SLEEP AND COGNITIVE DEFICITS IN OLDER ADULTS

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ABSTRACT

BREA SALIB: Sleep and Cognitive Deficits in Older Adults
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There has been much research examining the effects of sleep problems on cognitive function, and on cognitive decline in older adults. However, little has been done to examine the subclinical, age-related sleep changes in older adults in relation to cognitive function. Thus, the aim of this study was to explore the neuropsychological sequelae of mild sleep disordered breathing in community-dwelling older adults. It was found that desaturations, repeated decreases in blood oxygenation, negatively impacted blood oxygenation. Furthermore, desaturations had a negative relationship to performance on tests of attention, speed, and working memory. Moreover, deficits in attention, speed, and working memory were associated with poor performance on tests of verbal and visual long term episodic memory. Notably, EEG arousals, thought to be another component of sleep disordered breathing, were not related to desaturations or cognitive performance. Cardiovascular disease was also examined to determine is associations with the sleep, oxygenation, and cognitive variables. Although cardiovascular disease, particularly heart-related symptoms, was related to some aspects of sleep disordered breathing, it did not explain the relationship between desaturations and cognitive deficits.
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Specific Aims

The purpose of this study was to use secondary data analysis to examine the degree to which performance on cognitive measures in a sample of community-dwelling older adults is related to mild sleep-disordered breathing. There has been much research examining the effects of sleep problems on cognitive function, and on cognitive decline in older adults. However, little has been done to examine the subclinical, age-related sleep changes in older adults in relation to cognitive function. Research in sleep-disordered breathing has shown associations between arterial oxygenation during sleep, desaturations, and EEG arousals on cognition. Thus, the aim of this study was to explore the neuropsychological sequelae of mild sleep-disordered breathing in older adults in an attempt to provide a meaningful link between the sleep and aging literatures. This study also sought to explicate the relationship among measures of arterial oxygenation during sleep, arterial oxygenation during wake, desaturations, and arousals. Lastly, this study investigated whether the relationship between arterial oxygenation, EEG arousals, and cognitive performance was influenced by symptoms of cardiovascular disease.

Background and Significance

Sleep in Older Adults

Sleep problems in older adults are well documented, both with respect to subjective and objective measures (Ancoli-Israel & Ayalon, 2006; Bliwise, 2000; Martin, Shohat, & Ancoli-Israel, 2000). With respect to subjective measures, many studies have shown that older adults report a subjective experience of “poor sleep.” For instance, in a survey of more
than 9000 older adults, more than half reported at least one sleep problem, such as waking
during the night and waking without feeling rested in the morning (Foley et al., 1995). Only
12% of the sample reported no sleep complaints (Foley et al., 1995). The sample of older
adults in the aforementioned study included community-dwelling participants with physical
disabilities, depressive symptoms, and poor self-perceived health; yet even older adults in
good health appeared to have sleep problems. Older adults also report an increase in the
number of awakenings they experience at night, and also in their daytime napping (Bliwise,
Ansari, Straight, & Parker, 2005).

Some studies have suggested that the increase in sleep problems in older adults may
be the result of medical and psychiatric illnesses (Foley, Monjan, Simonsick, Wallace, &
Blazer, 1995; Foley, Ancoli-Israel, Britz, & Walsh, 2004). Conditions such as depression,
diabetes, and lung disease, among others, appear to be associated with sleep-related
problems. In fact, in one study, among a group of older adults free of health problems, only
10% reported their sleep as fair or poor (Foley et al., 2004). It should be noted, however, that
it can be difficult to discriminate between sleep problems associated with age-related medical
problems versus developmentally normal change in sleep in older adults. Using statistical or
recruiting methods to control for psychiatric and medical illness is essential to rule out their
influence on both sleep and cognition in the study of developmental changes.

In addition to subjective reports of poor sleep, evidence indicates that older adults are
more likely to experience multiple objective causes of poor sleep, one of which is sleep-
disordered breathing. Sleep-disordered breathing refers to a group of disorders of breathing
primarily characterized by pauses in airflow during sleep. The severity of sleep-disordered
breathing occurs on a continuum, from severe cases of obstructive sleep apnea, characterized
by the frequent repeated collapse of the airway during sleep, to milder non-clinical forms of occasional interrupted airflow. Two effects associated with obstructive sleep apnea are decreased blood oxygen saturation in the brain, known as hypoxemia, and arousals. An arousal is a shift in EEG activity from a deeper to a lighter stage of sleep. The severity of obstructive sleep apnea symptoms is quantified by assessing via polysomnography the number of apnea and hypopnea events that occur per hour of sleep. Apneas occur when airflow ceases and hypopneas occur when airflow during sleep decreases but does not completely stop. To be diagnosed with obstructive sleep apnea, a person must have 10 or more apnea/hypopnea events per hour, and someone with severe sleep apnea would have more than 30 apnea/hypopnea events per hour. The severity of sleep-disordered breathing in older adults spans this continuum.

Compared to their younger counterparts, there is a higher incidence of clinically diagnosable sleep disorders in older adults (Ancoli-Israel & Ayalon, 2006; Bliwise, 2000; Tishler, Larkin, Schluchter, & Redline, 2003; Zamarron, et al., 1999). Obstructive sleep apnea occurs in approximately 15% of adults 65 and older, compared to 2-4% of younger adults (Ancoli-Israel et al., 1991). Not only do older adults demonstrate an increase in obstructive sleep apnea, but they also evidence an increase in mild sleep-disordered breathing, a reduction in air intake during sleep that does not meet diagnostic criteria for obstructive sleep apnea. One study found that more than 30% of older adults 70 and over exhibited mild sleep-disordered breathing, with at least five breathing interruptions per hour, despite the fact that the participants described themselves as healthy and were not diagnosed with a sleep disorder (Hoch et al., 1990). Several studies of community-dwelling older adults
found that approximately 25% of its sample evidenced sleep-disordered breathing (Mehra et al., 2007; Phillips et al., 1992).

Sleep-disordered breathing is detrimental for two reasons. First, sleep-disordered breathing is associated with desaturations, defined as frequent, repeated drops in blood oxygenation by 4% or more. These desaturations consequently negatively affect the average arterial oxygenation during sleep, such that the more frequently an individual has desaturations, the lower his or her average arterial oxygenation will be for that period of sleep. A study examining the prevalence of desaturations in healthy older adults found that these desaturations were occurring more than five times per hour in more than 30% of their sample, and more than 10 desaturations per hour in more than 25% of the sample (Philip, Dealberto, Dartigues, Guillemainault, & Bioulac, 1997). A second consequence of breathing disturbances is that the body compensates by increasing respiratory effort, disrupting the continuity of the pattern of EEG brain waves (Kimoff et al., 1994). This disrupted pattern of brain activity can be objectively measured by polysomnography, a method of measuring sleep that monitors brain activity (via EEG), respiration, eye and jaw muscle activity, and heart rate.

As shown in Figure 1, the EEG component of polysomnography measures the amount of time spent in each of the five sleep stages. Stage 1 represents the lightest stage of sleep, and is characterized by theta waves, which are relatively low amplitude, high frequency brain waves. Stage 2 sleep is similar to Stage 1, except that it includes sleep spindles, which are sudden increases in wave frequency, and K-complexes, which are short bursts of increased wave amplitude. Stages 3 and 4 of sleep are characterized by delta waves, which have a slower frequency and greater wave amplitudes compared to Stages 1 and 2. Stages 3 and 4
are referred to as “slow wave sleep” because of the slow delta waves, and they represent the deepest stages of sleep. The fifth stage of sleep is Rapid Eye Movement, or REM sleep, characterized by rapid brain waves similar to those seen during the waking state, and it is the stage during which most dreaming occurs.

Most young and middle aged adults have a fairly predictable pattern of sleep stages during a night’s sleep. Many older adults, however, exhibit a pattern of disrupted sleep characterized by frequent arousals (see Figure 2). As indicated earlier, the interruption of any stage of sleep due the appearance of a lighter stage of sleep (e.g. shifting from Stage 3 to Stage 2 sleep) or to an increase in the frequency of brain activity is called an arousal (ASDA, 1992). The term “sleep fragmentation” connotes the pattern of EEG sleep that results when the normal continuity of sleep stages is disrupted by repeated arousals. One effect of fragmentation is a reduction in the amount of time spent in deeper, slow wave sleep (Stages 3 and 4), and an increased amount of time spent in lighter stages of sleep (Stages 1 and 2).

Polysomnography studies have shown that older adults’ sleep is characterized by more arousals than younger adults, and as a result their sleep is quite fragmented (Bliwise, 2000). Resulting in part from this fragmentation, the composition of sleep changes with age. In a meta-analysis of 65 studies of sleep problems in older adults, Ohayon, Carskadon, Guilleminault, and Vitiello (2004) showed that the percent of sleep spent in slow wave sleep was reduced with age, whereas percent of sleep time in Stages 1 and 2 of sleep increased. Stage 1 sleep increases to about 8-15% in older adults, compared to about 3-5% in younger adults, and slow wave sleep decreases (Bliwise, 1993).

As previously noted, arousals may be associated with interruptions in breathing. In support of this relationship between sleep-disordered breathing and fragmented sleep in older
adults, it has been shown that older adults with increased sleep-disordered breathing show increased arousals and reduced slow wave sleep (Ondze, Espa, Dauvilliers, Billiard, & Besset, 2003). Arousals occur in the normal sleep process, but a person may also abnormally arouse from sleep, such as from sleep-disordered breathing. However, older adults’ arousals may also result from non-breathing related events, such as the need to get up during the night in order to urinate, periodic limb movements, and waking to external stimuli (Bliwise, 2000). Furthermore, some researchers have noted that older adults are generally more prone to arousing with environmental stimuli, such as low decibel noises (Bliwise, 2000). Studies have thus shown that arousals are more prevalent with age (Bonnet & Arand, 2007), though these studies do not specify the sources of these arousals, so it is unclear the degree to which sleep-disordered breathing may be contributing to these sleep disruptions.

To summarize, older adults demonstrate poorer sleep than younger adults, both on subjective and objective measures. One cause of poor sleep is sleep-disordered breathing, a condition which is characterized by increased desaturations and arousals. Although arousals may be associated with sleep-disordered breathing, arousals may also represent other age-related sleep problems independent of sleep-disordered breathing (nocturia, periodic limb movement). Hence, arousals may have multiple sources, so the exact nature of the relationship between reduced arterial oxygenation and arousals in older adults remains unclear. This study seeks to understand that relationship and its impact on cognition in older adults. There is little research on the impact of mild sleep-disordered breathing on cognitive function in non-sleep disordered, community-dwelling older adults. Consequently, the primary evidence elucidating the potential connection between sleep-disordered breathing.
arousals, and cognitive dysfunction comes from research on patients with obstructive sleep apnea.

**Relationship Between Desaturations, Oxygenation, and Arousals**

Much of the evidence concerning the relationships among desaturations, arterial oxygenation during sleep, and arousals comes from studies of patients with obstructive sleep apnea. During an apneic event, airflow is reduced and arterial oxygen saturation falls, causing a desaturation. A number of events take place following these desaturations. Chemoreceptors are groups of cells in the body that sense the decline in oxygen and rise in carbon dioxide in the blood, and in response send a message to the brain to activate the sympathetic nervous system (Flemmons, 2002). The obstructive sleep apnea patient often arouses briefly as the body increases its respiratory effort to stabilize oxygen levels (Bassiri & Guilleminault, 2000).

Given that arousals may be important for restoring ventilation after desaturations during sleep, prolonged desaturations might be a result of either failure to initiate an arousal or an inability to alter breathing patterns when an arousal occurs. Previous studies in middle age adults (30-50 years) report that when associated with apneas, EEG arousals evoke such large increases in the amplitude of breathing cycles that they shorten the duration of desaturations during sleep (Badr et al., 1997; Basner, Onal, Stepanski, & Lopata, 1995; Carlson, Carley, Onal, Lopata, & Basner, 1994). Similar studies in young adults indicate that it is the magnitude of increase in the amplitude of breathing cycles that follow an apnea or hypopnea that is predictive of the rate of return of the oxygen level to normal following the event (Bradley et al., 1985; Findley et al., 1983). Thus, the interaction between desaturations
and arousals may be critical to understanding the relationship between older adults’ sleep and cognitive deficits.

**Cognitive Sequelae of Sleep-disordered breathing**

Cognitive decline in healthy older adults is a well-documented phenomenon. Older adults experience changes in a number of cognitive domains, including attention, memory, visuospatial, and executive functions (see Bialystok & Craik, 2006; Craik & Salthouse, 2000, for reviews). As previously discussed, it is also evident that aging is associated with increased sleep-disordered breathing. The degree to which age-associated mild sleep-disordered breathing may be associated with cognitive dysfunction is less well researched. Studies with sleep apnea patients indicate that the intermittent hypoxemia and arousals in this more severe form of sleep-disordered breathing are associated with cognitive deficits. Thus, sleep apnea studies provide evidence for the cognitive sequelae of sleep-disordered breathing in a clinical population, and thus these associations may also be evident in the milder, non-clinical sleep-disordered breathing seen in some older adults.

One potential factor that may contribute to older adults’ diminished cognitive function is the increase in desaturations and arousals. A number of studies have examined the way in which these sleep problems may impact daytime cognitive function; however, most of these studies come from the sleep disorders literature and not from studies of aging. These studies of the neuropsychological sequelae of sleep-disordered breathing nevertheless provide valuable information about the potential negative cognitive consequences of the disorder.

Aloia, Arnedt, Davis, Riggs, and Byrd (2004) conducted a review of the neuropsychological effects of obstructive sleep apnea, examining a number of broad
cognitive domains, including language (measured by tests such as the Boston Naming Test), attention (which included such tests as the Digit Span subtest of the Wechsler Adult Intelligence Scale, Letter Cancellation, Paced Auditory Serial Addition Test, and Continuous Performance Test), executive function (which included tests such as the Controlled Oral Word Association test, Trail Making Part B, and Stroop Test), long-term, episodic memory (which included tests such as the California Verbal Learning Test and Visual Reproduction of the Wechsler Memory Test), visuospatial abilities (as measured by such tests as the Block Design subtest of the Wechsler Adult Intelligence Scale and the Rey Osterrieth Complex Figure), and psychomotor abilities (which included tests such as Pegboard and Finger Tapping). The authors found that in studies comparing obstructive sleep apnea patients to controls, language abilities were spared in the three studies that assessed language function. Attention was impaired in six of eight (75%) of the studies, executive functioning was impaired in six of nine (67%), and long-term memory was impaired in seven of eleven studies (63%). Visuospatial and psychomotor functioning impairments were found in four of five studies (80%). With respect to psychomotor functioning, psychomotor speed appears to be intact (finger tapping) and fine motor coordination significantly impaired in four of four studies (100%).

While Aloia et al.’s review (2004) provided broad evidence as to the cognitive deficits associated with sleep-disordered breathing, additional evidence for the role of sleep-disordered breathing in cognitive deficits comes from both group comparisons and treatment studies. In group comparisons, cognitive performance is compared across participants with and without obstructive sleep apnea. Treatment studies examine the change in cognitive deficits in obstructive sleep apnea patients following treatment with a Continuous Positive
Airway Pressure machine (CPAP), an apparatus that the sleeper wears to maintain a positive airflow during the night, reducing both fragmentation and hypoxemia, and also reducing some associated cognitive deficits (Bardwell, Ancoli-Israel, Berry, & Dimsdale, 2001; Engleman et al., 1998). Although the previously mentioned review suggested a number of cognitive domains may be affected by sleep apnea, group comparisons and treatment studies have focused primarily on the effect of sleep-disordered breathing on attention, memory, and processing speed.

Group comparisons and treatment studies have both provided evidence for the role of sleep apnea in attention. Bedard, Montplaisir, Richer, Rouleau, and Malo (1991) found that sleep apnea participants performed significantly worse on a visual search task. Naegele et al. (1998) also compared sleep apnea participants to controls and found differences in performance on one test of selective attention (Stroop Test), but failed to find differences on other tests of selective attention (Trail Making and a visual search task). There was, however, a significant improvement following CPAP treatment on participants’ performance on all of the selective attention tests, whereas performance on many other tests did not improve. Like Naegele and colleagues, Phillips et al. (1990) found that selective attention improved with treatment, and they noted that it was the most improved cognitive function. The ability to selectively attend to information and inhibit irrelevant information also seems to affect performance on tests such as the Wisconsin Card Sorting Test (WCST). Although tests such as the WCST are largely used to test planning, initiating, and flexibility, it seems that sleep apnea patients’ poor performance on tasks such as the WCST comes from a tendency to perseverate, or to repeat the same behavior or thought, which researchers have found to be associated with fragmentation (Redline et al., 1997). Some have asserted that the ability to
inhibit irrelevant information explained these perseverations (Naegele et al., 1998). Thus, studies suggest that selective attention deficits related to disrupted sleep can be seen on a number of tests, and there is evidence to suggest that these deficits may be improved once continuous sleep is restored.

Deficits in long-term episodic memory also appear to be associated with sleep apnea. Salorio, White, Piccirillo, Dunfley, and Uhles (2004) found that sleep apnea patients exhibited significant impairments in verbal episodic memory. Like Salorio and colleagues, Naegele et al. (1998) also found long-term episodic memory deficits. In addition to this support for the relationship between obstructive sleep apnea and episodic memory deficits, evidence indicates that patients with obstructive sleep apnea exhibit poor performance on tests of working memory performance as well (Redline et al., 1997).

Reduced processing speed is also associated with obstructive sleep apnea. Processing speed appears to be one of the deficits that improves with CPAP treatment (Engleman et al., 1999, Phillips et al., 1990; Sánchez, Buela-Casal, & Bermúdez, 2004). Verstraeten et al. (2004) suggested that the sleep problems experienced by sleep apnea patients may result in deficits in processing speed and attentional capacity, which lead to performance deficits on more complex cognitive tasks as well.

In addition to these findings in sleep apnea patients, evidence exists to suggest that even those with mild sleep-disordered breathing exhibit cognitive deficits. In particular, speed, attention, and working memory appear to be associated with mild sleep-disordered breathing (Boland et al., 2002; Kim et al., 1997; Quan et al., 2006). Moreover, there is some research that shows that these cognitive abilities (speed, attention, and working memory) improve with CPAP treatment (Engleman et al., 1999).
To summarize, evidence from obstructive sleep apnea studies regarding the impact of sleep-disordered breathing on cognition suggests these sleep problems result in a wide range of cognitive deficits. The few studies that have explicitly examined mild sleep-disordered breathing indicate that mild sleep-disordered breathing may particularly affect speed, attention, and working memory. Despite the evidence that older adults experience desaturations and arousals, however, few research studies have explicitly examined the relationship between subclinical sleep-related changes in older adults and cognition. Consequently, one question that remains to be answered is whether part of non-sleep disordered, community dwelling older adults’ cognitive deficits could be explained by reduced arterial oxygenation and arousals, the symptoms of sleep-disordered breathing.

Role of Cardiovascular Disease

Cardiovascular disease is closely associated with sleep-disordered breathing, even in middle-aged patients with mild to moderate forms of sleep-disordered breathing (Shahar et al., 2001). Cardiovascular disease may play a role in the relationship between sleep-disordered breathing and cognitive deficits in older adults. Cardiovascular disease is a broad term that comprises a variety of medical conditions that affect the health of the cardiac and circulatory systems. Obstructive sleep apnea is thought to be a risk factor for a number of cardiovascular symptoms including increased blood pressure (Hla et al., 1994), increased risk of heart failure (Javaheri et al., 1998), and stroke (Lavie, 2005). Several authors have posited the mechanisms by which sleep-disordered breathing and cardiovascular disease may be related.

There is a complex interplay between cardiovascular disease and sleep-disordered breathing. Repeated hypoxemic events affect the cardiovascular system such that the
cardiovascular system becomes less able to cope with reductions in arterial oxygenation.

Two key factors that may explain the association between sleep-disordered breathing and cardiovascular disease are chemoreceptor sensitivity and arterial distensibility.

Chemoreceptor sensitivity is the ability of chemoreceptors to sense and respond to changes in oxygen and carbon dioxide in the blood. In most cases, when blood oxygen levels drop, the chemoreceptors trigger the respiratory centers to increase the rate or depth of breathing.

There are conflicting reports as to whether individuals with frequent hypoxemia exhibit decreased or increased chemoreceptor sensitivity. Patients with obstructive sleep apnea may display decreased chemoreceptor sensitivity, exhibiting a blunted response to changes in oxygen and carbon dioxide (Berry & Gleeson, 1997; Osanai et al., 1999). If chemoreceptors are under-sensitive in people with sleep-disordered breathing, individuals would be less likely to arouse during sleep because the chemoreceptors would not respond to the reduction in oxygen by triggering a rapid increase in respiration. Thus, blood oxygen levels would be slow to return to normal, and the individual would remain in a hypoxemic state for a longer period of time, during which sympathetic nervous system activity and blood pressure would remain high.

In contrast to this reduced sensitivity of chemoreceptors, others have reported increased chemoreceptor sensitivity in response to repeated hypoxic episodes (Mahamed & Duffin, 2001; Narkiewicz et al., 1999). That is, people with sleep-disordered breathing may be highly likely to show increased chemoreceptor response to reductions in arterial oxygenation, which results in increases in ventilation. In this case, because their respiratory centers are being triggered, these individuals are more likely to arouse, to the detriment of sleep continuity. This arousal may also have a protective effect, however, if the blood oxygen
levels rapidly return to normal. In activating the respiratory response, chemoreceptors not
only restore oxygen levels, but also reduce stress on the cardiovascular system by reducing
sympathetic nervous system activity and blood pressure (Watenpaugh, Muenter, Wasmund,
& Smith, 1999).

A second factor that might explain the association between sleep-disordered breathing
and cardiovascular disease is arterial distensibility, the elasticity of blood vessels.
Distensibility is essential to the constriction and dilation of blood vessels in the control of
blood pressure. Although hypoxia typically results in immediate vasodilation to increase
blood flow to oxygen starved tissues, individuals with obstructive sleep apnea may lack this
response (Kato et al., 2000). Researchers have posited that cardiovascular dysfunction,
related to repeated hypoxemic events, may explain this lack of response (Lanfranchi &
Somers, 2001). As previously mentioned, repeated hypoxemic events results in increased
sympathetic nervous system activity, vasoconstriction, and increased blood pressure
(Leuenberger et al., 2005; Ng et al., 2005). Furthermore, investigators have found that
repeated hypoxic events in obstructive sleep apnea are associated with in changes to the
cardiovascular system, such as decreased arterial distensibility (Ng et al., 2005). This reduced
arterial distensibility results in virtually no vasodilation in response to hypoxia (Remsburg et
al., 1999). Taken together, these findings indicate that response to hypoxic challenge requires
a complex interaction between the cardiovascular and respiratory systems. It necessitates not
only sufficient sensitivity of chemoreceptors to detect changes in oxygen and carbon dioxide
levels, but it also requires sufficient capacity for the arteries to respond to fluctuating oxygen
levels. Both of these have been shown to be impaired in individuals with sleep-disordered
breathing.
The interaction between these two factors, chemoreceptors and arterial distensibility, may partly explain the mechanism by which sleep-disordered breathing and cardiovascular disease affect cognitive function in older adults. Older adults experience decreased chemoreceptor sensitivity, independent of changes related to sleep-disordered breathing (Cheitlin, 2003). Moreover, if older adults experience repeated hypoxemic events related to sleep-disordered breathing, it is likely that their chemoreceptor sensitivity is further compromised. In support of the reduced chemoreceptor activity hypothesis in older adults, researchers have found that the respiratory response to hypoxia is reduced in older adults (DiGiulio, Cacchio, Bianchi, Rapino, & De Ilio, 2003). Thus, if an older adult experiences a hypoxic event during sleep, but fails to respond to the reduction in arterial oxygenation with an arousal because of reduced chemoreceptor sensitivity, the older adult may experience more severe and prolonged oxygen deprivation and increased sympathetic nervous system activity and blood pressure. On the other hand, if older adults’ systems are overly sensitive to changes in oxygen, as has been found in some sleep apnea patients, frequent arousals resulting from increased ventilatory response may actually be associated with comparatively better cognition, as the length and overall severity of the hypoxemia would be minimized.

Cardiovascular disease itself has been associated with neurological and cognitive impairments. Cardiovascular disease is associated with an increased risk of stroke and dementia (White & Launer, 2006), and a growing literature has documented the close relationship between cardiovascular function and brain pathology. Cardiovascular disease’s association with brain pathology is seen in a reduction in brain volume and enlarged ventricles, and white matter disease, evidenced by white matter hyperintensities on imaging studies (Yiloski, Yiloski, & Raininko, 2000). White matter disease is thought to be caused by
blood vessel damage in the small penetrating arteries of the brain (Pantoni & Garcia, 1995), and it has also been implicated in sleep apnea. Recent research has established the association between severity of apnea and small vessel vascular disease in the brain (Aloia et al., 2001; Colrain et al., 2002), and imaging studies have shown that cerebral metabolism in apnea is significantly reduced in white matter, even after controlling for age (Kamba et al., 2001).

Cardiovascular disease, specifically athersclerosis and the presence of plaques in the arteries, has also been found to be associated with poorer cognitive performance (Aleman et al., 2005; Verhaeghen, Borchelt, & Smith, 2003), above and beyond what would be expected due to age and education (Breteler, Claus, Grobbee, & Hofman, 1994). Cardiovascular disease has been associated with deficits in cognitive abilities such as processing speed, attention, and memory (Hassing et al., 2004; Yiloski et al., 2000). It is interesting to note that the types of cognitive deficits associated with white matter disease show significant overlap with those associated with cardiovascular disease and sleep disorders. Thus, it is possible that repeated hypoxemic events in older adults may increase the risk for cardiovascular disease, which in turn increases the neural damage evident in white matter disease.

In review, numerous studies have documented the changes that occur to sleep with age. In subjective reports, many older adults endorse significant problems with sleep. Objective measures of sleep also document changes in sleep with age, with older adults evidencing a reduction in slow wave sleep and wide range of sleep related breathing problems, from clinically diagnosable obstructive sleep apnea to milder forms of sleep-disordered breathing. The interruptions in breathing experienced by older adults result in reduced arterial oxygenation and may cause arousals during sleep.
The exact nature of the relationships between desaturations, oxygenation, arousals, and cognition in older adults is unclear. (See Figure 3 for a flowchart depicting the entire theoretical model.) Older adults exhibit both sleep-disordered breathing and increased arousals, but it is not known whether arousals are part of a sleep-disordered breathing phenomenon, or whether they are independent of breathing problems. If arousals occur in response to reduced arterial oxygenation, they may protect the older adult from the detrimental effect of hypoxemia by signifying an increase in arterial oxygenation and reduction in sympathetic nervous system activity. These arousals, however, may come at the cost of reduced sleep quality. In contrast, failure to arouse during a reduction in arterial oxygenation may result in better quality sleep but longer periods of time in a hypoxemic state, starving cells of oxygen and maintaining high levels of blood pressure. Even if arousals occur for reasons not related to sleep-disordered breathing events, however, numerous arousals during sleep may fragment the continuity of sleep such that slow wave sleep is severely reduced and daytime cognitive performance is significantly impaired.

If desaturations, arousals, and cognition are related, the mechanism likely involves a complex interplay of sleep, arterial oxygenation, and cardiovascular function. Findings from sleep apnea studies suggest that desaturations and arousals result in daytime cognitive deficits, and sleep-disordered breathing also appears to be closely related to cardiovascular disease. Support for these inter-connections comes from the consistency among findings regarding cognitive deficits in sleep apnea, cardiovascular disease, and white matter disease. What remains to be determined is whether this model can be applied to the sleep and cognitive deficits seen in older adults.
The Current Study

The present study tested whether cognitive deficits in a sample of community-dwelling older adults may be related to subclinical sleep-disordered breathing. This study also sought to determine whether the impact of desaturations on cognitive function depends on whether arousals are associated with desaturations. Moreover, because of the potential relationship between sleep-disordered breathing and cardiovascular disease in obstructive sleep apnea, and because of the potential role of chemoreceptor sensitivity and vascular response to hypoxemia, this study also attempted to determine whether the effect of arousals and reduced arterial oxygenation on cognitive function in older adults is affected by cardiovascular disease.

This study employed a secondary data analysis of data gathered from the “Respiratory Periodicity and Cognitive Decline in Elders” project at the UNC Chapel Hill School of Nursing (Barbara Carlson, Principle Investigator). Participants were in the study for two years, but only baseline data were considered here. All participants underwent a physical examination conducted by a nurse practitioner, answered questions about their health status, daytime activities, and sleep, and underwent a two-night sleep study at the School of Nursing Biobehavioral Laboratory. The sleep data were collected via polysomnography, and arterial oxygenation during sleep was monitored via a fingertip pulse oximeter, a small device worn on the finger that continually measures the oxygen saturation of blood. Participants were assessed on the Cumulative Illness Rating Scale for Geriatrics (CIRS-G, Linn, Linn, & Gurel, 1968; Miller et al., 1992), an interview measure administered by a nurse practitioner that assesses illness severity across a variety of domains. In the present study, cardiovascular disease was measured using scores from the vascular and heart subscales of the CIRS-G. A
number of neuropsychological assessment instruments were also administered. Neuropsychological measures included tests of verbal and visual long-term episodic memory, processing speed, working memory, and attention. These neuropsychological functions represent cognitive abilities that have consistently been implicated in studies of sleep apnea, cardiovascular disease, and white matter disease.

To study the relationships among the variables as described above, several statistical techniques were employed. First, correlations were computed to evaluate the broad patterns of relationships among variables. Regression analyses were used to determine the degree to which desaturations, arousals, and arterial oxygenation during wake contributed to mean arterial oxygenation during sleep. Lastly, structural equation modeling (SEM) was used to examine the relationships among sleep, cardiovascular, and cognitive variables. In the measurement model of the SEM, five latent endogenous cognitive variables were modeled: verbal memory, visual memory, attention, processing speed, and working memory. Exogenous latent variables for cardiovascular disease, oxygenation during sleep, arousals, and arterial oxygenation while awake were initially comprised of their respective indicator variables. The structural model was then assessed for relationships among latent variables (see Figure 4).

**Hypotheses**

The hypotheses below seek to answer the following questions: 1) What is the relationship among desaturations, arousals, and mean arterial oxygenation during sleep? 2) How does oxygenation while awake affect the relationship between desaturations, arousals, and mean arterial oxygenation during sleep? 3) How are arousals, desaturations, and arterial oxygenation related to cognitive performance, and do arousals moderate the effect of
One purpose of this study was to determine the degree to which desaturations and arousals are associated with arterial oxygenation. As previously discussed, repeated desaturations during sleep reduces arterial oxygenation. It was thus hypothesized that desaturations, as measured by the oxygen desaturation index (ODI), would be a significant determinant of mean arterial oxygenation during sleep. Arousals that occur during sleep may or may not be associated with desaturations. Arousals frequently accompany reductions in mean arterial oxygenation during sleep because they are associated with increased respiratory effort. On the other hand, arousals may occur independently of sleep-disordered breathing, and may represent an inability to maintain continuous sleep from other causes. It is not clear from the literature how frequently older adults experience non-sleep-disordered breathing arousals, and given the high rate of sleep related breathing problems in older adults, it seems more likely that arousals would occur in the context of sleep-disordered breathing as opposed to other causes. It was thus hypothesized that there would be a significant positive correlation between the oxygen desaturation index and the number of arousals (i.e., the arousal index). If this is the case, the arousal index was also proposed to be a significant predictor of mean arterial oxygenation during sleep in a regression model. Thus, there may be a close relationship between desaturations and arousals in older adults such that individuals who have repeated desaturations and increased arousals may show higher overall arterial oxygenation than those who have frequent desaturations but do not have arousals. It was therefore hypothesized that arousals would act as a moderator in the relationship between desaturations and mean arterial oxygenation during sleep. In a regression analysis on mean
arterial oxygenation during sleep, there was hypothesized to be a significant interaction between desaturations and arousals.

The second aim of the study was to examine the degree to which arterial oxygenation during sleep was associated with arterial oxygenation while awake. Arterial oxygenation while awake provides a measure of baseline arterial oxygenation. This measure of arterial oxygenation while awake may provide an indication of the degree to which low arterial oxygenation while awake contributed to reduced respiratory response to sleep-disordered breathing events and consequently reduced mean arterial oxygenation during sleep. Thus, arterial oxygenation while awake was hypothesized to be significantly related to the mean arterial oxygenation during sleep. Furthermore, the degree to which desaturations and arousals impact oxygenation during sleep may be related to how oxygenated the blood is before sleep onset. In other words, baseline arterial oxygenation may affect the body’s reaction to reduced arterial oxygenation during sleep. Arterial oxygenation while awake was thus hypothesized to moderate the relationship between desaturations, arousals, in their prediction of oxygenation during sleep in a regression analysis. I also hypothesized a two-way interaction between arterial oxygenation while awake and desaturations in their prediction of mean arterial oxygenation during sleep in a regression analysis. In other words, individuals with decreased arterial oxygenation while awake and increased desaturations during sleep would have the lowest mean oxygenation during sleep. There was also hypothesized to be a two-way interaction between arterial oxygenation while awake and arousals in their prediction of mean arterial oxygenation during sleep in a regression analysis. This two-way interaction would demonstrate that individuals with the lowest mean oxygenation during sleep would have both low arterial oxygenation while awake and low
arousals. Individuals with low oxygenation at wake, before sleep onset, may be less likely to arouse during sleep after a desaturation, possibly because of reduced chemoreceptor sensitivity. I also therefore hypothesized that there would be a significant three-way interaction between the desaturation index, arousal index, and arterial oxygenation while awake in the prediction of mean arterial oxygenation during sleep. The interpretation of this expected three-way interaction is that individuals with low arterial oxygenation at wake have reduced respiratory response to the desaturations and therefore have reduced arousals. Thus, those with low arterial oxygenation at wake, many desaturations, and few arousals were expected to have the lowest mean blood arterial oxygenation during sleep.

In addition to these proposed relationships between arterial oxygenation during sleep and multiple other physiological factors, sleep-disordered breathing was also expected to be a determinant of cognitive function. It was hypothesized that sleep-disordered breathing, characterized by repeated desaturations and reduced arterial oxygenation, would be significantly related to performance in the five cognitive domains evaluated: verbal memory, visual memory, attention, processing speed, and working memory. Cognitive performance in these domains was also hypothesized to be related to arousals. If arousals occur in the context of sleep-disordered breathing, they may reduce the negative effect of decreased arterial oxygenation on cognitive performance in the aforementioned domains. Thus, it was hypothesized that arousals would moderate the relationship between arterial oxygenation during sleep and cognitive function, such that the relationship between reduced arterial oxygenation and cognitive functioning depends on whether the person arouses as a result of the hypoxemic episode. Individuals with diminished response to desaturations would be less likely to arouse, and consequently they would have lower arterial oxygenation, which over a
period of time would result in lower cognitive performance. I therefore hypothesized that in the proposed SEM model (see Figure 4), paths from the latent variables comprising sleep-disordered breathing (mean arterial oxygenation during sleep, desaturations, etc.), and arousals, to the latent cognitive domains would be significant, as would the paths between the interaction variable (mean arterial oxygenation during sleep x arousals) and the cognitive domains.

In addition to these assessments of sleep-disordered breathing and cognitive function, the study also examined the relation of cardiovascular variables to sleep-disordered breathing and cognitive performance. In addition to direct relationships between cardiovascular disease, sleep-disordered breathing variables, and cognition, cardiovascular disease was proposed to act as a moderator of arterial oxygenation during sleep and arousals in their relationship to cognitive performance. It was proposed that fewer arousals and increased hypoxemia would be related to poorer cognitive performance in those who also exhibit cardiovascular disease. Therefore, I hypothesized that there would be significant relationships in the SEM model between the latent interaction variable comprised of cardiovascular disease, arousals, and oxygenation during sleep, and the cognitive latent variables. I also planned to assess whether the simpler relations exemplified by the paths between the two-way interaction terms (desaturations and arousals each with cardiovascular disease) and cognitive variables each would be significant. Whether these two-way interactions would be significant was unclear, as the relationship between mean arterial oxygenation during sleep and cognitive function should depend on both cardiovascular function and arousals.

In summary, the present study proposed the following hypotheses:
1) With regard to the relationship between desaturations, arousals, and mean arterial oxygenation during sleep, it was hypothesized that desaturations, as measured by the desaturation index, would be a significant determinant of mean arterial oxygenation during sleep. There was also hypothesized to be a significant positive correlation between the oxygen desaturation index and the arousal index. If this relationship held, it was also hypothesized that the arousal index would be a significant determinant of mean arterial oxygenation during sleep. It was also hypothesized that arousals would act as a moderator in the relationship between desaturations and mean arterial oxygenation during sleep. Thus, in a regression analysis on mean arterial oxygenation during sleep, there was hypothesized to be significant main effects of desaturations and arousals and an interaction between desaturations and arousals.

2) In examining the degree to which arterial oxygenation while awake, the baseline measure of arterial oxygenation, affects oxygenation during sleep, it was hypothesized that arterial oxygenation while awake would be a significant determinant of mean oxygenation during sleep, and there would be significant two-way interactions between arterial oxygenation while awake and desaturations and between arterial oxygenation while awake and arousals in predicting arterial oxygenation during sleep. There was also hypothesized to be a three-way interaction between the desaturation index, arousal index, and arterial oxygenation while awake in predicting mean oxygenation during sleep.

3) In correspondence with the relationships hypothesized in the first two hypotheses, with regard to the exogenous variables of the structural equation model, it was hypothesized that there would be significant relationships between arousals and oxygenation during
sleep, oxygenation while awake and oxygenation during sleep, and arousals and oxygenation while awake.

4) It was hypothesized that there would be significant paths in the structural equation model between the following exogenous latent variables related to sleep: arousals, arterial oxygenation during sleep, and the interaction variable (arterial oxygenation during sleep x arousals) and the endogenous variables representing cognitive function.

5) It was hypothesized that there would be significant paths in the structural equation model between the following exogenous latent variables involving cardiovascular disease: cardiovascular disease and the interaction variables (cardiovascular disease x arterial oxygenation during sleep, cardiovascular disease x arousals, and arterial oxygenation during sleep x arousals x cardiovascular disease) and the endogenous variables representing cognitive function. Thus, the structural equation model would be used to determine whether cardiovascular disease may explain the relationship between arousals, reduced oxygenation during sleep, and cognitive function.

Methods

Participants

Participants in this study included 115 community-dwelling participants over the age of 70, 64% of whom were female and 36% of whom were male. The study’s exclusion criteria included alcohol and drug use (three or more alcoholic drinks per week or use of illegal drugs), neurological disorders (dementia, schizophrenia, Parkinson’s, bipolar disorder, medication managed depression), neuroimmune disorders (tuberculosis, hepatitis, seasonal asthma, HIV/AIDS, syphilis, meningitis), history of a cerebrovascular events in the previous 6 months (stroke, TIA, loss of consciousness, general anesthesia, seizure), presence of an
implanted device (pacemaker, internal defibrillator), recent history of a sleep problems (pain that prevents sleep, waking to urinate 3 or more times per night, easily wakened by sounds, difficulty sleeping away from home, walking during sleep, falling out of bed, waking from sleep violent or confused) and not being able to speak or read English.

Measures

Arousals. EEG arousals were scored from the polysomnogram and were measured in terms of the total number and the average hourly rate. From the polysomnography data, sleep-disordered breathing was measured in terms of the total number and hourly rate of arousals. Polysomnographic recordings were scored by 30-s epochs, following the international criteria outlined by Rechtschaffen and Kales (1968), and arousals were determined using the American Sleep Disorders Association criteria (1992). Arousals were counted when there was an abrupt shift in EEG frequency that included theta or alpha waves, or frequencies greater than 16 Hz, but no spindles (aburst of 12-16Hz waves). Ten seconds of continuous sleep were required to precede each scored arousal, and each arousal had to last at least three seconds and be accompanied by an increase in chin EMG if it occurred during REM sleep. The polysomnography was scored independently by two trained sleep researchers so as to ensure optimal accuracy of the scoring. Agreement between scorers for sleep states in the present study was excellent (kappa = .90). Scores for arousals included the total number of arousals and the arousal index (number of arousals per 5-minute period).

Blood oxygenation. Participants’ arterial oxygenation was monitored via fingertip pulse oximetry. Pulse oximetry is a non-invasive method of measuring the oxygenation of the blood. A sensor placed on the finger passes an infrared light from one side to the other.
Based on the changes in wavelength measured by the sensor, the device can assess the difference in color for blood that is more or less oxygenated.

There were two derived measures of oxygenation: arterial oxygenation and oxygen desaturation index. Arterial oxygenation was measured at baseline, while awake, and continuously during sleep. Arterial oxygenation while awake corresponded to the mean baseline blood oxygen saturation collected during the 10 minute period prior to lights out when the individual was awake. Arterial oxygenation during sleep was averaged across the entire night and included the mean and minimum values, as well as the percent of time spent below 90% saturation, a measure used to quantify the severity of oxygen desaturation during sleep (Chaudhary et al., 1998). Arterial oxygenation during sleep was also assessed via the oxygen desaturation index. The oxygen desaturation index (ODI) quantifies desaturations as the decrease of arterial oxygenation by 4% or more in a 3-second moving window. This measure is expressed in terms of an average hourly rate during sleep.

*Cardiovascular disease.* Vascular disease was measured using the Cumulative Illness Rating Scale – Geriatrics (CIRS-G; Linn, Linn, & Gurel, 1968; Miller et al., 1992), which was employed to assess the severity of illnesses. The CIRS-G, an interview measure, was administered by a nurse practitioner, and included a number of illness subscales. For the present study, I examined two subscales of the measure, the Heart and Vascular subscales (see Figure 5). Both subscales include a four-item rating scale (from 0 to 4), with a score of 0 representing no symptoms of illness, and 4 representing increased symptoms reflecting the most severe illness. Participants with a score of 4 on either of the scales were excluded from the study, so all participants obtained scores in the 0 to 3 range. Researchers have reported good inter-rater reliability, discriminative validity, and face validity in the CIRS-G (Miller et al., 1992).
Neuropsychological tests. Five cognitive domains were assessed in this study: verbal episodic memory, visual episodic memory, attention, speed of processing, and working memory. The two verbal memory tests were the Logical Memory and Word List subtests of the Wechsler Memory Scale-III (Wechsler, 1997b). The two visual memory tests were the Visual Reproduction subtest of the WMS-III (Wechsler, 1997b) and the Rey-Osterrieth (Osterrieth, 1944; Rey, 1941). The tests that assessed attention were the Trail Making Test (Halstead, 1947; Reitan & Davidson, 1974) and the Stroop Test (Golden, 1978). Speed of processing was assessed with the Symbol Digit Modalities Test (Smith, 1973). Working memory was assessed with the Letter Number Sequencing subtest of the WAIS-III (Wechsler, 1997a). Test-retest reliabilities for most of the neuropsychological tests have been judged to be good, ranging from .79 to .89 (Dikmen, Heaton, Grant, & Temkin, 1999), though the reliability of the memory tests is somewhat lower, notably for the Visual Reproduction Test, which has been found to have a test-retest reliability of .62 (Dikmen et al., 1999). The scoring system developed for the Rey Osterrieth Complex Figure has also been found to be high in both interrater and internal consistency reliabilities (Rapport, Charter, Dutra, Farchione, & Kingsley, 1997).

Logical Memory is a subscale of the Wechsler Memory Scale. In this test, the examiner read a brief story and the participant had to recall as much of the story as possible. Following this immediate recall condition, the participant also completed a delayed memory condition after approximately 15 minutes. In the delayed condition, the participant was asked to recall as much of the story as possible. On both the immediate (i.e. Logical Memory I) and delayed (i.e. Logical Memory II) conditions of the Logical Memory test, one point was awarded for each phrase or gist of a phrase that the participant accurately recalls. For the
purposes of this study, both immediate and delayed memory were entered into the structural equation model to represent the factor “verbal memory.”

The Word Lists subtest of the Wechsler Memory Scale was also administered. The subtest included two conditions, an immediate (i.e. Word Lists I) and delayed (i.e. Word Lists II) recall condition. In the immediate recall condition, the examiner read aloud a list of ten words, and participants were asked to recall as many words as possible. This was repeated four times. Following these trials for the immediate recall condition, a second word list (List B), was read aloud by the examiner, and the participant was instructed to recall as many as possible from this list. After this second, interfering list, the person had to recall as many words from the original list as possible. Following a delay of approximately 15 minutes, the delayed recall condition was administered. This condition required the participant to recall as many words as possible from the original list. For both conditions, one point was awarded for each word recalled. The score of the immediate recall condition consisted of the sum of the five trials. The delayed condition score reflected the total number of words recalled during the delayed condition. Both the immediate and delayed conditions were entered into the structural equation model to represent the “verbal memory” factor.

The Visual Reproduction subtest of the Wechsler Memory Scale is a visual memory test that includes both immediate (i.e. Visual Reproduction I) and delayed (i.e. Visual Reproduction II) conditions. Five different line drawings were each presented one at a time for 10 seconds, and after each drawing was removed, the participant was asked to draw that figure from memory. After a delay, the participant was asked to draw as many of the figures as he or she recalls. The figures were scored according to standardized scoring criteria, and scores for both the immediate and delayed conditions were derived by adding scores across
all five figures on each condition. In the present study, interrater reliabilities were high for scoring in both the immediate and delayed conditions ($r = .92$ and $.94$, respectively).

The Rey Osterrieth Complex Figure test is a test of visuospatial construction and memory. This instrument included four conditions: Copy, Immediate Recall, Delayed Recall, and Recognition. The participant was presented with the visual stimulus, a complex black-and-white line drawing on a laminated 8.5 x 11” piece of paper. In the Copy condition, the participant was instructed to copy the figure on a separate sheet of paper. The examiner timed the participant while they copied the figure, and when the participant was finished, the examiner removed the stimulus and the drawn copy from the participant’s view. In the Immediate Recall condition, administered after 3 minutes, the participant was given a blank piece of paper and was asked to draw the figure from memory. In the Delayed Recall condition, the participant was asked once again to draw the figure from memory 30 minutes after the Copy trial. Lastly, the Recognition condition was administered, in which the participant was asked to circle line drawings that represent elements of the larger complex figure, and distinguish those from novel line drawings. Each of the figures in the three drawing conditions (Copy, Immediate, and Delayed Recall) was scored according to criteria in the scoring manual. The total score in each of these three conditions ranged from 0 to 36, depending on the accuracy of the drawn figure. The Recognition score ranged from 0 to 24, and was computed based on the recognition of true positives and true negatives. The Immediate and Delayed Recall scores were used in analyses. Interrater reliabilities in the present study were high for scoring in both the immediate and delayed conditions ($r = .91$ and .99, respectively).
The Trail Making Test, a test that assesses selective attention and the ability to switch attention, was administered. It included two parts. Part A consisted of the numbers 1 to 25 arranged pseudo-randomly on an 8½ x 11 inch piece of paper. Participants were asked to draw lines to connect the numbers in sequential order. Part B consisted of 25 items consisting of the numbers 1 to 13 and the letters A to L that are pseudo-randomly arranged on the paper. Participants were asked to connect the items in sequential order, alternating between numbers and letters (e.g. 1, A, 2, B, etc.). In both parts, participants were given 2.5 minutes, but were instructed to work as quickly as possible without lifting the pencil from the paper. If the participant made an error, the examiner stopped him or her immediately, pointed out and marked an “x” over the error, and asked the participant to resume the task from the last correctly connected letter or number. The Trails B score was used to represent attention in the statistical analyses.

The Stroop Test is a commonly used test of attention that assesses selective attention. It included three subtests, each of which had 100 items presented on an 8½ by 11 inch piece of laminated white paper. The first subtest consisted of the words “red”, “green” and “blue” arranged randomly in columns and printed in black ink; participants read the words as quickly as they could. The second subtest consisted of “XXXX”s printed in rows and columns, printed in red, green, or blue ink, and participants named the ink colors as quickly as they could. The third subtest consisted of the words from the first condition printed in the colors from the second condition; in no case did the word and the color of the word match. Participants were asked to name the ink colors as quickly as they could. In each of these conditions, a score was derived that reflects the total amount of time to complete the page. This procedure produced three scores: the Word Score (W) from the first condition, the Color
Score (C) from the second condition, and the Color-Word Score (CW) from the third condition. The Color Word Score was used in analyses.

The Symbol Digit Modalities Test was used to assess processing speed. In this task, each of the numbers 1 through 9 was assigned a unique symbol. Participants were presented with a piece of paper on which the nine numerals and corresponding symbols is printed at the top. Below this key, there were double rows of boxes, in which there was a number in the lower box and the top box is blank. Participants were asked to write in the empty box the symbol that corresponded to the number that appeared below it. The score for this subtest was derived by counting the number of boxes correctly filled in 90 seconds.

To test working memory, the Letter Number Sequencing task from the Wechsler Adult Intelligence Scale was used. In the Letter Number Sequencing test, participants were read a combination of letters and numbers and they were asked to repeat them. They were first required to say the numbers in ascending order, then the letters in alphabetical order. Each item consisted of three trials, and the sequences of letters and numbers in each item progressed from two up to eight numbers and letters. One point was awarded for each correct response, and the score for the Letter Number Sequencing test ranges from 0 to 21.

Socioeconomic status. The Hollingshead Index was used to estimate socioeconomic status. The Hollingshead Index (Hollingshead, 1965) comprised a weighted combination of ordinal rankings of education and occupation. Occupation was ranked by assigning scores ranging from 1, for professional executives or proprietors, to 7, for unskilled employees. Education was also rated with seven categories of ranking, from 1, for individuals with a professional degree (e.g. M.A., Ph.D.) to 7, for individuals with less than seven years of
schooling. The occupational score was weighted by 7 and the education score was weighted by 4, and the two were summed to create an index score with a maximum score of 77.

Procedure

Participants underwent a physical examination conducted by a nurse practitioner, completed the previously described neuropsychological tests, answered questions about their health status, daytime activities, and sleep, and underwent a two-night sleep study at the School of Nursing Biobehavioral Laboratory. The two-night sleep study occurred one week from this initial physical examination and testing period. For the first night of the sleep study, the participants arrived at the Biobehavioral Laboratory before dinner between 3:00 and 4:00 p.m. and had their temperature, pulse, blood pressure, weight, and height measured, and completed neuropsychological tests. After the testing, the participants had dinner and some time to relax and get ready to go to bed. Sensors were applied and recordings initiated between 10:30-11:00 p.m.. Participants were awakened at 6:00-6:30 a.m., sensors were removed, and the participant ate breakfast and left the laboratory around 8:00 a.m. They returned on the second night at 6:00 p.m., had dinner and underwent the second night of monitoring.

Results

This study included 115 older adults, mean age 78.3 (SD = 5.8). The data included records from 41 male and 74 female participants. The ethnicities were such that 86% of participants were Caucasian, 12% were African American, 1% were Hispanic, and 1% were Asian.

Participants in this study averaged 5.8 hours of sleep (SD = .85). On average, participants were awake for 93.8 minutes during the night (SD = 51.6). They took
approximately 16 minutes to fall asleep ($SD = 18.14$). Participants had frequent desaturations, an average of 15.7 per hour of sleep, with a minimum of 0 and a maximum of 69.2. (See Table 1 for means and standard deviations of sleep and oxygenation variables.) Even though over half of the sample exhibited fewer than 10 desaturations per hour, about a quarter of the participants exhibited more than 20 desaturations per hour. (See Figure 6 for a graph representing the relative frequencies of desaturations.) Participants also had numerous arousals, averaging 193.4 arousals in that single night. Despite these frequent desaturations and arousals, none of the participants met diagnostic criteria for sleep apnea, with an average AHI score of 1.07.

All test scores were examined for outliers, and only one of the participant’s oxygenation data consistently fell more than three standard deviations from the mean. Regression diagnostics showed that this participant’s baseline oxygenation was particularly outstanding, and these data exhibited undue influence ($DFFITS = -1.35$, $DFBETAS = 1.24$). Whereas the mean blood oxygen saturation while awake for all other participants was approximately 97%, this participant’s baseline oxygen saturation was 90%. This participant was thus excluded from the regression analyses.

To determine the relationship between desaturations, arousals, and mean arterial oxygenation during sleep, a series of regression analyses was conducted. Means and standard deviations for the sleep, oxygenation, and vascular disease variables are presented in Table 1. Desaturations were first examined to assess the degree to which desaturations negatively impact arterial oxygenation during sleep. The desaturation index contributed significantly to mean oxygenation during sleep, $F (1, 113) = 8.21$, $MSe = 22.94$, $p = .005$, accounting for 6% of the variation in mean oxygenation during sleep. (Table 2 summarizes the regression results
predicting mean oxygen saturation during sleep.) Thus, desaturations, as measured by the desaturation index, were a significant determinant of mean arterial oxygenation during sleep such that individuals with frequent desaturations exhibited lower arterial oxygenation than those without desaturations. The desaturation index was not correlated with the arousal index, however, and the arousal index did not significantly contribute to mean arterial oxygenation during sleep when entered as a single predictor in a regression equation.

Furthermore, in a regression analysis with the desaturation and arousal indices as predictors of mean arterial oxygenation during sleep, the arousal index did not reduce the effect of desaturations on mean arterial oxygenation during sleep, $F(2,113) = 4.15, MSe = 11.67, p = .018$, as the desaturation index still accounted for 6% of the variation in oxygenation during sleep. To determine whether arousals acted as a moderator in the relationship between desaturations and mean arterial oxygenation during sleep, a regression was conducted with the desaturation index, arousal index, and interaction term (desaturation index x arousal index) as predictors of mean arterial oxygenation during sleep. The results of this analysis suggested that the arousal index did not significantly contribute to oxygenation during sleep, nor did it moderate the relationship between the desaturation index and mean oxygenation during sleep. The desaturation index, however, remained a significant contributor to mean oxygenation during sleep, $F(3, 113) = 2.96, MSe = 8.35, p = .036$, uniquely accounting for 7% of the variance in mean oxygenation during sleep in this regression equation.

The degree to which mean arterial oxygenation while awake contributed to mean oxygenation during sleep was also examined (see Table 3). In effect, these analyses were conducted to assess the degree to which baseline arterial oxygenation affected oxygenation during sleep. In addition to the previously mentioned excluded outlier case, two additional
cases were excluded because of missing values for oxygenation while awake. A regression analysis showed that oxygenation while awake explained 55% of the variance in oxygenation during sleep, \( F (1, 111) = 137.61, MSe = 182.06, p < .0001 \). Mean oxygenation while awake, the desaturation index, and the arousal index together accounted for a significant amount of variance when entered as predictors of oxygenation during sleep, \( F (3, 111) = 49.41, MSe = 63.17, p < .0001 \), though only mean oxygenation while awake and the desaturation index were unique contributors to mean oxygenation during sleep, accounting for 51% and 2% of the variance, respectively. The arousal index did not account for any variance in this regression equation. Two-way interactions between arterial oxygenation while awake and desaturations and between arterial oxygenation while awake and arousals were tested, as was a three-way interaction among these variables. None of the interaction terms was significant.

To rule out the potential effects of age and socioeconomic status on these sleep and breathing variables, the above regression analyses were repeated with age and the Hollingshead Index included. When entered singly in regression equations predicting mean oxygenation during sleep, neither age nor the Hollingshead index significantly contributed to mean oxygenation during sleep. Furthermore, when age and the Hollingshead index were added to the regression equations discussed above, neither age nor the Hollingshead Index affected any of the previously mentioned relationships between the desaturation index, arousal index, mean oxygenation while awake, and mean oxygenation during sleep.

These regression analyses provided evidence as to the relationships among the sleep and oxygenation variables, and structural equation modeling was used to examine the factor structure of the oxygenation, arousal, and neuropsychological variables, as well as the relationships among latent variables. Analyses were conducted using LISREL 8.71 (Joreskog
and Sorbom, 2004). As a preliminary examination, prior to conducting the SEM analyses, means and standard deviations were computed for sleep and cognitive variables (see Tables 1 and 4, respectively), as were correlations (see Tables 5 and 6).

Correlational analyses provided initial evidence as to the relationships among the sleep and oxygenation variables. All of the variables assessing oxygenation during sleep were significantly correlated with one another, though the relationship between the desaturation index and the other oxygenation variables were notably lower than other the correlations. The number of arousals and the arousal index were highly correlated ($r = .94$), but neither measure was significantly associated with any of the oxygenation measures. One exception was that the number of arousals was significantly correlated with the desaturation index, though this relationship is difficult to interpret, as the correlation was rather weak. Moreover, this single correlation should probably not be interpreted as meaningful, as the correlation between the arousal index and desaturation index was not significant.

Oxygenation while awake was significantly correlated with other measures of oxygenation during sleep, but was not associated with the desaturation index.

With regard to the CIRS variables, the heart and vascular subscales were significantly but weakly correlated. There were only two significant correlations between the CIRS measures and sleep variables. The heart subscale was significantly related to the measure of percent of sleep time spent below 90% oxygen saturation. The vascular subscale was related to the desaturation index. Despite these two significant correlations, these findings failed to demonstrate a consistent and meaningful pattern of relationships between the CIRS subscales and sleep variables.
Examination of the correlations between cognitive tests and other variables yielded an interesting pattern of results. There were few significant relationships between the cognitive variables and either the sleep oxygenation or arousal variables. The exception was that the desaturation index was significantly related to a number of the cognitive variables, including scores from the immediate and delay conditions for Word Lists, the delay condition for Visual Reproduction, Stroop Color Word, Symbol Digit Modalities, and Letter-Number Sequencing. With regard to the cardiovascular variables, the vascular subscale was not consistently related to the cognitive tests, but the heart subscale was related to the Trail Making Part B and Stroop Color Word scores.

In data included in the SEM analyses, there were 5 missing values in the data set, and these missing values were imputed using multiple imputation in LISREL prior to running the SEM model. All variables were entered into the model in their original metrics, except that the scores from the Stroop and Trail Making tests were reverse coded such that higher values represented better performance for all cognitive measures. Residuals for latent variables with single indicators were estimated using the following equation: (1-reliability) x standard error. (See Table 7 for a list of reliability estimates.) Model fit was assessed by examining the chi-square value ($\chi^2$), Root Mean Square Error of Approximation (RMSEA), and Comparative Fit Index (CFI).

Researchers have suggested that for appropriate power, SEM analyses should in general have at least 100 participants (Ding, Velicer, & Harlow, 1995; Medsker et al., 1994). Others have suggested that five participants per indicator variable would provide sufficient power (Bentler & Chou, 1987). With 21 indicator variables in the present model and 115 participants, the present proposed model appears to have a sufficient sample size.
Furthermore, some estimates of model fit overestimate goodness of fit in small samples (<200), but RMSEA and CFI, the model fit indices used in this study, are less sensitive to sample size (Fan, Thompson, & Wang, 1999). For structural equation models, RMSEA values of .05 to .08 represent adequate fit, and values .05 or less represent good fit (Kline, 2005). CFI values of .95 or greater represent good fit (Hu & Bentler, 1999). Relationships among latent variables were assessed by examining the standardized path coefficients. Weak relationships are suggested by path coefficients less than .10, moderate relationships are indicated by paths around .30, and path coefficients of .50 or greater suggest strong relationships (Kline, 2005).

Several steps were taken to derive the final structural equation model. First, the exogenous and endogenous variables were assessed to determine appropriate measurement model configuration. Next, the entire model was run to assess the relationships among the exogenous and endogenous variables. Lastly, in the final full model, paths were added between the latent variable representing attention, speed, and working memory, and the latent variables of verbal and visual memory. Details regarding each of the steps in the modeling process are described below.

As a first step in the structural equation modeling, the measurement models for the exogenous and endogenous variables were examined to determine whether the indicators used to represent each of the latent variables in the proposed model sufficiently fit (see Figure 7). The measurement model for the exogenous variables demonstrated that with the exception of the CIRS-G variables, each of the indicator variables loaded on to its respective latent variable. Model fit was not optimal, however, $\chi^2 (18, N=115) = 52.03, p < .001, CFI =$
.91, RMSEA = .14, and several changes were made to the configuration of the exogenous measurement model.

Changes to this initial measurement model were made to the cardiovascular, oxygenation during sleep, and arousal latent variables. The measurement model indicated that the two cardiovascular indicators (vascular and heart CIRS-G subscales) did not load onto a single factor; thus the heart and vascular subscales from the CIRS-G were subsequently entered as separate latent variables. Each of the paths between the latent variable oxygenation during sleep and the four indicator variables were significant. Correlated errors existed between the desaturation index and the three other sleep oxygenation variables, however, indicating potential redundancy of the measures or omission of a latent factor. Further investigation revealed that although each of the indicator variables significantly loaded onto the latent variable of arterial oxygenation during sleep, only 8% of the variability in the desaturation index was explained by that latent variable. In contrast, the latent construct explained 47% of the variation in the minimum oxygenation indicator variable, 93% of the variability in the mean oxygenation during sleep indicator variable, and 75% of the variability in the indicator representing percent of sleep time spent with less than 90% oxygen saturation. Taken together, these findings suggested that the desaturation index may represent a distinct pattern of data separate from the latent construct indicated by the three other oxygenation variables. It was also found that the two measures of arousals, number of arousals and arousal index, were so highly correlated (r = .94) that including them both was unnecessary. Given the high correlation between the measures for number of arousals and the arousal index, the latent variable for arousals comprised the single indicator of the arousal index score. As previously planned, the latent variable of oxygenation while
awake was represented by a single indicator, the mean level of oxygenation during the 10 minutes before lights out. Thus, the best model fit was obtained by including the two CIRS-G scales and the arousal and desaturation indices as single indicators for their respective latent variables, $\chi^2 (10, N=115) = 36.36, p < .001, CFI = .93, RMSEA = .15$ (see Figure 8).

As for the endogenous variables, the four variables that each represent verbal and visual long-term memory significantly loaded on their respective latent variables, and model fit was good, $\chi^2 (43, N=115) = 58.06, p = .16, CFI = .99, RMSEA = .04$ (see Figure 9). Correlated errors were included between the immediate and delay conditions for each of the memory tests (Word Lists, Logical Memory, Rey-Osterrieth, and Visual Reproduction). Despite this reasonably good fit, modification indices for the measurement model analysis showed that the indicators representing processing speed (Symbol Digit Modalities Test) and working memory (Letter Number Sequencing) fit best when included as indicators for the attention latent variable. Thus, four variables were used to indicate the latent variable of attention/speed/working memory (Trail Making Part B, Stroop Color-Word, Symbol Digit Modalities Test, and Letter-Number Sequencing). The final measurement model for the endogenous variables resulted in good model fit, $\chi^2 (47, N=115) = 59.75, p = .10, CFI = .99, RMSEA = .04$ (see Figure 10).

Standardized parameter estimates for the initial full structural model are presented in Figure 11. The fit statistics indicated that the fit in this initial model was moderate, $\chi^2 (138, N=115) = 196.22, p < .001, CFI = .96, RMSEA = .07$. Because the model fit was not optimal, modification indices were examined to assess potential loci of model misfit. Modification indices indicated that paths between the attention/speed/working memory latent construct and the two latent variables representing verbal and visual memory should be included.
Including the paths between attention/speed/working memory and verbal and visual memory significantly improved model fit, \( \Delta \chi^2 (2) = 4.37, p < .05 \). Good fit was achieved in this final model, \( \chi^2 (136, N=115) = 191.85, p = .001, CFI = .97, RMSEA = .05 \). (See Figure 12 for the final model. Tables 8 and 9 summarize the factor loadings for each of the latent variables. Tables 10 and 11 summarize the coefficients for paths among latent variables.) Of note, several paths between exogenous latent constructs were significant. Both of the subscales of the CIRS-G were related to desaturations, and the heart subscale was related to oxygenation during sleep. Neither CIRS-G subscale was related to oxygenation while awake. Oxygenation while awake was shown to be significantly associated with the latent variable oxygenation during sleep. All other relationships among exogenous variables were not significant. Notably, arousals were not associated with any other latent exogenous variable.

With regard to the relationships among exogenous and endogenous variables, both desaturations and the heart subscale of the CIRS-G were significant predictors of the attention/speed/working memory latent variable. Moreover, attention/speed/working memory was related to verbal and visual memory. In contrast, arousals did not appear to be related to poorer cognitive performance, nor were oxygenation during sleep, oxygenation while awake, or vascular disease. Interaction terms were added to this final model to assess whether arousals and cardiovascular disease affect the relationship between desaturations and cognitive function. Addition of these interaction terms did not improve model fit, nor were they significantly associated with any of the cognitive latent variables.

To rule out the potential confounding effects of age, intellectual ability, and SES on these relationships, age, the NAART Full Scale IQ estimate, and the Hollingshead Index were each entered as individual indicators in the model (see Figure 13). Model fit remained
good with the inclusion of these control variables, \( \chi^2 (169, N=115) = 234.80, p < .001, CFI = .97, RMSEA = .045. \) Age was significantly associated with attention/speed/working memory. The IQ estimate also was directly associated with attention/speed/working memory and long-term episodic memory, and its inclusion in the model rendered the relationship between attention/speed/working memory and the verbal memory variable non-significant. The Hollingshead Index was associated with the IQ estimate, but it was not related to any other variable and was thus excluded from the model. As in the previous model, the attention/speed/working memory variable remained related to verbal and visual long-term memory. Importantly, the path coefficients from the heart subscale and desaturations to the attention/speed/working memory variable remained significant after the addition of the three control variables (age, IQ, SES). (See Table 12 for path coefficients in the model with IQ and demographics.)

**Discussion**

The purpose of this study was to examine the effect of mild sleep-disordered breathing on cognitive function in community-dwelling older adults. Despite the fact that participants in this study were free from diagnosable sleep disorders such as obstructive sleep apnea, they exhibited numerous desaturations and arousals. These findings are consistent with other studies which show that sleep-disordered breathing is prevalent among older adults (Hoch et al., 1990; Ancoli-Israel et al., 1991). Studies of sleep apnea patients indicate that the desaturations and arousals that accompany the disorder have a negative impact on cognitive function (Aloia et al., 2004), but it had yet to be determined whether the subclinical sleep-disordered breathing exhibited by many older adults had any impact on cognitive performance. This study thus serves to shed some light on this question, and additionally
raises some interesting issues concerning the relationships among sleep-disordered breathing, cardiovascular disease, and cognitive function.

*Sleep-disordered breathing, effect on oxygenation during sleep*

The first goal with regard to the examination of sleep-disordered breathing in this study was to investigate the relationships among desaturations, arousals, oxygenation while awake, and oxygenation during sleep. Although arterial oxygenation while awake was a significant determinant of arterial oxygenation during sleep, desaturations negatively impacted arterial oxygenation during sleep above and beyond oxygenation while awake. Thus, participants in this study exhibited numerous desaturations, and desaturations negatively affected arterial oxygenation during sleep. Participants in this study also exhibited numerous arousals, but contrary to the initial prediction, arousals were not related to desaturations, nor did they moderate the relationship between desaturations and oxygenation during sleep.

There are several possible explanations for the lack of findings regarding the relationship between desaturations and arousals. One possible explanation is that the relationship between desaturations and arousals could have been masked by noise in the arousal data. Arousals were not scored in a time-locked fashion with desaturations, so they represent not only arousals due to desaturations, but all arousals. In other words, arousals may have multiple sources, such as pain, periodic limb movements, and frequent need to urinate, and the arousals arising from these other sources would not be associated with desaturations. A second possibility is that arousals may not necessarily be closely related to desaturations. In fact, some research suggests that desaturations and arousals, while frequently co-occurring, may occur alone as well (Ayappa, Rapapart, Norman, & Rapoport,
2005), and arousals are not necessary for the termination of breathing disruptions (Younes, 2003). This explanation aligns with the hypothesis that individuals with sleep-disordered breathing may have insufficient chemoreceptor sensitivity to register the change in arterial oxygenation (Berry & Gleeson, 1997; Osanai et al., 1999), and thus arousals are not initiated in response to desaturations. Lastly, given the potential influence of breath amplitude on the relationship between desaturations, arousals, and oxygenation during sleep (Badr et al., 1997; Basner, Onal, Stepanski, & Lopata, 1995; Carlson, Carley, Onal, Lopata, & Basner, 1994), it is possible that participants in the study did indeed exhibit arousals in response to desaturations, but the arousals did not cause increased breath amplitude. Consequently, arousals failed to moderate the effect of desaturations on arterial oxygenation.

**Impact of desaturations on cognition**

Another goal of this study was to understand the impact of mild sleep-disordered breathing on cognitive function in this sample of older adults. The most notable finding was that desaturations were related to a single construct representing attention, speed, and working memory. Although initially unplanned, the fact that these measures all loaded on to the same latent construct is not surprising. Each of these three domains may be defined in terms of separate functions: attention is theorized to involve the selection, control, and coordination of information; speed is considered the speed at which the brain carries out lower level cognitive processes; working memory is commonly conceptualized as a simple storage-capacity function. These three cognitive domains also comprise overlapping cognitive processes, however, that correspond to a complex, multidimensional construct pertaining to higher-level executive function. In this multidimensional construct, attention is related to working memory in that passive storage of verbal and visual information is actively
monitored and updated via the limited attentional capacity central executive (Baddeley, 1986; Engle, 2002). Thus, working memory involves the ability to control attention so as to maintain information in an active, accessible state (Cowan, 1999). This attentionally-controlled storage of visual and verbal information is time-limited, meaning that information in working memory decays with time. Consequently, the present findings may be interpreted such that desaturations are associated with poor performance on this multidimensional construct that represents time-sensitive attentional and working memory performance.

This finding that desaturations were related to attention/speed/working memory corroborates results from studies with younger (Adams et al. 2001, Aloia et al. 2004) and older (Aloia et al., 2003) sleep apnea patients. The present study builds on previous research in obstructive sleep apnea populations by establishing that desaturations affect these cognitive processes above and beyond mean oxygenation level, a finding which suggests that there is something unique about the desaturation process that affects cognitive performance other than its effects on oxygen. Moreover, this study demonstrates that this relationship occurs not just in severe sleep apnea patients, but in non-sleep disordered, community-dwelling older adults as well.

Another finding was that impairments in speed, attention, and working memory were related to poor performance on visual and verbal long-term episodic memory tasks. This finding is consistent with the aging literature. Specifically, researchers have suggested that age-related slowing prevents successful execution of operations required for higher level cognitive abilities such as attention and working memory (Salthouse, 1996). Thus, cognitive performance suffers when slowed processing prevents operations from being completed, or causes information to be lost and unavailable for additional processing (Salthouse, 1996;
Salthouse, 2005). In combination with this processing-speed theory, age-related deficits in attention and working memory are attributed to difficulties inhibiting irrelevant information from the focus of attention (Hartman, 1995; Hasher & Zacks, 1988; Lustig, Hasher, & Zacks, 2007; May, Hasher, & Kane, 1999; Zacks & Hasher, 1998). Hence, desaturations in this study were associated with inability to quickly and optimally carry out attentional and working memory processes. The fact that this deficit in attention, speed and working memory was associated with impaired performance on long-term episodic memory tasks, is consistent with studies in the aging literature which have demonstrated that age-related impairments in long-term memory can be explained in part by reduced speed, attention, and working memory abilities (Park et al., 1996; Verhaeghen & Salthouse, 1997).

**Impact of arousals on cognition**

In contrast to desaturations, arousals were not related to cognitive performance, nor did they moderate the relationship between desaturations and cognitive function. One possible interpretation of these findings is that arousals are unrelated to cognitive performance in mild sleep-disordered breathing. There is indeed some support to suggest that cognitive deficits are more closely related to hypoxemic episodes than arousals (Findley et al., 1986). Older adults in this study nevertheless exhibited numerous arousals, and given the evidence that frequent arousals result in reduced daytime cognitive performance (Martin, Engleman, Deary, & Douglas, 1996), these repeated arousals would still be expected to negatively impact cognitive function.

One potential explanation for the lack of relationship between arousals and cognitive function is that instead of conducting cognitive testing following a night of sleep in the lab, cognitive testing was conducted on the first day of the study, which followed a night of sleep
at home. Under the assumption that daytime cognitive deficits result from disruption of the previous night’s sleep, if there was night-to-night variability in arousals, we might expect the relationship between cognitive function and arousals in this study to be weakened. Unfortunately this explanation is not very plausible, because evidence suggests there is in fact little night-to-night variability in sleep and respiratory variables such as arousals and desaturations (Pittsley et al., 2005; Loredo, Clausen, Ancoli-Israel, &Dimsdale, 1999), and there is little difference between sleep variables such as arousals when assessed in the home versus laboratory (Iber et al., 2004). Thus, it remains unclear why arousals are unrelated to cognitive performance in this study.

*Role of demographics and IQ*

Of note, the relationship between desaturations, attention/speed/working memory, and long-term episodic memory remained intact when IQ and demographic variables representing age and SES were considered. This suggests the effect of desaturations on these cognitive functions is indeed due to something related to the desaturations themselves, and the relationship is not confounded by those extraneous demographics factors. Age was associated with the attention/speed/working memory construct, but controlling for age did not negate the relationship between desaturations and cognitive function. This suggests that desaturations produce cognitive deficits not attributable to increasing age among these older adults. These are difficult findings to interpret, though, as the age range of the participants in this study was restricted to individuals 70 and over. Replicating this study with a broad range of younger and older participants may help to clarify whether these desaturations and their effect on cognitive function is age-related. Another issue related to the effect of these demographic variables in the model was that IQ accounted for the relationship between
attention/speed/working memory and long-term episodic verbal memory. This finding could likely be explained by the fact that both the long-term verbal episodic memory latent construct and the IQ estimate are heavily reliant on verbal skills. Unlike age and IQ, SES was found to be unrelated to any of the cognitive variables.

*Sleep-disordered breathing and cardiovascular disease*

This study also examined the relationship of cardiovascular disease to mild sleep-disordered breathing. Cardiovascular disease refers to a range of conditions that affect the heart and blood vessels. In the present study, cardiovascular disease was assessed using the heart and vascular subscales of the CIRS-G. The heart subscale assesses conditions such as myocardial infarction, whereas the vascular scale concerns conditions such as high blood pressure. Previous research has provided support for the association between cardiovascular disease and sleep-disordered breathing, even in patients with mild to moderate forms of sleep-disordered breathing (Newman et al., 2001; Shahar et al., 2001).

The present study investigated arterial oxygenation while awake and aspects of sleep-disordered breathing (desaturations, arterial oxygenation during sleep, and arousals) to determine the association of each of these to cardiovascular disease. It was found that arterial oxygenation while awake was not related to the cardiovascular symptoms. As for the sleep-related variables, arterial oxygenation during sleep was related to the vascular symptoms, and desaturations were associated with both heart and vascular symptoms. In contrast to the arterial oxygenation-related sleep variables, arousals were not related to either measure of cardiovascular disease. Although this negative finding may be attributed to the previously discussed issue regarding the inclusive nature of the arousal measure, other studies have also failed to find relationships between arousals and cardiovascular disease (Shahar et al., 2001).
These findings that measures of cardiovascular disease were related to desaturations and sleep arterial oxygenation, but not arterial oxygenation while awake, suggest that intermittent hypoxemia during sleep is uniquely related to cardiovascular disease. This is consistent with other data which show that the intermittent hypoxemia in sleep-disordered breathing is related to such cardiovascular conditions as hypertension and ischemic heart disease (Nieto et al., 2000; Shahar et al., 2001; Shamsuzzaman, Gersh, & Somers, 2003). Convincing evidence exists to suggest that sleep-disordered breathing is an etiologic factor in the development of cardiovascular disease (Drager et al., 2007; Lanfranchi & Somers, 2001), but whether cardiovascular symptoms exacerbate sleep apnea symptoms remains to be seen.

In addition to examining the relationship of cardiovascular variables to sleep, this study also explored their relationships to cognitive function. Multiple studies have found support for the relationship between cardiovascular disease and deficits in cognitive abilities such as processing speed, attention, and memory (Hassing et al., 2004; Yiloski et al., 2000). In the present study, the heart subscale of the CIRS-G was related to attention/speed/working memory and long-term episodic memory. Thus, those individuals with a history of myocardial infarction or congestive heart failure showed reduced performance on the attention/speed/working memory construct, and attention/speed/working memory was associated with verbal and nonverbal long-term episodic memory. Contrary to initial hypotheses, however, vascular symptoms were not related to cognitive function. This finding is surprising, given the consistent evidence linking poor vascular health and cognitive impairments (Phillips & Mate-Kole, 1997; Rao, Jackson, & Howard, 1999).

It is difficult to speculate as to why the heart symptoms were associated with cognitive function and vascular symptoms were not. One possibility is that participants may
have endorsed fewer items on the vascular scale compared to the heart scale, creating a floor effect. In actuality, a number of participants endorsed one or more of the symptoms on the vascular scale, whereas few people endorsed high scores on the heart scale, thus floor effects on the vascular scale do not account for the present findings. It is important to note, however, that individuals with severe cardiovascular symptoms were excluded from the study, so although there did not appear to be floor effects, ceiling effects perhaps reduced the likelihood of finding relationships among the variables. Another possible explanation is that the heart subscale may represent more severe symptoms than the vascular subscale. The lowest level item on the heart subscale corresponds with a history of myocardial infarction, whereas the lowest level item on the vascular subscale corresponds to hypertension controlled by diet alone. Therefore, the symptoms on the vascular scale are not only seemingly more mild than the heart scale, but a high score on the vascular subscale is associated with blood pressure that was well-controlled by diet or medications. Because individuals with well-controlled hypertension exhibit no more cognitive deficits than normotensive individuals (Brady, Spiro, & Gaziano, 2005; Nilsson, Gullberg, Ekesbo, Von Schenck, & Gustafson, 1998), it might be expected that the vascular scale would be less likely to be related to cognitive function. To combat these measurement issues in the examination of vascular symptoms in future studies, more sensitive and varied assessment of vascular symptoms may be achieved by including individuals with more severe vascular symptoms, and to use physiological measures of vascular function (e.g. Doppler ultrasound, systolic and diastolic blood pressure).

In addition to the direct effects of the cardiovascular variables on cognition, this study also investigated whether the cardiovascular variables moderated the effects of desaturations
and arousals on cognitive function. The finding that the cardiovascular symptoms did not moderate the effect of desaturations or arousals on cognition was surprising, especially because there were relationships between cardiovascular symptoms and desaturations. This lack of relationship would suggest that although cardiovascular symptoms are associated with sleep-disordered breathing, they do not act together to produce or protect against cognitive deficits. At first consideration, this finding would suggest that vascular damage may not be the mechanism by which intermittent hypoxemia affects cognitive performance. As previously discussed, there is nevertheless compelling research evidence supporting the relationship between sleep-disordered breathing and cardiovascular disease, and there is also persuasive evidence that links both sleep-disordered breathing and cardiovascular disease to cognitive function. While there is compelling evidence for the relationships among these variables, the degree to which cardiovascular disease moderates or acts as a mechanism by which sleep-disordered breathing affects cognitive function is less well known. Future studies may better explicate the nature of these relationships by employing a longitudinal study, and by assessing cardiovascular disease with more sensitive and specific physiological measures.

Conclusions

In summary, despite the fact that participants in this study were free from diagnosable sleep disorders such as obstructive sleep apnea, they exhibited numerous desaturations and arousals. Desaturations were found to uniquely impact arterial oxygenation, above and beyond arterial oxygenation while awake. Desaturations were found to be associated with a single construct representing attention, speed, and working memory, and this multidimensional construct was associated with the constructs representing verbal and visual
long-term episodic memory. Desaturations were also found to be related to measures of cardiovascular disease, and although the exact nature of this relationship has yet to be determined, desaturations may be associated with cardiovascular disease, which in theory may result in neurological damage and cognitive deficits. Notably, arousals were related to nothing in this study. They had no impact on arterial oxygenation or any cognitive test, nor were they related to measures of cardiovascular disease.

There were several limitations in this study, some of which have already been discussed, and others which bear mentioning here. As previously noted, the negative findings concerning arousals may have been affected by measurement difficulties, and in the future, scoring arousals so that they are time-locked with desaturations may yield more interpretable findings regarding their relationship with sleep-disordered breathing and cognitive function. The limited range of ages and the cross sectional design of this study preclude any conclusions about age-related or causal effects. Future studies may benefit from either inclusion of younger adults in the study sample, or use of a longitudinal design to examine the changes in sleep-disordered breathing, cardiovascular disease, and cognition with age. A final limitation is related to the small sample size. Although the sample size was deemed sufficient for adequate level of power, findings should be considered preliminary and the model should be replicated with additional large samples to confirm the model’s veracity.

In conclusion, the findings from the current study are theoretically important in that they suggest that even mild sleep-disordered breathing may have an impact on cognitive function in community-dwelling older adults. The broader, clinical implications of the findings from this study also deserve further study and consideration. Although remediating interventions for sleep-disordered breathing are primarily geared toward diagnosable cases of
sleep apnea, the findings from this study suggest that mild sleep-disordered breathing is not without consequences, and therefore there may be important treatment considerations for older adults with mild sleep-disordered breathing as well.
Table 1

*Means and Standard Deviations for Oxygenation, Sleep, and CIRS-G Measures*

<table>
<thead>
<tr>
<th></th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood oxygenation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean arterial oxygenation</td>
<td>93.9</td>
<td>1.9</td>
</tr>
<tr>
<td>during sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum arterial oxygenation</td>
<td>89.0</td>
<td>3.5</td>
</tr>
<tr>
<td>during sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent of sleep time</td>
<td>10.0</td>
<td>15.4</td>
</tr>
<tr>
<td>spent &lt;90% saturation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desaturation index</td>
<td>15.7</td>
<td>15.3</td>
</tr>
<tr>
<td>Arterial oxygenation</td>
<td>94.6</td>
<td>1.6</td>
</tr>
<tr>
<td>while awake (baseline)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Arousals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of arousals</td>
<td>193.4</td>
<td>80.6</td>
</tr>
<tr>
<td>Arousal index</td>
<td>2.4</td>
<td>0.9</td>
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<tr>
<td><strong>CIRS-G</strong></td>
<td></td>
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</tr>
<tr>
<td>Heart Subscale</td>
<td>0.6</td>
<td>1.0</td>
</tr>
<tr>
<td>Vascular Subscale</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Sum CIRS-G score</td>
<td>1.8</td>
<td>1.7</td>
</tr>
<tr>
<td>(Heart and Vascular)</td>
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Table 2

Hierarchical Regression Analysis Predicting Mean SaO2 During Sleep (N = 114)

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>sr2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desaturation index</td>
<td>-.45**</td>
<td>.15</td>
<td>-.26</td>
<td>.07</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arousal index</td>
<td>-.13</td>
<td>.16</td>
<td>-.08</td>
<td>.01</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desaturation index</td>
<td>-.44**</td>
<td>.16</td>
<td>-.26</td>
<td>.06</td>
</tr>
<tr>
<td>Arousal index</td>
<td>-.06</td>
<td>.16</td>
<td>-.04</td>
<td>.00</td>
</tr>
<tr>
<td><strong>Model 4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desaturation index</td>
<td>-.47**</td>
<td>.17</td>
<td>-.27</td>
<td>.07</td>
</tr>
<tr>
<td>Arousal index</td>
<td>-.07</td>
<td>.16</td>
<td>-.04</td>
<td>.002</td>
</tr>
<tr>
<td>Desaturation index*Arousal index</td>
<td>.10</td>
<td>.13</td>
<td>.07</td>
<td>.005</td>
</tr>
</tbody>
</table>

Note: $R^2 = .07$ for Model 1 (p = .005). $R^2 = .003$ for Model 2 (n.s.). $R^2 = .05$ for Model 3 (p=.02). $R^2 = .05$ for Model 4 (p = .04).

* p<.05. ** p<.01. ***p<.001.
Table 3

Hierarchical Regression Analysis for Variables Predicting Mean SaO2 During Sleep (N = 112)

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>sr2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wake SaO2</td>
<td>1.28***</td>
<td>.11</td>
<td>.75</td>
<td>.56</td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desaturation index</td>
<td>-.23*</td>
<td>.11</td>
<td>-.13</td>
<td>.02</td>
</tr>
<tr>
<td>Arousal index</td>
<td>-.09</td>
<td>.11</td>
<td>-.05</td>
<td>.00</td>
</tr>
<tr>
<td>Wake SaO2</td>
<td>1.24***</td>
<td>.07</td>
<td>.72</td>
<td>.51</td>
</tr>
<tr>
<td>Model 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desaturation index</td>
<td>-.23*</td>
<td>.11</td>
<td>-.13</td>
<td>.02</td>
</tr>
<tr>
<td>Arousal index</td>
<td>-.09</td>
<td>.11</td>
<td>-.05</td>
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<tr>
<td>Wake SaO2</td>
<td>1.29***</td>
<td>.12</td>
<td>.75</td>
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</tr>
<tr>
<td>Desaturation index* Arousal index</td>
<td>.03</td>
<td>.09</td>
<td>.02</td>
<td>.00</td>
</tr>
<tr>
<td>Desaturation index* Wake SaO2</td>
<td>.007</td>
<td>.14</td>
<td>.004</td>
<td>.00</td>
</tr>
<tr>
<td>Arousal index* Wake SaO2</td>
<td>-.06</td>
<td>.13</td>
<td>-.03</td>
<td>.00</td>
</tr>
<tr>
<td>Desaturation index* Arousal index* Wake SaO2</td>
<td>-.13</td>
<td>.12</td>
<td>-.09</td>
<td>.005</td>
</tr>
</tbody>
</table>

Note: $R^2 = .55$ for Model 1 (p < .0001). $R^2 = .57$ for Model 2 (p < .0001). $R^2 = .56$ for Model 3 (p < .0001).   * p<.05. ** p<.01. ***p<.001.
Table 4

*Means and Standard Deviations for Cognitive Measures*

<table>
<thead>
<tr>
<th>Category</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Verbal Memory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logical Memory I</td>
<td>38.9</td>
<td>9.2</td>
</tr>
<tr>
<td>Logical Memory II</td>
<td>22.5</td>
<td>8.1</td>
</tr>
<tr>
<td>Word Lists I</td>
<td>6.7</td>
<td>2.5</td>
</tr>
<tr>
<td>Word Lists II</td>
<td>6.5</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Visual Memory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Reproduction I</td>
<td>67.6</td>
<td>15.8</td>
</tr>
<tr>
<td>Visual Reproduction II</td>
<td>42.4</td>
<td>21.8</td>
</tr>
<tr>
<td>Rey-Osterrieth Immediate</td>
<td>13.4</td>
<td>6.3</td>
</tr>
<tr>
<td>Rey-Osterrieth Delayed</td>
<td>13.2</td>
<td>6.6</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making B</td>
<td>107.4</td>
<td>55.8</td>
</tr>
<tr>
<td>Stroop CW</td>
<td>169.5</td>
<td>51.1</td>
</tr>
<tr>
<td><strong>Processing Speed</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symbol Digit Modalities Test</td>
<td>39.7</td>
<td>10.0</td>
</tr>
<tr>
<td><strong>Working Memory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letter Number Sequencing</td>
<td>9.6</td>
<td>2.2</td>
</tr>
</tbody>
</table>
Table 5

*Intercorrelations Among Variables*

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Mean SaO2 during sleep</td>
<td>----</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Minimum SaO2 during sleep</td>
<td>.66***</td>
<td>----</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Percent of sleep &lt;90% SaO2</td>
<td>-.86***</td>
<td>-.65***</td>
<td>----</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Desaturation index</td>
<td>-.23*</td>
<td>-.39***</td>
<td>.35***</td>
<td>----</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Total # of arousals</td>
<td>-.08</td>
<td>-.01</td>
<td>.04</td>
<td>.23*</td>
<td>----</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Arousal index</td>
<td>-.05</td>
<td>.08</td>
<td>.02</td>
<td>.16</td>
<td>.94***</td>
<td>----</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Mean SaO2 while awake</td>
<td>.78***</td>
<td>.54***</td>
<td>-.63***</td>
<td>-.15</td>
<td>-.04</td>
<td>.01</td>
<td>----</td>
<td></td>
</tr>
<tr>
<td>8. CIRS-G heart</td>
<td>-.15</td>
<td>-.06</td>
<td>.19*</td>
<td>.18</td>
<td>.15</td>
<td>.10</td>
<td>-.05</td>
<td>----</td>
</tr>
<tr>
<td>9. CIRS-G vascular</td>
<td>.04</td>
<td>-.10</td>
<td>.01</td>
<td>.21*</td>
<td>-.04</td>
<td>-.03</td>
<td>.09</td>
<td>.22*</td>
</tr>
</tbody>
</table>

* p<.05. ** p<.01. ***p<.001.
Table 6

*Intercorrelations Among Sleep and Cognitive Variables*

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Minimum</th>
<th>Percent of sleep time</th>
<th>SaO2 while awake</th>
<th>CIRS-G heart</th>
<th>CIRS-G vascular</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Minimum</td>
<td>&lt;90% SaO2 during sleep</td>
<td>Desat. index</td>
<td>Total # of arousals</td>
<td>Arousal index (baseline)</td>
</tr>
</tbody>
</table>

†p<10. *p<.05. **p<.01. ***p<.001.
Table 7

*Reliability Estimates for Single Indicator Variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reliability estimate</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digit Symbol</td>
<td>.74</td>
<td>Hinton-Bayre et al., 2005</td>
</tr>
<tr>
<td>Letter Number Sequencing</td>
<td>.78</td>
<td>Psychological Corp., 1997</td>
</tr>
<tr>
<td>CIRS</td>
<td>.80</td>
<td>Miller et al., 1992</td>
</tr>
<tr>
<td>desaturations</td>
<td>.90</td>
<td>Whitney et al., 1998</td>
</tr>
<tr>
<td>arousals</td>
<td>.84</td>
<td>Loredo et al., 1999</td>
</tr>
</tbody>
</table>
Table 8

*Standardized Factor Loadings for Exogenous Variables in the Final Structural Model*

<table>
<thead>
<tr>
<th></th>
<th>Heart symptoms</th>
<th>Vascular symptoms</th>
<th>Desaturations</th>
<th>O₂ during sleep</th>
<th>Arousals</th>
<th>O₂ while awake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart symptoms †</td>
<td>.98</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Vascular symptoms †</td>
<td>-</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Desaturation index †</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mean O₂ during sleep †</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.99</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Minimum O₂ during sleep</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.68</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% sleep time &lt;90%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-.87</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Arousal Index †</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.90</td>
<td>-</td>
</tr>
<tr>
<td>Wake O₂ †</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.91</td>
</tr>
</tbody>
</table>

O₂ = arterial oxygenation

† these items were fixed to 1.00 for model identifying purposes.

* significant at p <.05; ** significant at p <.01
Table 9

*Standardized Factor Loadings for Endogenous Variables*

<table>
<thead>
<tr>
<th></th>
<th>Verbal memory</th>
<th>Visual Memory</th>
<th>Attention/ speed/ working memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>LM1†</td>
<td>.58</td>
<td>- -</td>
<td>- -</td>
</tr>
<tr>
<td>LM2</td>
<td>.64</td>
<td>- -</td>
<td>- -</td>
</tr>
<tr>
<td>WL1</td>
<td>.52</td>
<td>- -</td>
<td>- -</td>
</tr>
<tr>
<td>WL2</td>
<td>.53</td>
<td>- -</td>
<td>- -</td>
</tr>
<tr>
<td>VR1†</td>
<td>- -</td>
<td>.81</td>
<td>- -</td>
</tr>
<tr>
<td>VR2</td>
<td>- -</td>
<td>.79</td>
<td>- -</td>
</tr>
<tr>
<td>Rey-Osterrieth Immediate</td>
<td>- -</td>
<td>.72</td>
<td>- -</td>
</tr>
<tr>
<td>Rey-Osterrieth Delay</td>
<td>- -</td>
<td>.70</td>
<td>- -</td>
</tr>
<tr>
<td>Trail Making B†</td>
<td>- -</td>
<td>- -</td>
<td>.79</td>
</tr>
<tr>
<td>Stroop CW</td>
<td>- -</td>
<td>- -</td>
<td>.77</td>
</tr>
<tr>
<td>Symbol Digit Modalities Test</td>
<td>- -</td>
<td>- -</td>
<td>.85</td>
</tr>
<tr>
<td>Letter-Number Sequencing</td>
<td>- -</td>
<td>- -</td>
<td>.47</td>
</tr>
</tbody>
</table>


† these items were fixed to 1.00 for model identifying purposes.

* significant at $p < .05$; ** significant at $p < .01$
Table 10

Interrelations Among Exogenous Variables in Full Structural Model

<table>
<thead>
<tr>
<th></th>
<th>CIRS-G heart</th>
<th>CIRS-G vascular</th>
<th>O₂ during sleep</th>
<th>Desaturations</th>
<th>Arousals</th>
<th>O₂ while awake</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIRS-G heart</td>
<td>14.32</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIRS-G vascular</td>
<td>14.71*</td>
<td>130.11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O₂ during sleep</td>
<td>-1.86*</td>
<td>1.31*</td>
<td>5.49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desaturations</td>
<td>12.54*</td>
<td>42.72*</td>
<td>-8.91*</td>
<td>233.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arousals</td>
<td>0.34</td>
<td>-0.59</td>
<td>-0.10</td>
<td>2.26</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td>O₂ while awake</td>
<td>-0.63</td>
<td>1.81</td>
<td>3.04*</td>
<td>-3.74</td>
<td>0.02</td>
<td>2.24</td>
</tr>
</tbody>
</table>

* significant at p <.05
Table 11

*Standardized Path Coefficients Showing Interrelations Among Latent Variables*

<table>
<thead>
<tr>
<th></th>
<th>Verbal memory</th>
<th>Visual memory</th>
<th>Attention/speed/WM</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIRS-G heart</td>
<td>-.06</td>
<td>-.10</td>
<td>-.30*</td>
</tr>
<tr>
<td>CIRS-G vascular</td>
<td>-.02</td>
<td>-.05</td>
<td>.20</td>
</tr>
<tr>
<td>Desaturations</td>
<td>-.19</td>
<td>-.04</td>
<td>-.27*</td>
</tr>
<tr>
<td>Arterial oxygen. during sleep</td>
<td>-.46</td>
<td>-.41</td>
<td>.16</td>
</tr>
<tr>
<td>Arousals</td>
<td>.14</td>
<td>-.17</td>
<td>.02</td>
</tr>
<tr>
<td>Arterial oxygen. while awake</td>
<td>.29</td>
<td>.26</td>
<td>-.25</td>
</tr>
</tbody>
</table>

* * significant at p <.05
Table 12

*Standardized Path Coefficients Showing Interrelations Among Latent Variables*

<table>
<thead>
<tr>
<th></th>
<th>Verbal memory</th>
<th>Visual memory</th>
<th>Attention/speed/WM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CIRS-G heart</strong></td>
<td>-.04</td>
<td>.10</td>
<td>-.15</td>
</tr>
<tr>
<td><strong>CIRS-G vascular</strong></td>
<td>-.05</td>
<td>-.05</td>
<td>.15</td>
</tr>
<tr>
<td><strong>Desaturations</strong></td>
<td>-.15</td>
<td>-.06</td>
<td>-.20*</td>
</tr>
<tr>
<td>Arterial oxygen. during sleep</td>
<td>-.45</td>
<td>-.41</td>
<td>-.10</td>
</tr>
<tr>
<td><strong>Arousals</strong></td>
<td>.13</td>
<td>-.17</td>
<td>.02</td>
</tr>
<tr>
<td>Arterial oxygen. while awake</td>
<td>.20</td>
<td>.24</td>
<td>-.02</td>
</tr>
<tr>
<td><strong>age</strong></td>
<td>-.18</td>
<td>-.03</td>
<td>-.37*</td>
</tr>
<tr>
<td><strong>NAART IQ</strong></td>
<td>.54*</td>
<td>-.02</td>
<td>.66*</td>
</tr>
</tbody>
</table>

* significant at $p < .05$
Figure 1. Example of EEG waves for each stage of sleep (http://holisticonline.com/Remedies/Sleep/stages-of-sleep-eeg1.GIF).
Figure 2. Example of younger adults’ sleep architecture (top), and older adults’ sleep architecture (bottom), (http://www.aafp.org/afp/990501ap/2551.html).
Figure 3. Proposed theoretical model representing the relationships between aging, sleep-disordered breathing, vascular disease, and cognitive deficits.
Figure 4. Hypothesized structural equation model depicting relationship between arousals, sleep and arterial oxygenation while awake, vascular disease, and cognitive performance.
**Figure 5. Vascular and Heart Subscales of the CIRS-G.**

<table>
<thead>
<tr>
<th>Vascular</th>
<th>Hypertension</th>
<th>Peripheral</th>
<th>Aortic</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 No problem</td>
<td>No problem</td>
<td>No problem</td>
<td>No problem</td>
</tr>
<tr>
<td>1 Hypertension compensated with salt restriction and weight loss / serum cholesterol &gt; 200 mg/dl</td>
<td>Managed drug free</td>
<td>No problem</td>
<td>No problem</td>
</tr>
<tr>
<td>2 Daily antihypertensive meds/one symptom of atherosclerotic disease (angina, claudication, bruit, amaurosis fugax, absent pedal pulses) / aortic aneurysm &lt; 4 cm)</td>
<td>Single daily antihypertensive</td>
<td>At least 1 physical symptoms or imaging evidence</td>
<td>No problem</td>
</tr>
<tr>
<td>3 Two or more symptoms of atherosclerosis [see above]</td>
<td>Two or more drug</td>
<td>Two or more symptoms</td>
<td>Palpable &lt; 4 cm</td>
</tr>
<tr>
<td>4 Previous surgery for vascular problem/aortic aneurysm &gt; 4cm)</td>
<td>Evidence of LVH</td>
<td>Bypass graph surgery</td>
<td>Palpable &gt; 4cm</td>
</tr>
<tr>
<td>Heart</td>
<td>Athero. Heart Disease</td>
<td>Congest Heart Failure</td>
<td>Arrhythmias</td>
</tr>
<tr>
<td>-------</td>
<td>------------------------</td>
<td>-----------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>0</td>
<td>No problem</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Remote MI (&gt;5 years ago) / occasional angina treated with prn meds</td>
<td>Detectable murmur, no activity restriction</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>CHF compensated with meds / daily anti-angina meds / left ventricular hypertrophy / atrial fibrillation/bundle branch block / daily antiarrythmic drugs</td>
<td>Requires daily meds</td>
<td>Atrial fibrillation, daily antiarrythmics, pacemaker for incident bradycardia</td>
</tr>
<tr>
<td>3</td>
<td>Previous MI within 5 yrs / abnormal stress test / status post percutaneous coronary angioplasty or coronary artery bypass graft surgery</td>
<td></td>
<td>Bifasicular block, pacemaker for cardiogenic syncope</td>
</tr>
<tr>
<td>4</td>
<td>Marked activity restriction secondary to cardiac status (i.e., unstable angina or intractable congestive heart failure)</td>
<td>Intractable CHF</td>
<td></td>
</tr>
</tbody>
</table>
Figure 6. Frequencies of desaturations.
Figure 7. Initial measurement model for endogenous variables.

Abbreviations: heart = heart subscale of CIRS-G; vasc = vascular subscale of the CIRS-G; wakeO2 = arterial oxygenation while awake; dsatIndx = desaturation index (ODI); minO2 = minimum arterial oxygenation during sleep; meanO2 = mean arterial oxygenation during sleep; pct90 = percent of sleep time spent at <90% arterial oxygenation; arousInd = arousal index; sleepox = oxygenation during sleep;
Figure 8. Final measurement model for endogenous variables.

Abbreviations: heart = heart subscale of CIRS-G; vasc = vascular subscale of the CIRS-G; dsatIndx = desaturation index (ODI); minO2 = minimum arterial oxygenation during sleep; meanO2 = mean arterial oxygenation during sleep; pct90 = percent of sleep time spent at <90% arterial oxygenation; arousInd = arousal index; sleepox = oxygenation during sleep;
Figure 9. Initial measurement model for endogenous variables.

Abbreviations: LM1 = Logical Memory Immediate; LM2 = Logical Memory Delayed; WL1 = Word Lists Immediate; WL2 = Word Lists Delayed; VR1 = Visual Reproduction Immediate; VR2 = Visual Reproduction Delayed; Rey = Rey-Osterrieth Delayed; TrailsB = Trail Making Test Part B; StroopCW = Stroop Test Color Word Condition; LNSeq = Letter Number Sequencing; attn = attention; verbal = verbal memory; visual = visual memory
Figure 10. Final measurement model for endogenous variables.

Abbreviations: heart = TrailsB = Trail Making Test Part B; StroopCW = Stroop Test Color Word Condition; LM1 = Logical Memory Immediate; LM2 = Logical Memory Delayed; WL1 = Word Lists Immediate; WL2 = Word Lists Delayed; VR 1 = Visual Reproduction Immediate; VR2 = Visual Reproduction Delayed; Rey = Rey-Osterrieth Delayed; attn = attention; verbal = verbal memory; visual = visual memory
Figure 11. Initial structural model.

Abbreviations: heart = heart subscale of CIRS-G; vasc = vascular subscale of the CIRS-G; dsatInd = desaturation index; minO2 = minimum arterial oxygenation during sleep; meanO2 = mean arterial oxygenation during sleep; pct90 = percent of sleep time spent at <90% arterial oxygenation; arousInd = arousal index; wakeO2 = arterial oxygenation while awake; LM1 = Logical Memory Immediate; LM2 = Logical Memory Delayed; WL1 = Word Lists Immediate; WL2 = Word Lists Delayed; VR 1 = Visual Reproduction Immediate; VR2 = Visual Reproduction Delayed; ReyImmed = Rey-Osterrieth Immediate; ReyDelay = Rey-Osterrieth Delayed; TrailsB = Trail Making Test Part B; StroopCW = Stroop Test Color Word Condition; LNSeq = Letter Number Sequencing; desats = desaturation index; sleepox = oxygenation during sleep; wakeox = oxygenation while awake; attn = attention; verbal = verbal memory; visual = visual memory.
Figure 12. Final structural model, including paths among the endogenous variables.

Note: All paths depicted in the model are significant

Abbreviations: heart = heart subscale of CIRS-G; vasc = vascular subscale of the CIRS-G; desats = desaturation index; sleepox = latent variable representing mean arterial oxygenation during sleep, min. arterial oxygenation during sleep, and percent of sleep time spent at <90% arterial oxygenation; arousals = arousal index; wakeox = arterial oxygenation while awake; attnSpdW = latent variable comprising attention, speed, working memory; verbal = verbal memory; visual = visual memory.
Figure 13. Final structural model with control variables included.

Abbreviations: heart = heart subscale of CIRS-G; vasc = vascular subscale of the CIRS-G; dsatIndx = desaturation index; minO2 = minimum arterial oxygenation during sleep; meanO2 = mean arterial oxygenation during sleep; pct90 = percent of sleep time spent at <90% arterial oxygenation; arousInd = arousal index; wakeO2 = arterial oxygenation while awake; LM1 = Logical Memory Immediate; LM2 = Logical Memory Delayed; WL1 = Word Lists Immediate; WL2 = Word Lists Delayed; VR 1 = Visual Reproduction Immediate; VR2 = Visual Reproduction Delayed; ReyImmed = Rey-Osterrieth Immediate; ReyDelay = Rey-Osterrieth Delayed; TrailsB = Trail Making Test Part B; StroopCW = Stroop Test Color Word Condition; LNSeq = Letter Number Sequencing; desats = desaturation index; sleepox = oxygenation during sleep; wakeox = oxygenation while awake; attn = attention; verbal = verbal memory; visual = visual memory.
References


