specifically, in several instances participants did not supply information on weight, income, or ethnicity, and in some cases did not fully answer the survey measures including the Gf/Gc sampler subtests. This further reduced sample size in analyses that included these items. Despite this potential problem, in the primary and secondary analyses, no missing data reduced the sample size as variables affected were not potential covariates.

Additionally, recruitment was more difficult than initially predicted, with most students opting to obtain extra credit for other available studies, which they could complete themselves, as compared to recruiting someone else and bringing that other person to campus for this study. As a result, length of recruitment period was consistently extended, and the IRB approval was modified to include payment to potential participants in lieu of extra credit for a student, with potential payout starting at $5 initially and increased to $20 by the end of the study. Recruitment was also more difficult than expected among the OSA patients, with many initially interested in participation but either not within the required age ranges or unable to take additional time from their day. In many cases, older OSA patients had been previously diagnosed and treated and

were unable to participate for that reason. In other cases patients chose not to implement CPAP treatment. Length of data collection for older OSA patients continued for three months after collection for older normal adults, even with the assistance of referrals from multiple physicians at the sleep medicine clinic. Data collection for this last group eventually had to be discontinued due to continually declining availability of older adults at the sleep medicine clinic rather than lack of interest. Indeed, quite a few participants in both the older normal and OSA groups declined payment, even at the highest reimbursement rate. Thus, the study may be composed of participants who had an interest in or concern for their own cognitive function, or perhaps who were motivated for other intrinsic reasons. Instead of harming the study, then, it is possible that the difficulty and length of recruitment period allowed for participants who had an interest in full study participation, as opposed to participants who may have simply sought external benefit and may not have had motivation to put forth their best efforts or answer honestly and accurately. Given the detailed nature of the survey (e.g. medication information, questions assessing intelligence) and the unique issues created by the use of a computer (e.g. learning curves, length of administration) more motivated participants adds crucially to the study's validity.

The necessity of extending the recruitment period itself resulted in other limitations for the study. Namely, halfway through the recruitment period, the study author relocated out of the North Texas area. As a result, additional research assistants had to be trained to administer the study beyond the one originally planned. In all, three additional students and one medical assistant were trained by the author, with a total of five administrators. This number of personnel increased the likelihood of differences in administration and introduced variability which may relate to administration or error as opposed to actual between-group differences. Importantly,

most of the data from participants without OSA was collected by one assistant, and the majority of the data from participants with OSA was collected by myself.

Use of a laptop computer to administer the study also imposed limitations. For instance, the screen size, although large among laptop choices, was at approximately 17" not as large as a desktop monitor. Nor was the touchpad feasible to use with the ANAM program, so instead of a mouse as preferred, the keyboard had to be used to administer the study. In addition to the hardware, a computer itself added concerns to the study. Participants may not regularly use a computer and may have lacked familiarity with the idea, particularly within the setting of a study as many college-based studies use only self-report measures. In terms of software, the ANAM has not been tested in as many situations as traditional neuropsychology measures, and it does not provide measures of effort, verbal memory or visuoconstruction ability or multiple measures of executive function. A case in point of software concerns occurred when a virus was discovered on one of the laptops used, which led to missing the opportunity to collect data from potential participants before removal, as well as concerns about data corruption (note later evaluation by a computer technician determined the virus did not affect software or already stored data, although it may have deleted files). Also, with a computer administrator for that portion of the study, behavioral observation of participants is shortened.

Despite these concerns, without the use of a laptop, the study may not have been feasible at all. More intensive training requirements for administrators, greater possibility for variation in administration procedures, lower accuracy on reaction times scored down to the millisecond, and lengthier study administration all would result from traditional neuropsychology measures. Once data is collected, computer administration allows for precise scoring, ease of working with large amounts of data, and transferability directly into the statistics programs. Moreover, in

consideration of the cost of traditional measures when new, the ANAM represents savings into the thousands of dollars. Given a tradeoff of no data on cognitive function, the availability of such precise data on the constructs measured reduces potential administration variability concerns over traditional measures and represents an advance over previous studies.

Another limitation related to use of technology, or lack thereof, is that participants who reported they did not have an OSA diagnosis were assumed to not have OSA. However, it is entirely possible that these participants may have had symptoms of OSA and/or an elevated AHI and simply had not been evaluated by a sleep medicine physician. No participant in the normal group reported they had undergone a polysomnography to formally rule out presence of OSA. Lack of funding and logistical difficulties precluded sending these normal participants to the sleep medicine clinic for an evaluation. Instead, participants were screened by a study administrator in regard to complaints of snoring, morning headache, morning dry mouth, or perception of obstructed nocturnal breathing. No normal participant endorsed more than two (or 50%) of the possible complaints, but complaints do not always predict presence or severity of OSA. Therefore the normal groups may be 'contaminated' with those who have OSA, which would significantly limit the ability to detect differences.

Beyond multiple limitations, the study has multiple strengths as well. Firstly, unlike many studies based out of a college setting, the study utilized a variety of multiple objective measures, including a mental status exam, the ANAM, and for OSA patients, polysomnography and data recorded by the CPAP device, as opposed to solely self-report measures. Although covariates and some aspects of cognitive function (as measured by the Gf/Gc sampler) relied on self-report, the main dependent variables in this study were collected via objective measurement. This strengthens the validity of findings. Also, numerous potential covariates were included,

such as measures of mood, anxiety, and SOC; not all of these demonstrated significant between-group differences but their inclusion represents a step forward in the literature.

In addition to objective measurement, although Experiment I had a cross-sectional design, overall the study had a prospective quasi-experimental design. This design enabled troubleshooting of potential problem areas, such as the use of the Geriatric Depression Scale versus another measure that may be less applicable to older adults like the Beck Depression Inventory. Other potential problem areas included not utilizing a-priori power analyses to suggest a target N or not preparing to administer practice ANAM sessions in order to overcome any learning curve or not using identical laptops for administration; all of these concerns were avoided with the prospective design. Although such a design can not overcome all eventual concerns, it reduces the likelihood of concerns. Moreover, a quasi-experimental design allows study authors to conclude with a greater measure of certainty the effect of an intervention on outcomes. In this study, the quasi-experimental aspect is captured largely in Experiment II, when patients used the CPAP device as an intervention for OSA and completed the ANAM both pre- and post-treatment. This enables more firm conclusions about the relationship between age, OSA, and cognitive function than without a quasi-experimental design as it provides information on changes to the dependent variables with independent variable "manipulation." Although prior studies often focused on between group differences or changes with OSA patients after treatment, this study combined both of these aspects with the same sample pool.

Also, this study had a similar N at a range of 12-17 per group as compared to previous studies (see Table 1), as well as a relatively high overall N of 60. Unlike previous studies, however, age groups were firmly separated by a gap of ten years, which was purposely set to ensure differences based on age emerged cleanly; the cutoff for participation in the older adult

group was a minimum age of 65. Previous studies have not only used groups close in age, but described adults 50-55 or so as "older" despite the use of 65 in literature on aging. Other studies may have found an effect of OSA as compared to age without clear separation of age groups or a wide enough range of ages extending into older adulthood. A strength of this study, then, is that while the sample size of this study approximates that of similar prior studies, age is more clearly and accurately defined.

The study exhibits both multiple limitations and multiple strengths. Yet several of the potential limitations may have less of a negative effect than presumed at first glance. The limitations also offer clear direction as to how to set up future studies on this topic. Combined with strengths that relate to study design and measurement, the study appears to yield valid current results.

Future Directions

Future studies should expand on the current findings by addressing limitations of relatively low power and technology concerns. To increase power, group sizes should increase through a larger recruitment pool, such as in print and online ads throughout a geographic area and at multiple sleep medicine clinics. All participants once recruited should then undergo both an overnight polysomnography and follow-up testing to exclude those with undiagnosed OSA from "normal" groups and to assess whether changes observed in this study's ANAM scores are simply variation within a normal range or whether changes actually reflect greater room for improvement among OSA patients, both of which would increase power. If possible, participants without OSA should take home a "sham" CPAP (i.e. CPAP at a non-therapeutic level of pressure), which would help rule out a placebo effect of actual CPAP. Certainly, this would significantly increase study costs, especially with a larger overall sample size, but these changes

would enhance validity and generalizability. Importantly, the cost of an overnight polysomnography ranges from $1500-3000 including interpretation, and CPAP devices cost $500-1000 each, with a special device and software needed for each brand of device in order to extract data on sleep parameters and utilization; assuming an N of 100 total, such a study would cost $200,000, excluding the costs of CPAP device data extraction, participation reimbursement, paying research assistants, and procuring the cognitive function measures. In part for this reason, these aspects were not included in the current study.

In terms of technology concerns, results from a computerized measure of cognitive function could be corroborated with sections of a brief neuropsychological screener, such as the Repeatable Battery for the Assessment of Neuropsychological Status, that measure similar constructs of processing speed, attention, spatial flexibility, and working/short term visual memory. Additionally, traditional measures could incorporate assessment of visuoconstructional ability and verbal and visual memory. Other included assessments should gauge effort, such as the Test of Memory Malingering.

There were a number of between-group differences in terms of both number of medications and number of medical diagnoses. However, this information was determined by self-report, and all types of both variables were lumped in together, such as over the counter, prescriptions, and herbal supplements under ‘medications’ and current chronic, previous diagnosis, and history of medical conditions under ‘diagnoses’. Unfortunately, chart data at the sleep medicine clinic is typically based on patient self-report, so obtaining objective and accurate information in these areas may pose a challenge. Future differentiation of medications and clarification of types, length, and recency of medical conditions would likely help determine

whether regular use of prescriptions and verified, current co-morbid medical conditions also have a relationship with cognitive function, although none were discovered in the current study.

Beyond the obvious need to address limitations, future research should further explore the role of potential mediators of cognitive function, including low mood, anxiety, and fatigue, in persons with OSA. Also future research should include multiple measures of each variable given the large overlap of physical complaint questions on the measurements used to assess the latter two constructs in this study. Post-treatment assessment of these variables would enhance future research to the extent that change or lack of change indicates the need for additional psychotherapeutic treatment of these patients in addition to CPAP treatment, in order to improve cognitive function. Of course, a determination as to whether or not patients actually perceive themselves as having reduced cognitive function and in need of treatment for this concern should come from future research. Anecdotally, in this study many OSA patients requested information on their results and upon learning of the study expressed their belief that their diagnosis does, in fact, alter their pre-morbid level of function. Statistically, on a Likert-type scale created for the purposes of this study, OSA patients indeed rated their cognitive function lower, albeit still at an average level. It is possible that the physical symptoms triggered by OSA, rather than simply the hypoxia and sleep disruption, cause actual decrement in function whereas receiving the diagnosis of OSA draws awareness to the possibility of such decrements. Thus, it would be of particular salience to explore both potential mediators and subjective cognitive deficits more specifically and systematically.

Summary

This study demonstrated an effect of age on attention and short-term visual memory as well as measures of executive function including processing speed, rapidly distinguishing stimuli, spatial ability/flexibility, and working memory, which is consistent with previous literature. The study also found differences between participants with and without OSA on measures of mood, anxiety, and fatigue, and further demonstrated an effect of these measures on attention, processing speed, and accuracy of responding. No clear role of these measures as mediators was detected.

This study also demonstrated an effect of treatment on attention among middle-aged adults, and on short term memory and measures of executive function including processing speed, rapidly distinguishing stimuli, and mental flexibility among both age groups. It did not demonstrate an effect of age when pre- and post-treatment scores are collapsed, however. Overall, findings reflect the ability of treatment to improve cognitive function among OSA patients, regardless of lack of deficits at baseline when compared to those without OSA.

Table 1

Studies of Cognitive Dysfunction in OSA

Study	Sample	Construct Measured	Findings
Block et al., 1986	OSA (*n* =6) vs. Snorers (*n* = 28)	Verbal IQ, Performance IQ, verbal fluency	# of oxygen saturation decreases correlated with all measures for all participants; performance IQ and verbal fluency scores ↓ among OSA compared to controls
Lee et al., 1999	Apnea w/o OSA diagnosis (*n* = 17) vs. control (*n* = 16)	Mental flexibility, short term memory, sensory-motor* ability	Pts w/apnea had ↑ errors shifting responses and on memory retrieval; ↑ sensory-motor accuracy; ↓ speed
Bedard et al., 1991	Severe and moderate OSA vs. controls (*n* = 10 per group)	Full scale IQ, verbal IQ, performance IQ, verbal fluency, figure reproduction, manual dexterity, problem solving	Scores ↓ in severe compared to moderate and controls; performance and manual dexterity scores ↓ in moderate compared to controls
Naegele et al., 1995	OSA vs. controls (*n* = 17 per group)	Mental flexibility w/changing rules, problem solving	OSA pts ↓ scores compared to controls; severe pts ↓ scores on mental flexibility than moderate; OSA pts had difficulty initiating task, but could complete once started
Salorio et al., 2002	OSA (*n* = 24) vs. controls (*n* = 28)	Verbal learning	OSA pts ↓ scores on learning and delayed recall, semantic clustering ability; decreased abstract word-generating ability (frontal process) vs. categorical word-generating ability (temporal process)
Cheshire et al., 1992	OSA (*n* = 29)	Auditory verbal learning, estimated IQ, spatial ability	Oxygen desaturation correlated with ↓ auditory verbal learning and est. IQ scores; sleep fragmentation correlated with ↓ spatial ability

(table continues)

Table 1 *(continued)*

Study	Sample	Construct Measured	Findings
Greenberg et al., 1987	OSA (*n* = 14), sleepy medical (*n* = 10), controls (*n* = 14)	Processing speed, motor coordination	OSA pts scored ↓ on all measures than other groups; cognitive function lowest in OSA pts, then medical pts, then controls
Powell et al., 1999	OSA (*n* = 113) vs. intoxicated controls (*n* = 80)	Attention, reaction time	Reaction time ↑ for OSA than intoxicated .057 g/dL; 3 of 7 reaction time/attention measures ↑ or = impaired in OSA and intoxicated .08 g/dL
Findley et al., 1999	OSA pts, (*n* = 31) narcolepsy pts (*n* = 16), controls (*n* = 14)	Attention, reaction time, driving	Narcolepsy pts hit most obstacles, then OSA pts, then controls; as time passed, narcolepsy pts had ↑ deficits, OSA a trend for ↑ deficits, controls had none; attention and reaction time ↓ in OSA compared to normals
Findley et al., 1986	OSA pts (*n* = 26)	Attention, immediate and delayed recall	Pts with ↑ oxygen saturation had ↓ scores on all measures
Redline et al., 1997	OSA pts (*n* = 32), control (*n* = 20)	Attention, working memory	OSA pts had ↓ scores
Naegele et al., 1995	OSA vs. controls (*n* = 17 per group	immediate and delayed recall	OSA pts had ↓ scores, attributed to inability to learn rather than memory deficits (see above)
Bedard et al., 1991	OSA pts, controls	Attention, immediate and delayed recall	Severe OSA pts had ↓ scores than controls, but moderate OSA pts did not

(table continues)

Table 1 *(continued)*

Study	Sample	Construct Measured	Findings
Bartlett et al., 2004	OSA pts (n = 8), controls (n = 5)	Attention, Hippocampal creatine	Creatine was ↓ in OSA and correlated both with sleep fragmentation and ↓ attention scores
Morrell et al., 2003	OSA pts, control (n = 7 per group)	Hippocampal gray matter	OSA pts had ↓ left hippocampal gray matter than controls; no differences elsewhere in brain
Cheshire et al., 1992	OSA pts (n = 29)	Attention, immediate and delayed recall	Attention and memory deficits correlated with oxygen desaturation
Telakivi et al., 1998	OSA pts	Delayed recall	Delayed recall memory correlated with number of oxygen desaturations

(table continues)

Note. * Sensory-motor refers to movements in response to sensory input. OSA= Obstructive sleep apnea; COPD = Chronic obstructive pulmonary disease.

Table 2

Descriptions for ANAM Subtests

ANAM:	Construct Measured
Simple Reaction Time	Processing speed
2-Choice Reaction Time	Differentiation between two stimuli
Code Substitution	Attention
Code Substitution Delayed	Short term memory
Matching Grids	Spatial pattern comparison
Matching to Sample	Cognitive flexibility/spatial pattern working memory
Mathematical Processing	Arithmetic computation and comparison
Logical Relations	Ability to order symbols/cognitive flexibility
Running Memory	Working memory
Memory Search	Short term memory

Table 3

Demographic Characteristics for Experiment I Participants, by Group

Variable	Normal		Total	Obstructive Sleep Apnea		Total
	Middle-Aged	Older		Middle-Aged	Older	
	M (*SD*)	M (*SD*)		M (*SD*)	M (*SD*)	
N	17	15	32	17	12	29
Age	45.1 (6.5)	75.7 (5.5)	59.9 (16.7)	46.1 (6.7)	68.1 (2.7)	55.2 (12.3)
Gender	4 M / 12F	5 M / 10F	9 M / 22 F	8 M / 9F	5 M/ 7F	13 M / 16 F
BMI[a]	27.2 (7.3)	27.5 (4.8)	27.4 (6.0)	34.9 (8.4)	31.9 (7.7)	33.7 (8.1)
Ethnicity	12 White	13 White	25 White	13 White	9 White	22 White
	1 African American	2 Unreported	1 African American	1 African American	3 Unreported	1 African American
	1 Asian		1 Asian	1 Hispanic		1 Hispanic
	2 Hispanic		2 Hispanic	1 Other		1 Other
			2 Unreported	1 Unreported		4 Unreported
Years of Education	15.2 (2.3)	13 (5.2)	14.1 (4.0)	15.0 (2.6)	15.0 (2.7)	15.0 (2.6)
Highest Degree Completed	5 HS Diploma	5 HS Diploma	10 HS	7 HS Diploma	6 HS Diploma	13 HS
	3 Associate's	1 Associate's	4 Associate's	6 Bachelor's	3 Bachelor's	9 Bachelor's
	4 Bachelor's	4 Bachelor's	8 Bachelor's	3 Master's	1 Master's	4 Master's
	3 Master's	2 Master's	5 Master's		2 Doctoral	2 Doctoral

(table continues)

Table 3 *(continued)*

Variable	Normal			Obstructive Sleep Apnea		
	Middle-Aged	Older	Total	Middle-Aged	Older	Total
	M (*SD*)	M (*SD*)		M (*SD*)	M (*SD*)	
Highest Degree Completed		2 Doctoral	2 Doctoral			
Income	6 Under $25k	1 Under $25k	7 Under $25k	2 Under $25k	1 Under $25k	3 Under $25k
	4 $25k-$50k	1 $25k-$50k	5 $25k-$50k	1 $25k-$50k	4 $25k-$50k	5 $25k-$50k
	6 Over $50k	13 Over $50k	19 Over $50k	13 Over $50k	6 Over $50k	19 Over $50k
				1 Unreported	1 Unreported	2 Unreported
Number of Medical Diagnoses[a,b]	1.0 (1.5)	3.1 (2.4)	1.9 (2.0)	2.7 (1.9)	3.1 (1.6)	2.8 (1.6)
Number of Medications[a,b,c]	.88 (1.4)	3.9 (1)	2.3 (1.9)	2.9 (2)	4.0 (1.6)	3.3 (1.9)
AHI	N/A	N/A	N/A	44.2 (30.9)	29.8 (16.4)	38.2 (26.5)
GDS[a]	.94 (1)	1.2 (1.7)	1.1 (1.3)	3.1 (2.1)	2.8 (3.8)	3.0 (2.9)
BAI[a]	5.7 (4.4)	7.1 (6.4)	6.4 (5.4)	14.5 (10.3)	9.3 (7.8)	12.4 (9.6)
HAQ	28.3 (4)	28.5 (3.6)	28.4 (3.8)	31.5 (7.5)	30.4 (9.4)	31.1 (8.2)
SWAI-EDS[a]	62.6 (10.7)	61.1 (9.7)	61.9 (10.1)	46.3 (17.1)	49.9 (15.2)	47.8 (16.2)
SWAI-NS	12.8 (5.6)	14.3 (4.3)	13.5 (5.0)	14.1 (7.1)	14.6 (5.0)	14.2 (6.2)
FSS[a]	25.7 (9.9)	29.5 (13.8)	27.5 (11.9)	42.5 (14.8)	35.8 (10.7)	39.8 (13.5)
SOC (short form)	7.2 (2.9)	6.1 (2.4)	6.7 (2.7)	7.6 (2.9)	6.9 (2.2)	7.3 (2.6)
mMSE[b]	29.4 (.5)	28.5 (1.1)	28.9 (1.0)	29.6 (.6)	29.0 (1.0)	29.3 (.8)

(table continues)

Table 3 *(continued)*

	Normal			Obstructive Sleep Apnea		
Variable	Middle-Aged	Older	Total	Middle-Aged	Variable	Middle-Aged
	M (*SD*)	M (*SD*)		M (*SD*)		M (*SD*)
Common Analogies	15.1 (4.0)	16.3 (4.6)	15.7 (4.3)	14.7 (4.7)	15.8 (4.9)	15.1 (4.7)
Letter Series	9.0 (4.0)	7.1 (4.8)	8.1 (4.4)	8.5 (2.6)	7.5 (4.1)	8.1 (3.3)
Letter Sets	5.1 (2.2)	2.8 (2.7)	4.0 (2.7)	3.4 (1.7)	3.8 (2.5)	3.5 (2.0)
Abstruse Analogies	10.4 (1.4)	11.3 (1.8)	10.8 (1.6)	10.9 (2.0)	11.7 (1.5)	11.3 (1.8)

Note. Data are reported as mean (SD). [a] Significant main effect of OSA; [b] Significant main effect of age; [c]

Table 4

Cronbach's Alpha for the ANAM Subtests

Subtest	Alpha
Simple Reaction Time	-.01
2-Choice Reaction Time	-.15
Code Substitution	.00
Code Substitution Delayed	-.04
Matching Grids	.00
Matching to Sample	-.03
Mathematical Processing	-.01
Logical Relations	.01
Running Memory	-.13
Memory Search	-.04

Table 5

ANAM Subtest Reaction Times in Milliseconds by Age Group

	Unadjusted Means				Adjusted Means			
	Middle-Aged		Older Adult		Middle-Aged		Older Adult	
	M	(*SD*)	M	(*SD*)	M	(*SD*)	M	(*SD*)
Simple Reaction Time*	323.4	(94.2)	412.3	(119.0)	319.4	(94.2)	418.3	(119.0)
2-Choice Reaction Time**	449.8	(92.5)	531.1	(90.8)	446.3	(92.5)	535.4	(90.8)
Code Substitution**	1441.5	(321.7)	2076.1	(457.4)	1446.6	(321.7)	2062.2	(457.4)
Code Substitution Delayed**	1283.0	(302.8)	1761.4	(423.6)	1281.1	(302.8)	1760.7	(423.6)
Matching Grids*	1991.5	(600.5)	2504.9	(680.7)	2007.3	(600.5)	2475.4	(680.7)
Matching to Sample*	1979.3	(673.6)	2748.3	(847.0)	1988.5	(673.6)	2709.4	(847.0)
Mathematical Processing	2884.7	(901.3)	3039.4	(972.2)	2867.3	(901.3)	3041.1	(972.2)
Logical Relations*	2234.6	(605.2)	2783.8	(728.9)	2220.9	(605.2)	2794.2	(728.9)
Running Memory*	585.0	(96.2)	639.3	(83.6)	584.6	(96.2)	640.0	(83.6)
Memory Search**	723.5	(160.8)	895.3	(133.1)	721.7	(160.8)	897.7	(133.1)

Note. * $p < .05$; ** $p < .001$. Data are reported as mean (SD). Adjustments means are marginal means taking GDS, BAI, and FSS into account.

Table 6

ANAM Subtest Percent Correct by Age Group

	Unadjusted Means				Adjusted Means			
	Middle-Aged		Older Adult		Middle-Aged		Older Adult	
	M	(*SD*)	M	(*SD*)	M	(*SD*)	M	(*SD*)
Simple Reaction Time	100.0	(0.0)	99.9	(0.5)	100.0	(0.0)	99.9	(0.5)
2-Choice Reaction Time	92.2	(18.0)	94.9	(6.8)	93.0	(18.0)	93.8	(6.8)
Code Substitution	97.5	(2.4)	96.8	(3.7)	97.6	(2.4)	96.6	(3.7)
Code Substitution Delayed*	84.2	(13.7)	72.7	(13.6)	84.2	(13.7)	72.6	(13.6)
Matching Grids	95.3	(5.6)	94.6	(7.8)	95.3	(5.6)	94.6	(7.8)
Matching to Sample	89.3	(14.8)	83.0	(16.7)	89.7	(14.8)	82.8	(16.7)
Mathematical Processing	94.1	(6.9)	95.0	(7.2)	94.1	(6.9)	95.2	(7.2)
Logical Relations	88.6	(15.7)	86.9	(14.8)	89.2	(15.7)	96.4	(14.8)
Running Memory**	85.7	(15.4)	67.9	(23.3)	86.1	(15.4)	67.9	(23.3)
Memory Search	97.9	(2.5)	94.0	(14.0)	97.8	(2.5)	93.8	(14.0)

Note. * $p < .05$; ** $p < .001$. Data are reported as mean (SD). Adjustments means are marginal means taking GDS, BAI, and FSS into account.

Table 7

ANAM Subtest Throughput Scores by Age Group

	Unadjusted Means				Adjusted Means			
	Middle-Aged		Older Adult		Middle-Aged		Older Adult	
	M	(*SD*)	M	(*SD*)	M	(*SD*)	M	(*SD*)
Simple Reaction Time**	196.9	(43.4)	155.9	(47.6)	198.3	(43.4)	153.9	(47.6)
2-Choice Reaction Time*	128.4	(32.1)	109.5	(19.8)	130.0	(32.1)	107.3	(19.8)
Code Substitution**	42.4	(8.5)	29.1	(6.4)	42.2	(8.5)	29.4	(6.4)
Code Substitution Delayed**	40.9	(13.3)	25.5	(7.8)	40.8	(13.3)	25.9	(7.8)
Matching Grids*	31.3	(9.7)	24.2	(6.2)	31.1	(9.7)	24.4	(6.2)
Matching to Sample**	30.6	(12.9)	19.4	(6.4)	30.7	(12.9)	19.6	(6.4)
Mathematical Processing	21.2	(6.2)	20.4	(5.9)	21.3	(6.2)	20.4	(5.9)
Logical Relations*	25.2	(6.6)	20.2	(6.7)	24.5	(6.6)	19.9	(6.7)
Running Memory**	88.1	(24.3)	59.6	(24.6)	88.5	(24.3)	59.7	(24.6)
Memory Search**	84.6	(16.7)	63.9	(15.0)	84.7	(16.7)	63.5	(15.0)

Note. * $p < .05$; ** $p < .001$. Data are reported as mean (SD). Adjustments means are marginal means taking GDS, BAI, and FSS into account.

Table 8

Gf/Gc Sampler Scores by Age Group

	Unadjusted Means		Adjusted Means	
	Middle-Aged	Older Adult	Middle-Aged	Older Adult
	M (*SD*)	M (*SD*)	M (*SD*)	M (*SD*)
Common Analogies	15.1 (4.4)	16.5 (4.3)	15.4 (4.4)	16.1 (4.3)
Letter Series	9.1 (3.0)	7.5 (4.4)	9.0 (3.0)	7.8 (4.4)
Letter Sets	4.2 (2.1)	3.1 (2.6)	4.5 (2.1)	2.9 (2.6)
Abstruse Analogies	10.7 (1.7)	11.5 (1.7)	11.0 (1.7)	11.3 (1.7)

Note. Data are reported as mean (SD). Adjusted means are marginal means taking FSS and number of total medications into account.

Table 9

MANOVA of ANAM Reaction Time Scores (in Milliseconds) by Groups, with Covariates

Source	df	F	Partial η^2	*p*	Observed Power	Wilks' Lambda
Age (A)	10, 44	6.5**	.60	<.001	1.0	.40
OSA Status (O)	10, 44	.77	.15	.66	.34	.85
A x O	10, 44	.57	.11	.83	.25	.89
GDS	10, 44	2.7*	.38	.01	.92	.62
BAI	10, 44	1.4	.24	.23	.60	.76
FSS	10, 44	1.4	.24	.24	.60	.7

Note. * p <.05; ** p <.01.

Table 10

MANOVA of ANAM Percent Correct Scores by Groups, with Covariates

Source	df	F	Partial η^2	*p*	Observed Power	Wilks' Lambda
Age (A)	10, 44	4.0**	.48	<.001	.99	.52
OSA Status (O)	10, 44	1.3	.23	.27	.58	.77
A x O	10, 44	1.1	.20	.37	.50	.80
GDS	10, 44	1.0	.19	.43	.46	.81
BAI	10, 44	1.5	.26	.16	.67	.74
FSS	10, 44	2.6*	.37	.02	.91	.63

Note. * p <.05; ** p <.01.

Table 11

MANOVA of ANAM Throughput Scores by Groups, with Covariates

Source	df	F	Partial η^2	*p*	Observed Power	Wilks' Lambda
Age (A)	10, 44	7.7**	.64	<.001	1.0	.36
OSA Status (O)	10, 44	1.3	.23	.24	.60	.77
A x O	10, 44	.4	.08	.94	.18	.92
GDS	10, 44	2.4*	.35	.02	.89	.65
BAI	10, 44	3.5*	.44	.002	.98	.56
FSS	10, 44	1.4	.24	.24	.60	.77

Note. * p <.05; ** p <.01.

Table 12

MANOVA of Gf/Gc Scores by Groups, with Covariates

Source	df	F	Partial η^2	*p*	Observed Power	Wilks' Lambda
Age (A)	4, 46	2.1	.16	.10	.58	.85
OSA Status (O)	4, 46	.5	.05	.71	.17	.96
A x O	4, 46	1.2	.10	.31	.35	.90
FSS	4, 46	2.6*	.18	.05	.68	.82
Total Number of Medications	4, 46	1.6	.12	.19	.46	.88

Note. * $p < .05$; ** $p < .01$.

Table 13

Demographic Characteristics for Experiment II Participants, by Group

Variable	Middle-Aged OSA	Older OSA
N	9	8
Age	47 (7.2)	68 (2.2)
Gender	4 M / 5 F	4 M / 4 F
BMI	36.2 (10.2)	30.3 (6.8)
Ethnicity	6 White	8 White
	1 African American	
	1 Asian	
	1 Unreported	
Number of Medical Diagnoses	3.2 (2.0)	3.5 (1.6)
Number of Medications	3.1 (2.0)	4.6 (.7)
Sleep Efficiency on PSG	77.5 (9.0)	63.2 (27.5)
Diagnostic AHI	33.8 (18.8)	32.7 (16.5)
Diagnostic O2 Saturation	94.1 (1.1)	93.0 (1.4)
CPAP AHI (Sleep Study)	16.1 (13.7)	7 (5.7)
CPAP O2 Saturation	95.4 (1.3)	95.4 (1.3)
CPAP AHI (Post Treatment)	8.0 (11.6)	10.9 (4.9)
Prescribed Pressure	8.6 (2.2)	8.3 (1.8)
Average Use on Nights Used	5:57 (1:18)	5:28 (1:43)
GDS	3.0 (1.7)	1.3 (1.3)
BAI	13.8 (11.9)	7.5 (5.5)
HAQ	29.8 (7.1)	26.4 (5.2)
SWAI-EDS	43.1 (18.6)	49.9 (13.1)
SWAI-NS	12.1 (6.5)	14.1 (5.4)
FSS	45.1 (14.5)	32.5 (8.6)

(table continues)

Table 13 *(continued)*

Variable	Middle-Aged OSA	Older OSA
SOC (short form)	7.8 (2.9)	6.1 (1.7)
mMSE	29.9 (0.3)	29.1 (0.8)

Note. Data are reported as mean (SD). PSG = polysomnography.

Table 14

Comparisons of Those Who Did and Did Not Follow-Up

	Middle-Aged		Older Adult	
	Follow-Up	No Follow-Up	Follow-Up	No Follow-Up
N	9	3	8	4
Gender	4 M / 5 F	1 M / 2F	4 M / 4 F	1 M / 3 F
BMI	36.2 (10.2)	33.8 (11.3)	30.3 (6.8)	42.8 (NA)
Number of Medical Diagnoses	3.2 (2)	2 (1)	3.5 (1.6)	2.3 (1.3)
Number of Medications	3.1 (2)	2.7 (2.1)	4.6 (.7)	2.8 (2.2)
Sleep Efficiency on PSG	77.5 (9)	79.5 (1.3)	63.2 (27.5)	86.2 (7.3)
Diagnostic AHI	33.8 (18.8)	68.8 (51.9)	32.7 (16.5)	23.9 (16.8)
Diagnostic O2 Saturation	94.1 (1.1)	93.5 (4.5)	93.0 (1.4)	94.2 (.7)
GDS	3 (1.7)	4.7 (3.1)	1.3 (1.3)	5.8 (5.6)
BAI	13.8 (11.9)	20 (12.2)	7.5 (5.5)	13 (11.3)
HAQ	29.8 (7.1)*	41 (8.7)	26.4 (5.2)	37.3 (12)
SWAI-EDS	43.1 (18.6)	48.7 (21.5)	49.9 (13.1)	50 (21)
SWAI-NS	12.1 (6.5)	15.7 (10.1)	14.1 (5.4)	15.5 (4.9)
FSS	45.1 (14.5)	45 (20.1)	32.5 (8.6)	42.5 (12.7)
SOC (short form)	7.8 (2.9)	9.3 (3.8)	6.1 (1.7)	8.5 (2.5)
mMSE	29.9 (0.3)	29.3 (1.2)	29.1 (0.8)	28.8 (1.3)
Common Analogies	16.4 (4.1)*	8 (3)	15.6 (5.4)	16 (4.5)
Letter Series	8.2 (3)	9.3 (3.1)	8.3 (2.9)	6 (6.3)
Letter Sets	3.2 (1.9)	2.7 (1.2)	4 (2.4)	3.3 (3.2)
Abstruse Analogies	11.1 (2)	9 (1.7)	12.4 (1.2)*	10.3 (1)
Simple Reaction Time	172.6 (52.6)	198 (16.1)	142.7 (44.9)	170.8 (43.5)
2-Choice Reaction Time	115.3 (46.7)	124.7 (14.5)	107 (30.2)	111.9 (7.7)
Code Substitution	42.3 (7.6)	38.5 (1.7)	30.9 (7.2)	26.8 (5.9)

(table continues)

Table 14 *(continued)*

	Middle-Aged		Older Adult	
	Follow-Up	No Follow-Up	Follow-Up	No Follow-Up
Code Substitution Delayed	43.7 (9.3)*	28.7 (11)	25.9 (10.4)	27.7 (6.4)
Matching Grids	32.2 (10.7)	28.9 (4.3)	26.5 (6.2)	22.5 (5.9)
Matching to Sample	30.8 (13.9)	19.3 (6.7)	20.2 (6.3)	23.5 (3.7)
Mathematical Processing	21.2 (4.6)*	11.9 (2.1)	21.9 (4.8)	21 (7.3)
Logical Relations	25.3 (7.4)	18.9 (6.6)	22 (5.4)	17.9 (3.8)
Running Memory	83.4 (28.3)	80.3 (18.4)	74.7 (12.9)*	40.5 (13.2)
Memory Search	79.8 (11.3)	74.4 (8)	56.4 (19.1)	67.6 (10)

Note. * $p < .05$; ** $p < .001$. Data are reported as mean (SD).

Table 15

ANAM Subtest Scores by Group at Baseline and Follow-Up

Variable	Pre-Treatment		Post-Treatment	
	Middle-Aged	Older	Middle-Aged	Older
Reaction Time (in Milliseconds)				
Simple Reaction Time	381.8 (131.7)	444.6 (142.1)	411 (206.1)	416.3 (135.9)
2-Choice Reaction Time [a,b]	477.8 (71.6)	538.1 (114.8)	410 (43.2)	503 (74.2)
Code Substitution [a]	1427.6 (297.5)	1945.3 (415.3)	1242.8 (140.8)	1904.6 (404.3)
Code Substitution Delayed [a]	1327.6 (241.8)	1737 (401)	1288 (247.3)	1617.7 (545.8)
Matching Grids [a]	1958.4 (584.4)	2342 (576.9)	1763.5 (425.4)	2272.7 (432)
Matching to Sample [a]	2014.4 (686.3)	2585.4 (665.4)	1873.2 (514.9)	2572 (520.2)
Mathematical Processing [b]	2736.5 (485.6)	2751.7 (606.2)	2552 (516.1)	2531.9 (566.9)
Logical Relations [b]	2313.2 (550.4)	2662.8 (476.8)	2062.1 (447.6)	2458 (382.4)
Running Memory	610.9 (96.5)	610 (61.6)	583.9 (62.4)	661 (96.1)
Memory Search [a]	741.1 (85.5)	892.6 (105.9)	612.7 (266.7)	842.7 (316.4)
Percent Correct				
Simple Reaction Time	100 (0.0)	99.7 (.9)	99.7 (.8)	100 (0.0)
2-Choice Reaction Time	87.5 (32.9)	93.6 (9.8)	955.5 (3.0)	97.8 (2.8)
Code Substitution	97.4 (3.0)	96.4 (3.0)	98 (2.4)	91.7 (11.8)
Code Substitution Delayed [a]	93.5 (6.1)	75 (14.8)	92.3 (10.3)	84.3 (16.7)
Matching Grids	96.7 (6.6)	98.1 (2.6)	93.9 (7.0)	93.1 (7.0)
Matching to Sample	90.2 (10.7)	83.1 (17.1)	95 (4.3)	85 (14.9)
Mathematical Processing	93.3 (7.1)	96.3 (5.2)	95 (5.6)	98.1 (2.6)
Logical Relations	92.1 (8.9)	93.8 (5.9)	94.9 (5.8)	92.7 (12.7)
Running Memory	83.2 (20.5)	79.1 (18.3)	92.6 (4.6)	80.4 (17.7)
Memory Search	97.2 (3.6)	87.5 (24.4)	98.6 (1.8)	98.2 (2.4)

(table continues)

Table 15 *(continued)*

Variable	Pre-Treatment		Post-Treatment	
	Middle-Aged	Older	Middle-Aged	Older
Throughput				
Simple Reaction Time	172.6 (52.6)	142.7 (44.9)	174.6 (67.2)	153.8 (35.0)
2-Choice Reaction Time	115.3 (46.7)	107 (30.2)	140.9 (12.2)	118.7 (16.4)
Code Substitution [a,c]	42.3 (7.6)	30.9 (7.2)	47.8 (4.7)	29.5 (7.3)
Code Substitution Delayed [a]	43.7 (9.3)	27.3 (10.4)	43.1 (15.1)	33.8 (11.2)
Matching Grids	32.2 (10.7)	26.5 (6.2)	33.7 (8.3)	25.2 (4.4)
Matching to Sample [a]	30.8 (13.9)	20.2 (6.3)	33 (11.2)	20.6 (6.0)
Mathematical Processing	21.2 (4.6)	21.9 (4.8)	23 (6.6)	23.7 (5.1)
Logical Relations [b]	25.3 (7.4)	22 (5.4)	29.1 (8.1)	23.4 (6.3)
Running Memory	83.4 (28.4)	73.2 (13.2)	95.2 (15)	71.5 (23.5)
Memory Search [b]	79.8 (11.3)	57.2 (20.5)	120.7 (67.2)	83.7 (48.8)

Note. Data are reported as mean (*SD*). [a] Significant main effect of age; [b] Significant main effect of time; [c] Significant interaction.

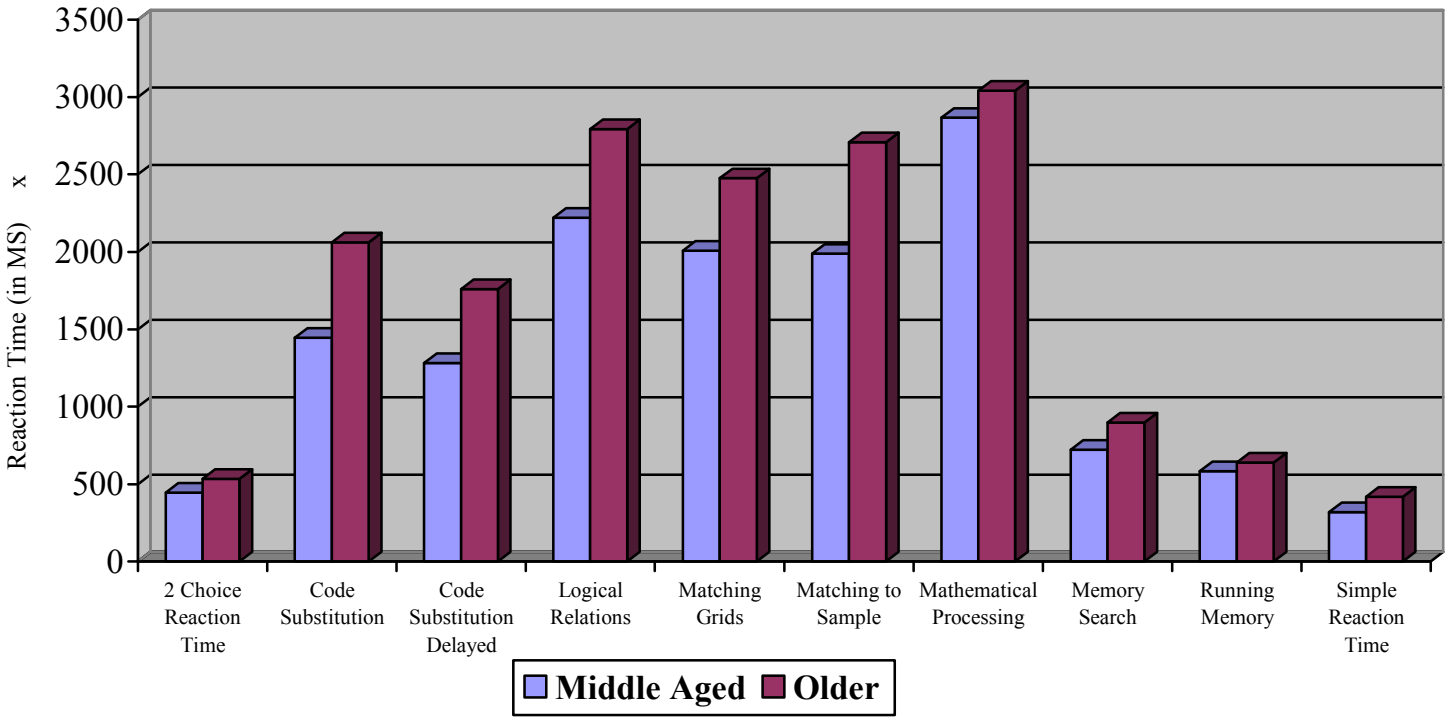

Figure 1.Differences by age group (middle-aged, older) on ANAM subtest response times in milliseconds.

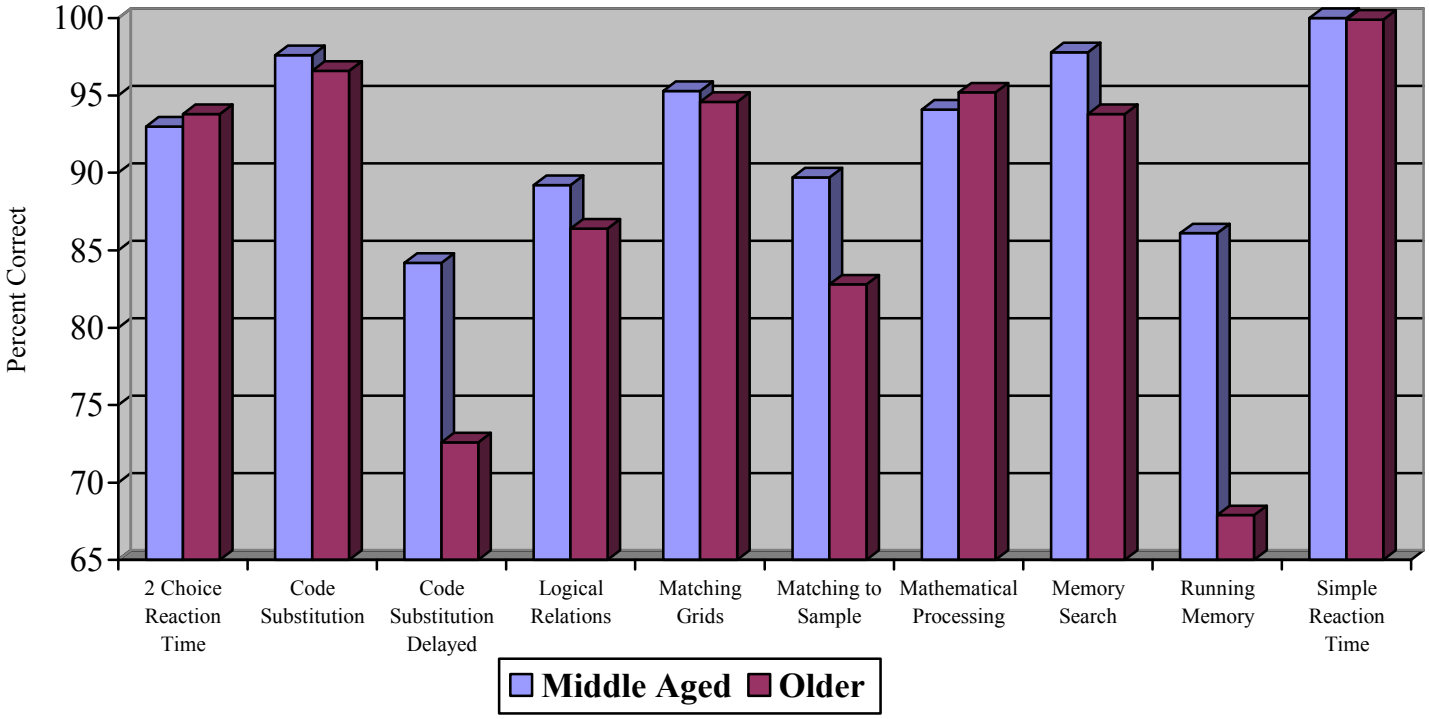

Figure 2. Differences by age group (middle-aged, older) on ANAM subtests' percent correct.

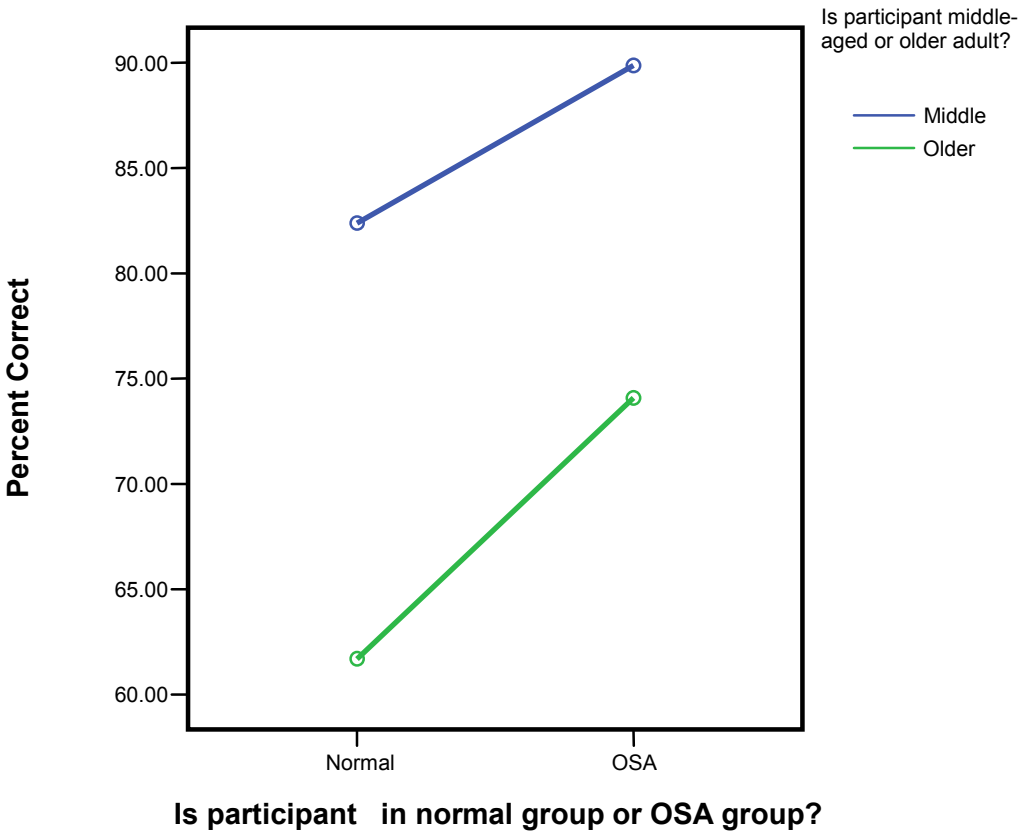

Figure 3. Relationship between age group and OSA group on the Running Memory subtest's percent correct; this subtest measures working memory. There was a main effect of age, with middle aged adults more accurate, but no effect of OSA and no interaction.

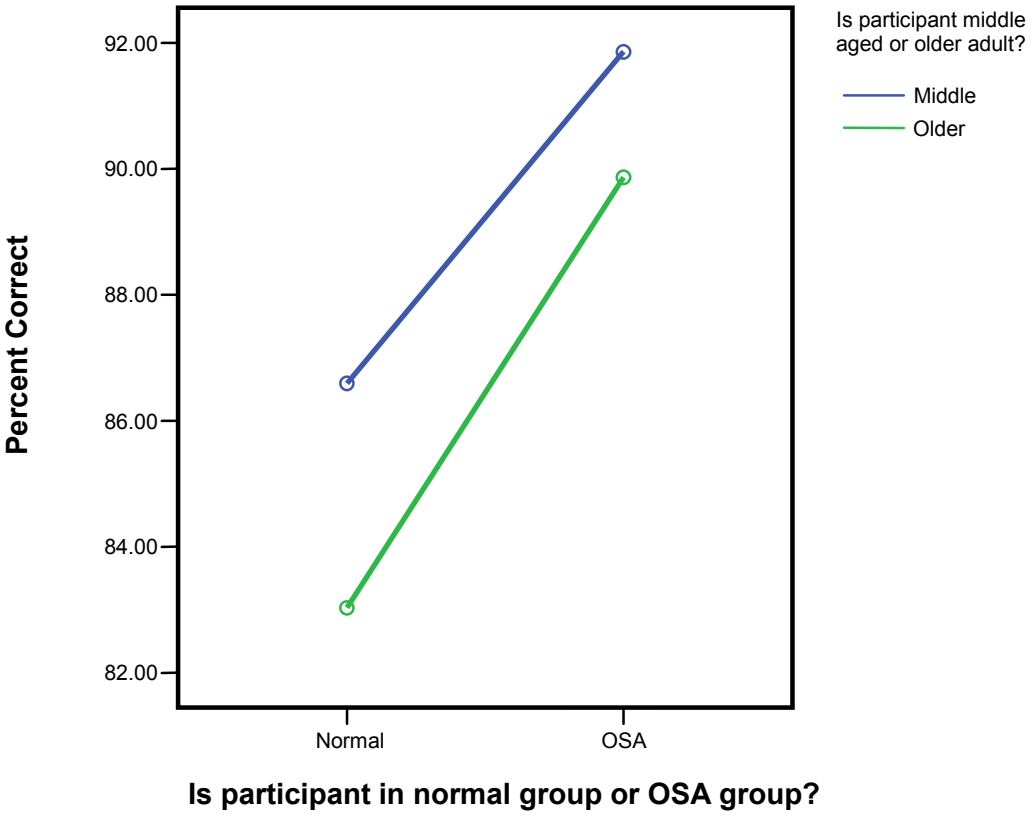

Figure 4. Relationship between age group and OSA group on Logical Relations subtest's percent correct; this subtest measures mental flexibility. There were no main effects of age group or OSA group and no interaction.

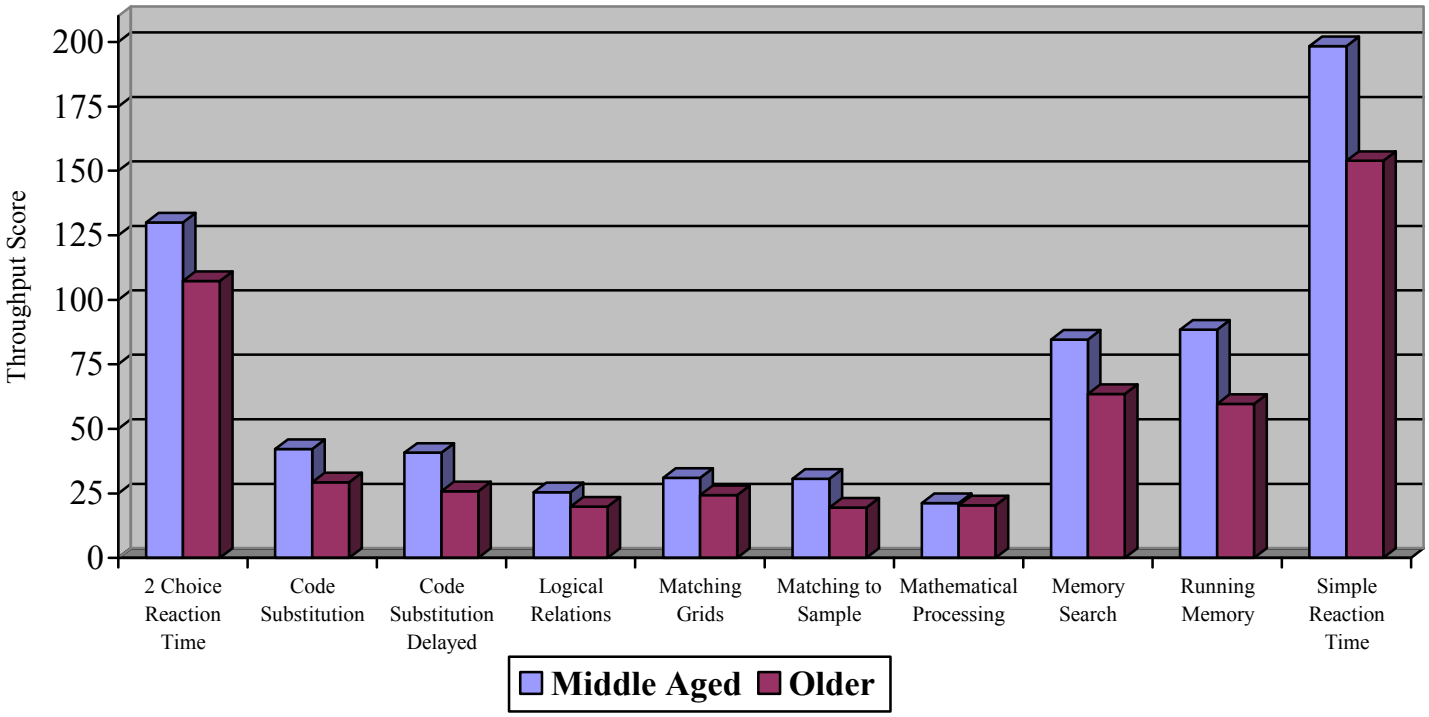

Figure 5. Differences by age group (middle-aged, older) on ANAM throughput scores by subtest.

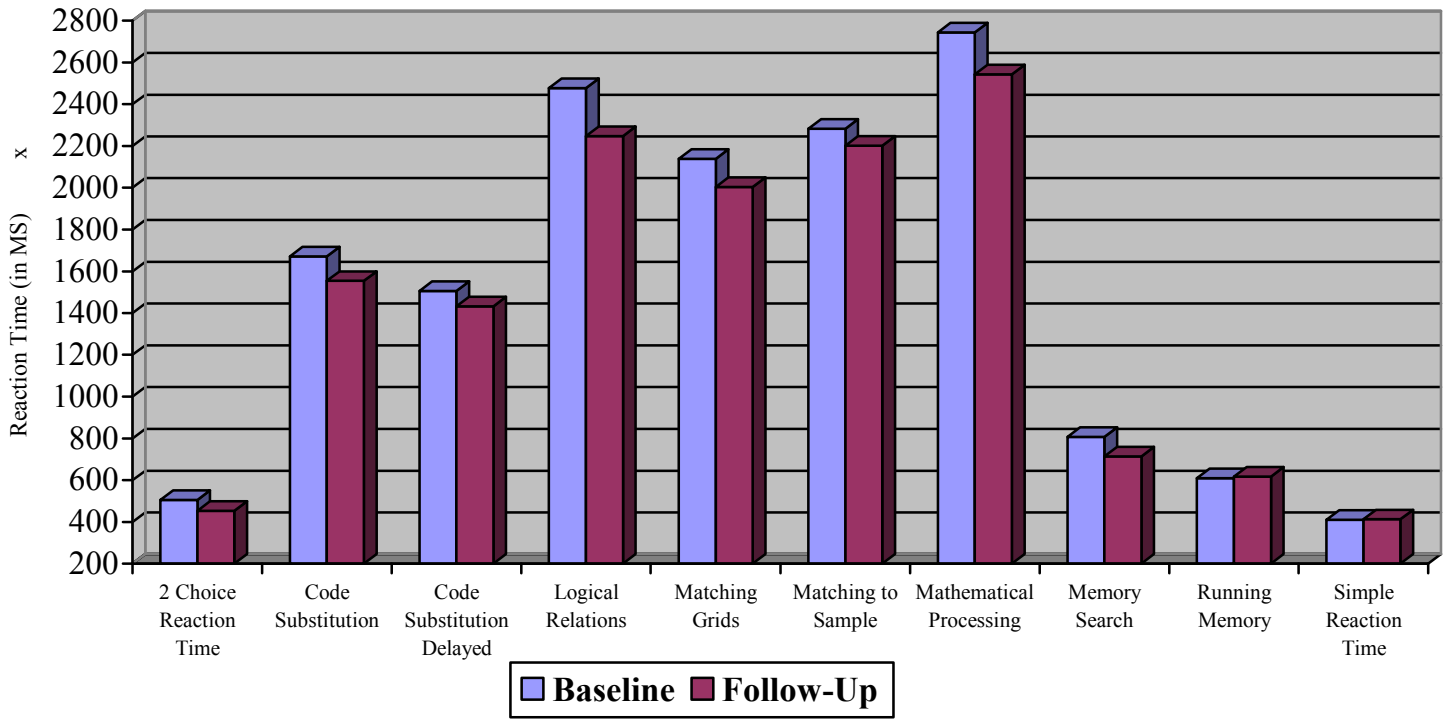

Figure 6. ANAM reaction time scores in milliseconds, by subtest, at baseline and after approximately one month of CPAP treatment.

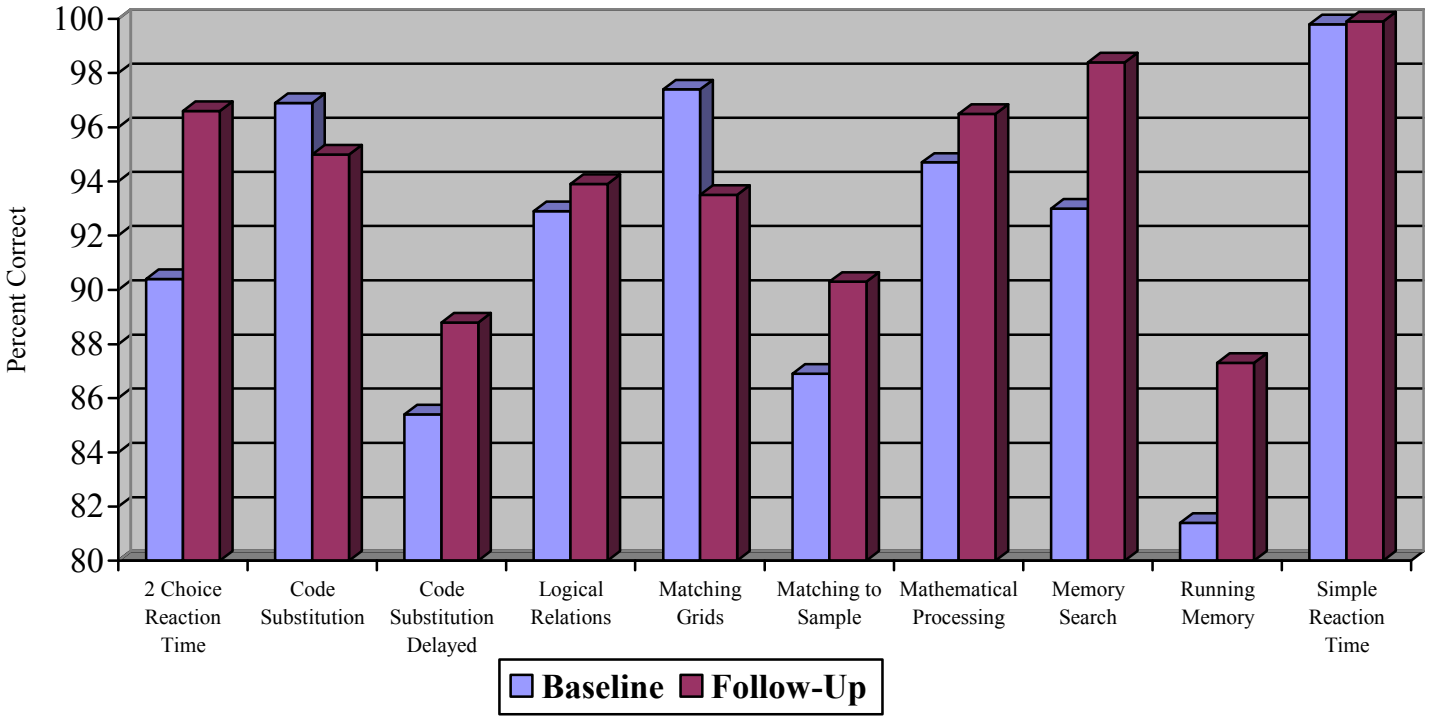

Figure 7. Percent correct on ANAM subtest scores at baseline and after approximately one month of CPAP treatment.

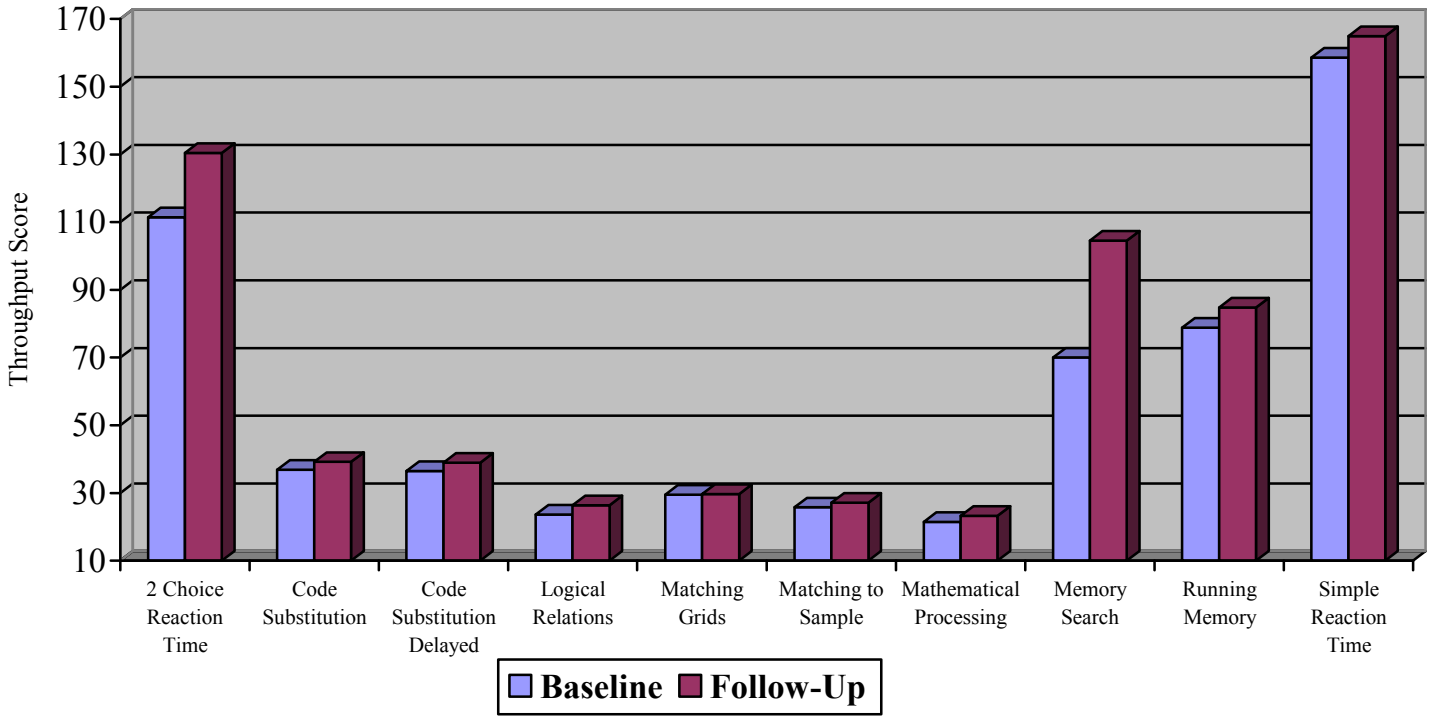

Figure 8. ANAM throughput scores at baseline and after approximately one month of CPAP treatment.

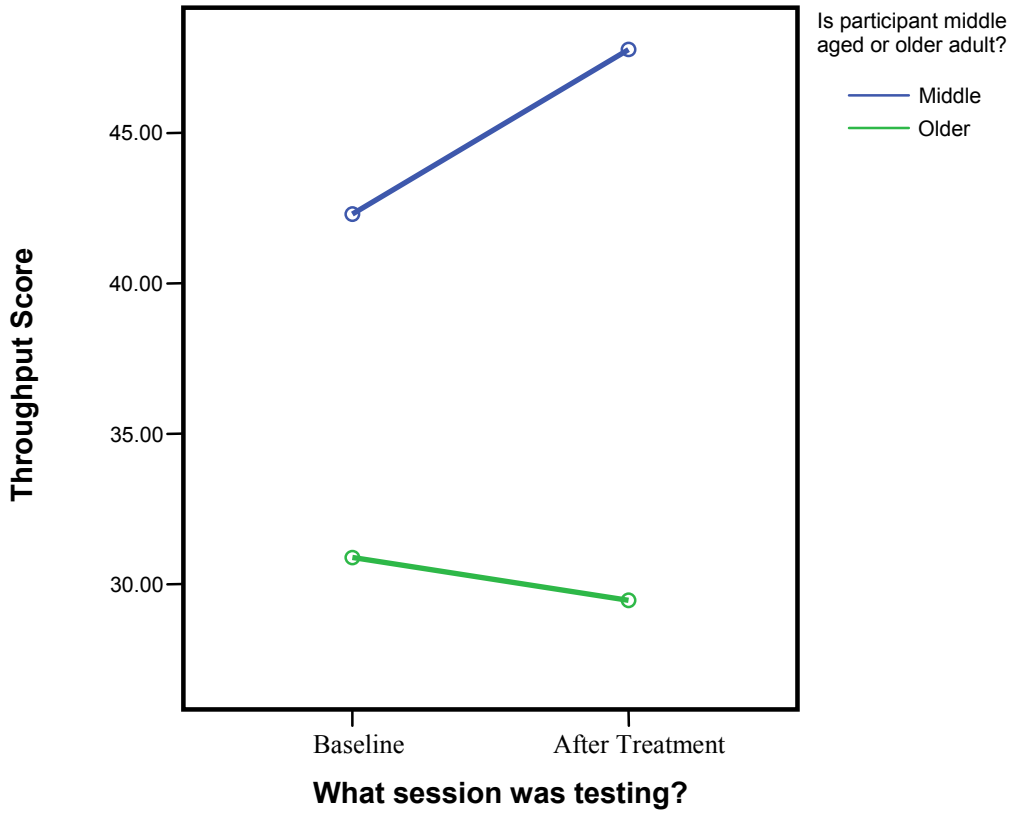

Figure 9. Relationship between age group and session (baseline, after treatment) on the throughput score of Code Substitution, which measures attention. There was a main effect of age and a significant interaction between age group and session..

REFERENCES

Alchanatis, M., Zias, N., Deligiorgis, N., Amfilochiou, A., Dionellis, G., & Orphanidou, D. (2005). Sleep apnea-related cognitive deficits and intelligence: An implication of cognitive reserve theory. *Journal of Sleep Research*, *14*, 69-75.

Alexander, G.E., Furey, M.L., Grady, C.L., Pietrini, P., Brady, D.R., Mentis, M.J., & Schapiro, M.B. (1997). Association of premorbid intellectual function with cerebral metabolism in alzheimer's disease: Implications for the cognitive reserve hypothesis. *American Journal of Psychiatry*, *154*, 165-172.

Aloia, M.S., Ilnickzky, N., Di Dio, P., Perlis, M.L., Greenblatt, D.W. & Giles, D.E. (2003). Neuropsychological changes and treatment compliance in older adults with sleep apnea. *Journal of Psychosomatic Research*, *54*, 71-76.

Aloia, M.S, Arnedt, J.T, Davis, J.D., Riggs, R.L., Byrd, D. (2004). Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: A critical review. *Journal of the International Neuropsychological Society*, *10*(5), 772-785.

Bardwell, W.A., Ancoli-Israel, S., Berry, C.C., & Dimsdale, J.E. (2001). Neuropsychological effects of one-week continuous positive airway pressure treatment in patients with obstructive sleep apnea: A placebo-controlled study. *Psychosomatic Medicine*, *63*(4), 579-584.

Barnes, D.E., Cauley, J.A., Lui, L., Fink, H.A., McCulloch, C., Stone, K.L., & Yaffe, K. (2007). Women who maintain optimal cognitive function in old age. *Journal of the American Geriatric Society*, *55*, 259-264.

Beck, A.T., Epstein, N., Brown, G., & Steer, R.A. (1988). An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology*, *56*(6), 893-897.

Bédard, M.A., Montplaisir, J.,Richer, F., Rouleau, I., & Malo, J. (1991). Obstructive sleep apnea syndrome: Pathogenesis of neuropsychological deficits. *Journal of Clinical and Experimental Neuropsychology*, *13*(6), 950-964.

Bédard, M.A., Montplaisir, J., Malo, J., Richer, F., Rouleau, I. (1993). Persistent neuropsychological deficits and vigilance impairment in sleep apnea syndrome after treatment with continuous positive airways pressure (CPAP). *Journal of Clinical and Experimental Neuropsychology*, *15*(2), 330-341.

Beebe, D.W., Groesz, L., Wells, C., Nichols, A., McGee, K. (2003) The neuropsychological effects of obstructive sleep apnea: A meta-analysis of norm-referenced and case-controlled data. *Sleep*, *26*(3) 298-307.

Bernstein, I.H., Rush, A.J., Thomas, C.J., Woo, A., & Trivedi, M.H. (2006). Item response analysis of the inventory of depressive symptomatology. *Neuropsychiatric Disorders Treatment*, *2*(4) 557-564.

Berry, D.T.R., Webb, W.B., Block, A.J., Bauer, R.M., & Switzer, D.A. (1986). Nocturnal hypoxia and neuropsychological variables. *Journal of Clinical and Experimental Neuropsychology*, *8*(3) 229-238.

Berry, D.T.R., Phillips, B.A., Cook, Y.R., Schmitt, F.A., Honeycutt, N.A., Arita, A.A. et al. (1990). Geriatric sleep apnea syndrome: A preliminary description. *Journal of Gerontology*, *45*(5), 169-174.

Bleiberg, J., Kane, R.L., Reeves, D.L., Garmoe, W.S., Halpern, E. (2000). Factor analysis of computerized and traditional tests used in mild brain injury research. *Clinical Neuropsychology*, *14*(3), 287-294.

Block, A.J., Berry, D., & Webb, W. (1986). Nocturnal hypoxemia and neuropsychological deficits in men who snore. *European Journal of Respiratory Disorders*, *69*, 405-408.

Borak, J., Cieslicki, J.K., Koziej, M., Matuszewski, A., & Zielinski, J. (1996). Effectsof cpap treatment on psychological status in patients with severe obstructive sleep apnoea. *Journal of Sleep Research*, *5*, 123-127.

Boron, J.B., Turiano, N.A., Willis, S.L., & Schaie, K.W. (2007). Effects of cognitive training on change in accuracy in inductive reasoning ability. *Journal of Gerontology*, *62B*(3), 179-186.

Camicioli, R.C., & Wild, K. (2006). *Assessment of the Elderly with Dementia.* In: Handbook of Neurology Rating Scales. R.M. Herndon (Ed.). Demos Medical Publishing, 195-260.

Carskadon M.A, Dement W.C. (1981) Respiration during sleep in the aged human. *Journal of Gerontology*, *36* 420–423.

Cheshire, K., Engleman, H., Deary, I., Shapiro, C., & Douglas, N.J. (1992). Factors impairing daytime performance in patients with sleep apnea.hypopnea syndrome. *Archives of Internal Medicine*, *152*, 538-541.

Cohen-Zion, M., Stepnowsky, C., Marler, Shochat, T., Kripke, D.F., & Ancoli-Israel, S. (2001). Changes in cognitive function associated with sleep disordered breathing in older people. *Journal of the American Geriatric Society*, *49*, 1622-1627.

Collins, L. (2000). Comparative validity of nart, nart-r, amnart, wrat-III reading, and act scores in predicting wais-III fsiqs: Implications for estimation of premorbid intelligence in adults. *Dissertation Abstracts International*, 60, 8B

Décary, A., Rouleau, I., Montplaisir, J. (2000). Cognitive deficits associated with sleep apnea syndrome: A proposed neuropsychological test battery. *Sleep*, *23*(3), 369-381.

Dolan, D.C., & Rosenthal, L. (2007). Subjective Evaluation of Sleepiness. In L. Shigley, M. Jones-Parker, & T. Lee-Chiong (Eds.), *Textbook of Polysomnography* (pp. 419-426). Philadelphia, PA: Lippincott, Williams, & Wilkins.

Engleman, H.M., Martin, S.E., Deary, I.J., & Douglas, N.J. (1994). Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. *The Lancet*, *343*, 572-575.

Engleman, H.M., Martin, S.E., Deary, I.J., & Douglas, N.J. (1997). Effect of cpap therapy on daytime function in patients with mild sleep apnoea/hypopnoea syndrome. *Thorax*, *52*, 114-119.

Engleman, H.M., Martin, S.E., Kingshott, R.N., Mackay, T.W., Deary, I.J., & Douglas, N.J. (1998). Randomised placebo-controlled trial of daytime function after continuous positive airway pressure (cpap) therapy for the sleep apnoea/hypopnoea syndrome. *Thorax*, *53*, 341-345.

Engleman, H.M., Kingshott, R.N., Wraith, P.K., Mackay, T.W., Deary, I.J., & Douglas, N.J. (1999). Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. *American Journal of Respiratory and Critical Care Medicine*, *159*, 461-467.

Engleman, H., & Joffe, D. (1999). Neuropsychological function in obstructive sleep apnoea. *Sleep Medicine Reviews*, *3(1)*, 59-78.

Eysenck, M.W., Derakshan, N., Santos, R., & Calvo, M.G. (2007). Anxiety and cognitive performance: Attentional control theory. *Emotion*, *7(2)*, 336-353.

Ferini-Strambi, L., Baietto, C., DiGioia, M.R., Castaldi, P., Castronovo, C., Zucconi, M. et al. (2003). Cognitive dysfunction in patients with obstructive sleep apnea (osa): Partial reversibility after continuous positive airway pressure (cpap). *Brain Research Bulletin*, *61*, 87-92.

Findley, L.J., Barth, J.T., Powers, D.C., Wilhoit, S.C., Boyd, D.G., & Suratt, P.M. (1986). Cognitive impairment in patients with obstructive sleep apnea and associated hypoxemia. *Chest*, *90(5)*, 686-690.

Findley, L.J., Suratt, P.M., & Dinges, D.F. (1999). Time-on-task decrements in "steer clear" performance of patients with sleep apnea and narcolepsy. *Sleep*, *22(6)*, 804-809.

Folstein, M., Folstein, S.E. & McHugh, P.R. (1975). "Mini-mental state" a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12(3)*, 189-198.

Folstein, M. F., Folstein, S. E., McHugh, P. R., & Fanjiang, G. (2001). *Mini-Mental State Examination user's guide.* Odessa, FL: Psychological Assessment Resources.

Freund, A.M., & Baltes, P.B. (1998). Selection, optimization, and compensation as strategies of life management: Correlations with subjective indicators of successful aging. *Psychology and Aging*, *13(4)*, 531-543.

Freund, A.M., & Baltes, P.B. (2002). Life management strategies of selection, optimization, and compensation: Measurement by self-report and construct validity. *Journal of Personality and Social Psychology*, *82(4)*, 642-662.

Friedman, B., Heisel, M.J., & Delavan, R.L. (2005). Psychometric properties of the 15-item geriatric depression scale in functionally impaired, cognitively intact, community dwelling elderly primary care patients. *Journal of the American Geriatric Society, 53*, 1570-1576.

Giambra, L.M., Arenberg, D., Zonderman, A.B., Kawas, C., & Costa, Jr., P.T. (1995). Adult lifespan changes in immediate visual memory and verbal intelligence. *Psychology and Aging*, *10(1)*, 123-139.

Gilliland, K. (2008, September). *Automated neuropsychological assessment metric ANAM: development, validation, and current use.* Lecture presented at the Blast Concussion and mTBI Assessment Across the Deployment Cycle conference, San Antonio, TX.

Greenberg, G.D., Watson, R.K., & Deptula, D. (1987). Neuropyschological dysfunction in sleep apnea. *Sleep*, *10(3)*, 254-262.

Grober, E. & Sliwinski, M. (1991). Development and validation of a method for estimating pre-morbid verbal IQ in the elderly. *Journal of Clinical and Experimental Neuropsychology*. *13(6)*, 933-949.

Guido, P., Rosenthal, L., Bishop, C., Roehrs, T.A., Michaelson, S., Syron, M., & Roth, T. (1995) The measurement of sleepiness in a sleep apnea population. *Sleep Research, 24*, 51.

Hayslip, Jr., B. & Maiden, R.J. (2005). Cognitive loss. In Dulmus, C.N. & Rapp-Paglicci, L.A. (Eds.), *Preventive interventions for adults* (pp. 27-55). Hoboken, NJ: Wiley & Sons.

Hayslip, Jr., B., & Sterns, H.L. (1979). Age differences in relationships between fluid and crystallized intelligences and problem solving. *Journal of Gerontology*, *34*, 404-414.

Hayward, L., Mant, A., Eyland, A., Hewitt, H., Purcell, C., Turner, J., Goode, E., Le Count, A., Pond, D., & Saunders, N. (1992). Sleep disordered breathing and cognitive function in a retirement village population. *Age and Aging*, *21*, 121-128.

Hiestand, D.M., Britz, P., Goldman, M., & Phillips, B. (2006). Prevalence of symptoms and risk of sleep apnea in the us population: results from the national sleep foundation sleep in america 2005 poll. *Chest*, *130*, 780-786.

Hogan, D.B., & Ebly, E.M. (2000). Predicting who will develop dementia in a cohort of Canadian seniors. *Canadian Journal of Neurological Science*, *27(1)*, 18-24.

Horn J.L. (1975). *Gf-Gc sampler*. University of Denver, Mimeo.

Ingram, F., Henke, K.G., Levin, H.S., Fishel Ingram, P.T., & Kuna, S.T. (1994). Sleep apnea and vigilance performance in a community-dwelling older sample. *Sleep*, *17(3)*, 248-252.

Janssens, J.P., Pautex, S., Hilleret, H., & Michel, J.P. (2000). Sleep disordered breathing in the elderly. *Aging Clinical and Experimental Research*, *12*, 417-429.

Kane, R.L., & Kay, G.G. (1992) Computerized assessment in neuropsychology: A review of tests and test batteries. *Neuropsychological Review, 3***,** 1–117.

Kane R.L., Roebuck-Spencer, T., Short, P., Kabat, M., & Wilken, J. (1997). Identifying and monitoring cognitive deficits in clinical populations using automated neuropsychological assessment metrics (anam) tests. *Archives of Clinical Neuropsychology*, *22(S1)*, S115-S126.

Kay, G.G., & Starbuck, V.N. (X) Computerized neuropsychological assessment. In Maruish, M.E. & Moses, J.A. (Eds.), *Clinical neuropsychology: theoretical foundations for practitioners* (pp. 143-161). Hillsdale, NJ: Erlbaum.

Kribbs, N.B., Pack, A.I., Kline, L.R., Getsy, J.E., Schuett, J.S., Henry, J.N. et al. (1993). Effects of one night without nasal cpap treatment on sleep and sleepiness in patients with obstructive sleep apnea. *American Review of Respiratory Disorders*, *147*, 1162-1168.

Krupp, L.B., LaRocca, N.G., Muir-Nash, J., & Steinberg, A.D. (1989). The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of Neurology*, *46(10)*, 1121-1123.

Lee, M.M., Strauss, M.E., Adams, N., & Redline, S. (1999). Executive functions in persons with sleep apnea. *Sleep and Breathing*, *3(1)*, 13-16.

Lesher, E.L., & Berryhill, J.S. (1994). Validation of the geriatric depression scale short form among inpatients. *Journal of Clinical Psychology*, *50(2)*, 256-260.

Lichstein, K. L., Means, M. K., Noe, S. L., & Aguillard, R. N. (1997). Fatigue and sleep disorders. *Behaviour Research and Therapy*, *35*, 733-740

Lopez, M.N., Charter, R.A., Mostafavi, B., Nibut, L.P., & Smith, W.E. (2005). Psychometric properties of the folstein mini-mental state examination. *Assessment*, *12(2)*, 137-144.

Lucock, M.P., & Morley, S. (1996). The health anxiety questionnaire. *British Journal of Health Psychology, 1,* 137-150.

Morrell, M.J., McRobbie, D.W., Quest, R.A., Cummin, A.R.C., Ghiassi, R., & Corfield, D.R. (2003). Changes in brain morphology associated with obstructive sleep apnea. *Sleep Medicine*, *4,* 451-454.

Munoz, A., Mayoralas, L.R., Barbe, F., Pericas, J., & Agusti, A.G.N. (2000). Long-term effects of CPAP on daytime functioning in patients with sleep apnoea syndrome. *European Respiratory Journal*, *15*, 676-681.

Naegele, B., Pepin, J.L., Levy, P., Bonnet, C., Pellat, J., Feuerstein, C. (1998). Cognitive executive dysfunction in patients with obstructive sleep apnea syndrome (OSAS) after CPAP treatment. *Sleep*, *21(4)*, 392-397.

Naegele, B., Thouvard, V., Pepin, J., Levy, P., Bonnet, C., Perret, J.E., Pellat, J. & Feuerstein, C. (1995). Deficits of cognitive executive functions in patients with sleep apnea syndrome. *Sleep*, *18(1)*, 43-52.

Nebes, R.D., Buysse, D.J., Halligan, E.M., Houck, P.R., & Monk, T.H. (2009). Self-reported sleep quality predicts poor cognitive performance in healthy older adults. *Journal of Gerontology*, *64B (2)*, 180-187.

Phillips, B.A., Berry, D.T.R., Lipke-Molby, T.C. (1996). Sleep disordered breathing in healthy, aged persons: Fifth and final year follow-up. *Chest*, *110*, 654-658.

Pilcher, J., & Huffcutt, A. (1996). Effects of sleep deprivation on performance: A meta-analysis. *Sleep*, *19(4)*, 318-326.

Powell, N.B., Riley, R.W., Schechtman, K.B., Blumen M.B., Dinges, D.F., & Guilleminault, C. (1999). A comparative model: Reaction time performance in sleep-disordered breathing versus alcohol-impaired controls. *The Laryngoscope, 109*, 1648-1654.

Rabbit, P., Diggle, P., Smith, D., Holland, F., & McInnes, L. (2001). Identifying and separating the effects of practice and of cognitive ageing during a large longitudinal study of elderly community residents. *Neuropsychologia*, *39*, 532-543.

Redline, S., Strauss, M.E., Adams, N., Winters, M., Roebuck, T., Spry, K., Rosenberg, C., & Adams, K. (1997). Neuropsychological function in mild sleep-disordered breathing. *Sleep*, *20(2)*, 160-167.

Roehrs, T., Merrion, M., Pedrosi, B., Stepanski, E., Zorick, F., & Roth, T. (1995). Neuropsychological function in obstructive sleep apnea syndrome (osas) compared to chronic obstructive pulmonary disease (copd). *Sleep*, *18(5)*, 382-388.

Rosenthal, L., Roehrs, T.A., & Roth, T. (1993). The sleep-wake activity inventory: a self-report measure of daytime sleepiness. *Biological Psychiatry*, *34*, 810-820.

Rosenthal, L., Dolan, D.C., & Taylor, DJ. (2006) Response to CPAP Therapy in Sleepy and Non-Sleepy OSA Patients. *Sleep*, *29*, A211. (Abstract Suppl.)

Rush, A.J., Gullion, C.M., Basco, M.R., Jarret, R.B., & Trivedi, M.H. (1996). The inventory of depressive symptomology (ids): Psychometric properties. *Psychological Medicine*, *26(3)*, 477-486.

Salorio, C.F., White, D.A., Piccirillo, J., Duntley, S.P., & Uhles, M.L. (2002). Learning, memory, and executive control in individuals with obstructive sleep apnea syndrome. *Journal of Clinical and Experimental Neuropsychology*, *24(1)*, 93-100.

Salthouse, T.A. & Davis, H.P. (2006). Organization of cognitive abilities and neuropsychological variables across the lifespan. *Developmental Review*, *26*, 31-54.

Saunamaki, T., & Jehkonen, M. (2007). Depression and anxiety in obstructive sleep apnea syndrome: A review. *Acta Neurologica Scandinacia*, *116(5)*, 277-288.

Schaie, K.W. (1994). The course of adult intellectual development. *The American Psychologist*, *49(4)*, 304-313.

Sheikh, V.I., & Yesavage, V.A. (1986). Geriatric depression scale (gds): Recent evidence and development of a shorter version. In: T.L. Brink (Ed). *Clinical gerontology: a guide to assessment and intervention* (pp 165-174). New York: Haworth Press.

Sternberg, D.E., & Jarvik, M.E. (1976). Memory functions in depression. *Archives of General Psychiatry*, *33(2)*, 219-224.

Tombaugh, T.M., & McIntyre, N.J. (1992). The mini-mental state examination: A comprehensive review. *Journal of the American Geriatrics Society*, *40(9)*, 922-935.

Valencia-Flores, M., Bliwise, D.L., Guilleminault, C., Cilveti, R., & Clerk, A. (1996). Cognitive function in patients with sleep apnea after acute nocturnal nasal continuous positive airway pressure (cpap) treatment: Sleepiness and hypoxemia effects. *Journal of Clinical and Experimental Neuropsychology, 18(2)*, 197-210.

Verstraeten, E., Cluydts, R., Pevernagie, D., & Hoffmann, G. (2004). Executive function in sleep apnea: Controlling for attentional capacity in assessing executive attention. *Sleep*, *27(4)*, 685-693.

Wahlin, A., MacDonald, S.W.S., deFrias, C.M., Nilsson, L., & Dixon, R.A. (2006). How do health and biological age influence chronological age and sex differences in gognitive aging: Moderating, mediating, or both? *Psychology and Aging*, *21(2)*, 318-332.

Willis, S.L., Tennstedt, S.L., Marsiske, M., Ball, K., Elias, J., Koepke, K.M. et al. (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. *Journal of the American Medical Association*, *296*, 2805-2814.

Yesavage, J., Bliwise, D., Guilleminault, C., Carskadon, M., & Dement, W. (1985). Preliminary communication: Intellectual deficit and sleep-related respiratory disturbance in the elderly. *Sleep*, *8(1)*, 30-33.

Zelinski, E.M., Gilewski, M.J., & Schaie, K.W. (1993). Individual differences in cross-sectional and three-year longitudinal memory performance across the adult life span. *Psychology and Aging*, *8(2)*, 176-18