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Effect of CPAP Compliance on a Cognitive Screening Test in a Memory Clinic Population with Sleep Apnea

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by

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We, the undersigned committee, having examined the attached doctoral research project, "Effect of CPAP Compliance on a Cognitive Screening Test in a Memory Clinic Population with Sleep Apnea," by Tatiana Marie Vallejo-Luces, M.S. hereby indicates its unanimous approval.

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Abstract

Title: Effect of CPAP Compliance on a Cognitive Screening Test in a Memory Clinic Population with Sleep Apnea

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Objectives: To determine whether the Montreal Cognitive Assessment (MoCA) was a sensitive indicator of cognitive improvement following introduction of continuous positive airway pressure (CPAP) in community memory clinic (CMC) patients who had been diagnosed with sleep apnea (SA).

Method: Twenty-six CPAP compliant CMC patients (61.5% male; 96.2% Caucasian/Non-Hispanic) with a diagnosis of SA (66-87 years (*M*=76.27(4.90)) completed a MoCA before initiation of treatment and again 4-9 months later. CPAP compliance was documented through CPAP machine compliance reports and/or clinical interview with patient and family member during subsequent medical visits. Twenty CPAP non-compliant CMC patients (85% male, 100% Caucasian/Non-Hispanic; 66-90 years (*M*=77.45 (6.88)) similarly diagnosed with SA completed MoCAs before initiation of treatment and again 4-8 months later. CMC diagnoses of the patients included: no cognitive impairment, Alzheimer's disease, mild cognitive impairment, cognitive disorder NOS, or other dementia.

Results: Post-treatment MoCA scores for the CPAP compliant group (*M*= 22.27) were significantly higher than pre-treatment scores (*M*= 20.38; *t*(25)= -4.992; *p*<0.001). Nineteen of the 26 compliant individuals evidenced increases in MoCA, three remained the same, and four declined. The non-compliant group showed no change over time (MoCA pre- *M*= 19.90, MoCA post- *M*= 20.50; *t*(19)= -.798; *p*= .435), with seven scores decreasing, eleven increasing, and two remaining the same. There was no significant interaction between CPAP compliance groups and MoCA change scores, *Wilks' Lambda*= .94, *F* (1, 44) = 2.67, partial eta squared= .057.

Conclusions: More patients with SA who complied with CPAP recommendation demonstrated improved MoCA performance than did those who did not comply with the recommendation. Within-subject comparison of pre- and post-CPAP usage via paired *t*-test was significant only for the compliant group. Finding no effect on change score or interaction between MoCA test time and compliance using the mixed-model ANOVA was likely due to the relative small sample size, which did not supply sufficient power to the study. This interpretation is supported by the t-test outcome as well as the numerical difference in numbers of patients whose MoCA scores increased from the pre-test to the post-test measurement (19 versus 7).

Key words: Sleep Apnea, CPAP, Compliance, MoCA, Memory Clinic

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Introduction

Poor sleep quality and daytime sleepiness are suspected causes of cognitive impairment in obstructive sleep apnea (OSA) patients. Cognitive dysfunction ranges from difficulties in attention and executive function to memory difficulties. Continuous Positive Airway Pressure (CPAP) is the most consistently effective treatment for moderate to severe OSA in adult, elderly, and dementia populations and has been shown to improve cognitive impairment in these populations as well. However, there are compliance issues that limit the effectiveness of this treatment. Typically, the instruments used to study cognitive changes with CPAP use involve extensive neuropsychological testing in research settings. Hence, it would be beneficial for patients and physicians to measure this cognitive change through a time sensitive screener such as the Montreal Cognitive Assessment (MoCA). In this project, the objective was to determine whether the MoCA is a sensitive indicator of cognitive improvement following introduction of CPAP in patients from a memory disorder clinic who have been diagnosed with sleep apnea. Compliant and non-compliant patients with a diagnosis of sleep apnea completed a MoCA before initiation of treatment and again at a follow-up appointment. CPAP compliance was documented through clinical interview with the patient and a family member during subsequent medical visits. A review of the literature of sleep apnea and CPAP compliance was examined to understand the cognitive impact of CPAP treatment on sleep apnea patients and to further emphasize the need to improve compliance.

Review of the Literature

Sleep Apnea

Sleep apnea (SA) is a common and serious sleep disorder that occurs when breathing is briefly and repeatedly interrupted during sleep (Mayo Foundation for Medical Education and Research, 2015). It affects about 18 million American adults and an estimated 10 million Americans that remain undiagnosed (American Association for Respiratory Care, 2016). The condition affects about 4 percent of middle-aged men and 2 percent of middle-aged women (American Association for Respiratory Care, 2016). Thus, the prevalence is higher among men than women. Sleep apnea occurs in all ages including children and it is likely it may be passed on across generations in families (American Association for Respiratory Care, 2016). There are several factors that increase the risk of sleep apnea, such as being overweight, having a large neck, small airways in their noses, throats, or mouths, smoking, alcohol use, and belonging to certain ethnicities including African Americans, Pacific Islanders, and Mexican-Americans, are at increased risk of developing sleep apnea (American Association for Respiratory Care, 2016). Sleep apnea has numerous adverse health consequences, such as high blood pressure, heart attack, stroke, transient ischemic attacks, coronary heart disease, and the likelihood of involvement in motor vehicle accidents is three times more likely (American Association for Respiratory Care, 2016; National Institute of Neurological Disorders and Stroke, 2015).

Sleep apnea is characterized by brief interruptions of breathing during sleep (NINDS, 2015). These interruptions involve at least 30 episodes of airflow cessations per hour at the mouth and nose for more than 10 seconds (Yoshida, 2010). During these periods of compromised breathing, arousal from sleep occurs to restore gas exchange (Eckert et al., 2007). There are three main types of sleep apnea: obstructive sleep apnea, the more common form, central sleep apnea, and a mixed or complex sleep apnea syndrome that is a combination of the other two forms (Mayo Foundation for Medical Education and Research, 2015). Common symptoms of both obstructive sleep apnea and central sleep apnea include loud snoring (most important in diagnosing obstructive sleep apnea), episodes of breathing interruptions, frequent and sudden awakenings along with shortness of breath (more common in central sleep apnea), dry mouth or sore throat, morning headache, insomnia, excessive daytime sleepiness, attention and memory difficulties, and mood changes such as irritability (Mayo Foundation for Medical Education and Research, 2015). Common complications of sleep apnea are daytime fatigue, high blood pressure or heart difficulties, type 2 diabetes, metabolic syndrome, complications with medications and surgery, liver difficulties, and sleep deprivation (Mayo Foundation for Medical Education and Research, 2015). Risk factors for obstructive sleep apnea include obesity, which increases the risk four times compared to individuals with normal weight, a neck circumference in men 17 inches and larger and 15 inches or more in women, a narrowed airway, the male sex, older age, family history, use of alcohol, sedatives or other substances that relax the muscles of the throat, smoking, which increases the likelihood three times, and nasal congestion (Mayo Foundation for

Medical Education and Research, 2015). In comparison, risk factors for central sleep apnea include older age, heart disorders, narcotic pain medications, and history of a stroke (Mayo Foundation for Medical Education and Research, 2015). On the other hand, OSA has been identified as a potential risk factor for mild cognitive impairment and other dementias. In a longitudinal study of 298 white women with a mean age of 82 years, sleep-disordered breathing was associated with an increased risk of cognitive impairment, particularly mild cognitive impairment or dementia (Alzheimer's disease; Yaffe et al., 2011). Specifically, hypoxia measures were consistently associated with mild cognitive impairment or dementia (Yaffe et al., 2011). After a mean of 4.7 years of follow-up, 35.9% of women with sleep-disordered breathing developed mild cognitive impairment and 15.8% developed dementia (Yaffe et al., 2011). Patients with OSA are also at risk for subcortical ischemic vascular dementia (Roman, Erkinjuntti, Wallin, Pantoni, & Chui, 2002). Subcortical ischemic vascular dementia is due to small-artery disease and hypoperfusion, specifically complete infarction or lacunar infarcts and microinfarcts, and incomplete infarctions of deep cerebral white matter (Roman et al., 2002). The effects of OSA on cerebral microvascular and neurovascular systems include mechanisms such as hypoperfusion, endothelial dysfunction, and neuroinflammation (Kerner & Roose, 2016). Hypoperfusion leads to the development or progression of cerebral small vessel disease (Kerner & Roose, 2016). In fact, intermittent hypoxia or a temporary absence of enough oxygen in the blood plays a role in initiating and worsening these processes (Kerner & Roose, 2016). Hypoxemia or low oxygen level in the blood also worsens the process resulting in white matter lesions, white matter integrity abnormalities, and gray matter loss

(Kerner & Roose, 2016). However, there is lack of research in the relationship between vascular dementia and OSA, as well as in other dementias including frontal temporal dementia, and Lewy Body Dementia.

Obstructive sleep apnea affects at least two to four percent of the adult population in the United States (Eckert et al., 2007). Specifically, two to three times greater in men than in women and in older adults ages 65 and older compared to middle-aged individuals (Eckert et al., 2007). On the other hand, central sleep apnea is seen in less than ten percent of patients presenting at sleep studies and in less than one percent in the general population (Becker & Wallace, 2015). It affects males predominantly and mostly affects middle-aged or elderly individuals with the prevalence increasing among older individuals greater than 60 years (Becker & Wallace, 2015). Therefore, the prevalence in patients with dementia is significantly high with 70-80% having five or more apneas-hypopneas per hour of sleep and about 38-48% having 20 or more (Ancoli-Israel et al., 2008). The greater prevalence in males is likely attributed to the presence of a lower apneic threshold of arterial oxygen and carbon dioxide ($PaCO_2$) in women compared to men (Becker & Wallace, 2015). Therefore, a greater reduction in $PaCO_2$ to initiate apnea is needed (Becker & Wallace, 2015). Moreover, different studies report the prevalence of complex sleep apnea syndrome to be between 0.56 and 18% (Verbraecken, 2013). Differences in prevalence data are due to CPAP titration, a supine sleep position, sleep duration, opioid medication, ethnicity, and health conditions such as chronic health failure and atrial fibrillation (Verbraecken, 2013).

The most common type of sleep apnea, obstructive sleep apnea, is caused by the relaxation of soft tissue in the back of the throat that blocks or narrows the passage of air (NINDS, 2015). This soft tissue is made of muscles that support the soft palate, uvula, tonsils, and the side walls of the throat and tongue (Mayo Foundation for Medical Education and Research, 2015). Their collapse narrows or closes the airway, limiting the level of oxygen breathed in and in turn lowering the level of oxygen in your blood (Mayo Foundation for Medical Education and Research, 2015). Consequently, the brain briefly awakens the person five to 30 times or more each hour throughout the night to reopen the airway (Mayo Foundation for Medical Education and Research, 2015). This brief awakening is snorting, choking, or a gasping sound and disrupts the ability to reach a restful sleep (Mayo Foundation for Medical Education and Research, 2015). In fact, many individuals with obstructive sleep apnea are unaware of these interruptions and believe they received adequate sleep, while experiencing fatigue and sleepiness during waking hours, especially when performing tasks that require less attention (Mayo Foundation for Medical Education and Research, 2015; Gagnon, et al., 2014). When waking up in the morning, individuals also report headaches and dry throat (Gagnon, et al., 2014).

In comparison, central sleep apnea is a least common form and is caused by irregular brain signals influencing breathing control and rhythm (Strohl, 2016). It is defined by the lack of respiratory effort during cessations of airflow (Eckert, Jordan, Merchia, & Malhotra, 2007). This contrasts with obstructive sleep apnea where ongoing attempts of respiratory efforts are detected. Several manifestations of central

sleep apnea include obesity hypoventilation syndrome, high altitude-induced periodic breathing, idiopathic central sleep apnea, narcotic-induced central apnea, and Cheyne-Stokes breathing (Eckert et al., 2007). Due to the increase of obesity over the years, the prevalence of obesity hypoventilation syndrome is on the rise (Eckert et al., 2007). However, idiopathic central sleep apnea is less common and may constitute less than five percent of the population referred to a sleep clinic (Eckert et al., 2007). These manifestations are classified into hypercapnic and nonhypercapnic groups based on the wakefulness CO_2 levels (Eckert et al., 2007). Overall, there is an overlap between central sleep apnea and obstructive sleep apnea that suggest similar mechanisms. For example, central respiratory events may lead to obstructive respiratory events in patients with a particular pharyngeal anatomy (Eckert et al., 2007). Furthermore, complex sleep apnea syndrome is initially diagnosed as an obstructive sleep apnea, yet once treatment is initiated, there are frequent occurrences of central sleep apnea after the elimination of obstructive events (Verbraecken, 2013). Therefore, although the mechanism is not well known, complex sleep apnea is believed to be a combination of an upper airway collapse and interrupted ventilator control (Verbraecken, 2013). A hypothesis proposes an altered carbon dioxide excretion occurring when the upper airway obstruction is opened through continuous positive airway pressure treatment (CPAP; Verbraecken, 2013). This leads to a decrease in “carbon dioxide partial pressure” and when this value falls below the “apneic threshold,” a central apnea will develop (Verbraecken, 2013).

Diagnosis

The most accurate way to diagnose sleep apnea is through a sleep study. The most common sleep studies used are a nocturnal polysomnography (PSG) or a home-based portable monitor (NHLBI, NIH., 2012). In a nocturnal polysomnography, the study records lung and brain activity, breathing patterns including movements through the nose while you breathe, snoring, and chest movements, eye movements, arm and leg movements, heart rate, and blood pressure while you sleep (NHLBI, NIH., 2012). The test is performed at sleep centers or laboratories using sensors attached to the scalp, face, chest, limbs, and a finger (NHLBI, NIH., 2012). Sleep stages are monitored using 3 studies: electroencephalography (EEG), electrooculography (EOG), and surface electromyography (EMG). Test results will confirm a diagnosis of sleep apnea and will indicate the severity to determine the appropriate treatment. Additionally, a PSG quantifies the number of respiratory events such as obstructive, central, or complex, as well as the hypoxemia, or an abnormally low concentration of oxygen in the blood, and arousals that result or occur independently from the respiratory events (Armon, Nowack, & Johnson, 2016). In other cases, a home-based sleep test using a portable monitor could also be recommended. This monitor records the amount of oxygen in your blood, air movement through your nose while you breathe, heart rate, and chest movements indicating your effort in breathing (NHLBI, NIH., 2012). Test results would indicate a decrease in oxygen level during apneas and subsequent awakenings (Mayo Foundation for Medical Education and Research, 2015). However, since these monitors do not detect all types of sleep apnea, a

polysomnography could still be recommended (Mayo Foundation for Medical Education and Research, 2015).

Impact on Cognition

Recent reviews of the neurocognitive effects of OSA have indicated deficits in the cognitive domains of attention, episodic and verbal memory, and executive functions (Stranks & Crowe, 2016). More specifically, there are reported deficits in attention/vigilance, delayed long-term visual and verbal memory, and constructional abilities (Stranks & Crowe, 2016). Reported cognitive complaints from patients with untreated OSA in sleep centers are similar to these deficits, such as difficulties concentrating on new tasks, attention, vigilance, performing monotonous tasks, and difficulties with memory and learning new tasks (Vaessen, Overeem, & Sitskoorn, 2015). For example, frequent cognitive complaints include a decrease in alertness, short-term memory problems, and a lack of concentration (Gagnon, et al., 2014). However, findings on more specific memory complaints were inconsistent (Vaessen, Overeem, & Sitskoorn, 2015). Regarding executive functioning, a study by Chen et al. stated OSA patients reported complaints of emotional control and motivation rather than abstract thinking and problem solving (Vaessen, Overeem, & Sitskoorn, 2015). Despite these similarities, subjective cognitive complaints from OSA patients are not necessarily related to objective cognitive functioning and many of these subjective complaints are reported in the absence of objective cognitive impairments (Vaessen, Overeem, & Sitskoorn, 2015). This is likely due to several reasons. First, cognitive complaints could be secondary to other daytime OSA symptoms and are possibly

unrelated to objective impairments in cognitive performance. Another reason may be that subjective cognitive complaints are determined over a longer period, while objective cognitive measures assess cognition at one point in time and under controlled conditions (Vaessen, Overeem, & Sitskoorn, 2015). However, the relationship between cognitive complaints and objective impairments warrant further investigation since current studies primarily concentrate on the relation between objective sleepiness and cognitive complaints (Vaessen, Overeem, & Sitskoorn, 2015). In neuropsychological testing, the greatest deficits were found in psychomotor speed and executive function, while tests measuring motor control, construction, attention, and speed of processing abilities were less affected in patients with OSA (Stranks & Crowe, 2016). However, more recent studies now support deficits in memory in OSA patients (Stranks & Crowe, 2016).

The causal mechanism between cognitive impairment and OSA is unknown and research continues to be in its infancy (Stranks & Crowe, 2016). A possible explanation includes cognitive impairment resulting from long-term consequences of regular intermittent hypoxia disrupting the blood-brain barrier and affecting the brain's microenvironment, as well as altering synaptic plasticity despite the blood-brain barrier's initial adaptivity (Stranks & Crowe, 2016). However, although sleepiness and hypoxemia might cause the neuropsychological deficits seen in these patients, many co-morbidities observed in these patients, such as obesity and cardiovascular diseases, could also affect their cognitive functioning (Sforza & Roche, 2012). Moreover, a relationship between cognitive impairment and symptoms of OSA

has been identified in patients with dementia (Ancoli-Israel et al., 2008). For example, a large study of patients in nursing homes demonstrated those with severe dementia had significantly more severe OSA symptoms and those with severe OSA had significantly more severe dementia (Ancoli-Israel et al., 2008). Although it is unlikely OSA causes dementia, the hypoxia and sleep disruption from OSA might worsen cognitive functioning (Ancoli-Israel et al., 2008).

Impact on Brain Structure and Function

Findings in a meta-analysis of fifteen studies identified consistent patterns of structural atrophy and functional disturbances that occur due to OSA. These studies demonstrated the involvement of the right basolateral amygdala/hippocampus complex and the right central insular cortex that play an important role in the subjective and objective cognitive and emotional complaints of OSA patients, specifically affect, attention, and memory-related functions, and somatosensory processing (Tahmasian et al., 2016). This area is part of a joint network that also incorporates the anterior insular, posterior-medial frontal cortex, and thalamus (Tahmasian et al., 2016). The hippocampus is known to be greatly affected by hypoxic and hypercapnic episodes (Kloepfer et al., 2009). Structural damage to this area results in cognitive deficits in memory, as well as attention and executive functioning due to the role of the hippocampus in these functions, as well as its indirect functional connections with the parietal and prefrontal cortex, which are also affected in OSA (Ferini-Strambi et al., 2013).

Impact on Mood

Affective disorders in patients with OSA occur frequently, yet vary widely (El-Ad & Lavie, 2005). For example, depression is frequent in OSA patients, yet it does not seem to be a universal finding (El-Ad & Lavie, 2005). This is likely due to many other contributing factors influencing affective disorders, such as age, body mass, and hypertension (El-Ad & Lavie, 2005). Other psychiatric disorders have been reported in OSA patients such as anxiety, somatization, obsession-compulsion, and hostility (El-Ad & Lavie, 2005). It appears that these affective disorders reported in OSA patients may be influenced by the sleep disruption and intermittent hypoxemia caused by sleep apnea (El-Ad & Lavie, 2005). Some models propose the involvement of the prefrontal cortex due to the common impairment of executive functions in patients with sleep apnea and state that it is particularly vulnerable to sleep disruption (El-Ad & Lavie, 2005). Specifically, sleep disruption and intermittent hypoxemia reduce the effectiveness of sleep-related restorative processes and leads to the disruption of homeostasis in certain regions of the brain (El-Ad & Lavie, 2005).

Treatment

Treatment for sleep apnea includes weight loss, positional therapy, treatment of associated medical problems (i.e. improving therapy for heart failure may eliminate central sleep apnea), oral appliance therapy, supplemental oxygen, continuous positive airway pressure (CPAP), and surgical methods such as uvulopalatopharyngoplasty, maxillomandibular advancement surgery, and tracheostomy (Yoshida, 2010). A 10% reduction in weight leads to a 26% reduction in the respiratory disturbance index

(RDI) and include numerous benefits such as improved pulmonary function and arterial blood gas values, possible reduction of CPAP pressure required, and improved sleep structure and snoring (Downey III, 2017). The purpose of oral appliance and airway pressure devices is to adjust the position of the mandible or lower jaw and tongue to enlarge the airway or reduce its collapsibility (Yoshida, 2010). Treatment success is determined by measuring the apnea-hypopnea index (AHI) being less than 10 (Yoshida, 2010). An AHI more than 30 demonstrates significant neuropsychological morbidity (Yoshida, 2010). Treatments are chosen from least invasive and effective to most invasive and effective (Downey III, 2017). Nasal CPAP therapy is offered first for patients suffering from mild to severe obstructive sleep apnea (Downey III, 2017). For those who do not tolerate or refuse nasal CPAP therapy, BiPAP therapy is the next recommendation followed by oral appliances (Downey III, 2017). When noninvasive medical therapy fail, surgical procedures are recommended. Moreover, pharmacological treatment is generally not recommended. However, central nervous system stimulants such as modafinil and armodafinil are used to treat fatigue and increase daytime wakefulness for patients who continue to suffer from this symptom despite CPAP treatment (Downey III, 2017).

The most common and reliable therapy for sleep apnea is an airway pressure device. CPAP is known as the most common and efficacious therapy for OSA (Mayo Clinic, 2015). Based on Medicare guidelines, CPAP is recommended for all patients with an AHI greater than 15 (Downey III, 2017). However, for patients with an AHI of 5-14.9, CPAP is recommended only if they have one of the following symptoms:

excessive daytime sleepiness, hypertension, and/or cardiovascular disease (Downey III, 2017). CPAP contains an airflow generator that provides constant pressurized air to prevent soft tissues in the airways from collapsing and becoming blocked (Wozniak et al., 2014). This airflow is applied to the nose and directed through the upper airway (Downey III, 2017). Physiological changes include an increase in lateral areas of the upper airway and thinning of lateral pharyngeal walls that are thicker in patients with OSA (Downey III, 2017). The CPAP machine consists of three main parts: a mask that covers the nose or the nose and mouth, a tube that connects the mask to the motor, and a motor that blows air into a tube (Wozniak et al., 2014). Current models are lightweight, small, quiet, and are designed for daily use (Wozniak et al., 2014). During or after a sleep study is conducted, proper titration is needed for CPAP machines depending on the patient's needs. Proper titration includes finding the minimum CPAP level that eliminates obstructive apneas and/or hypopneas, oxyhemoglobin desaturation, respiratory effort-related arousals, and snoring in all sleep stages and positions (Downey III, 2017). However, current CPAP devices automatically change pressures based on the presence and/or absence of OSA since it may vary over the course of the night, sleep stages, and body positions not captured in the one-night titration study (auto-positive airway pressure or auto-PAP; Downey III, 2017). CPAP effectively resolves apneas and hypopneas, decreases arousals, and normalizes oxygen intake (Downey III, 2017). Additionally, it has been shown to improve daytime sleepiness, mood, quality of life, cognitive function, decrease health care costs, and blood pressure in patients with mild to moderate sleep apnea (Downey III, 2017). Most importantly, patients who use CPAP report an immediate improvement in

alertness, concentration, and memory; however, maximum improvement in neurocognitive symptoms is generally seen within 2 months of consistent CPAP use (Downey III, 2017). Although CPAP has a better therapeutic effect than other treatments, there are many problems that lead to noncompliant usage such as nasal congestion, discomfort due to air-leak and pressure sensation, and mask intolerance (Yoshida, 2010). Thus, patients with mild symptoms are more likely to discontinue treatment.

Another similar airway pressure device is Bilevel Positive Airway Pressure (BiPAP). In comparison to CPAP, instead of delivering a constant pressure during both inspiration and expiration, BiPAP allows for an independent adjustment of pressure during both events (Downey III, 2017). BiPAP is generally used in patients who cannot tolerate high CPAP pressures, such as patients who suffer from difficult exhalations or who have injuries caused by increased air or water pressure (barotrauma; Downey III, 2017). However, generally this treatment is more expensive, has no known advantages over CPAP therapy, and does not have better compliance rates than CPAP (Downey III, 2017).

Since weight loss and positional therapies have not been effective in completely resolving the issue, a variety of oral appliances have been used when CPAP is not tolerated, or surgery is not recommended (Yoshida, 2010). Crossover studies examining the efficacy of CPAP and oral appliances reported the effectiveness of oral appliances in OSA patients, especially in mild to moderate cases due to fewer side effects (Yoshida, 2010). In fact, the American Academy of Sleep Medicine has

issued recommendations for the use of oral appliance therapy for simple snoring and mild sleep apnea and for moderate to severe sleep apnea, if CPAP or BiPAP therapy is not tolerated, and if patients do not respond to CPAP or BiPAP (Yoshida, 2010; Downey III, 2017). Oral appliance therapy includes mandibular advancement appliances and tongue retaining devices (Yoshida, 2010). Thus, a close collaboration with a dental professional experienced in oral appliance therapy is necessary. Mandibular advancement appliances are the most common and usually advance the posture of the mandible at an elevated vertical and protrusive position (Yoshida, 2010). However, the protrusion distance of these devices can be adjusted after the initial construction (Yoshida, 2010). Some appliances allow for flexible jaw movements and are commonly used in orthodontics and to treat sleep apnea in mentally impaired patients and patients with neuromuscular disabilities (Yoshida, 2010). In comparison, tongue retaining devices are used seldomly and usually when there are dental complications (Yoshida, 2010). These devices work by holding the tongue forward during sleep (Yoshida, 2010). The ideal treatment goal for oral appliance therapy is an AHI of less than 5 without snoring (Downey III, 2017). Adherence rates are not well defined and recorded due to a lack of objective measures and a reliance on self-report. The main reasons for nonadherence with oral appliances are temporomandibular joint problems, occlusal changes, excessive salivation, discomfort, and ineffectiveness (Downey III, 2017).

Patients with severe sleep apnea usually require surgical methods to relieve their obstruction. It is also indicated when conservative therapies are unsuccessful or

not tolerated, as well as for patients who have a dental or jaw abnormality that could be corrected through surgery (Yoshida, 2010). Additionally, a three-month trial of other treatment options is suggested before considering surgery (Mayo Clinic, 2015). The goal of surgery would be to enlarge the airway through the nose or throat; this narrow airway may be causing the individual to snore or block the upper airway passages causing sleep apnea (Mayo Clinic, 2015). For example, the most common surgical procedure performed for patients with OSA is uvulopalatopharyngoplasty, which removes tissue from the rear of the mouth and top of the throat that may be contributing to the vibrating of structures leading to snoring, as well as reshaping the soft tissues in the lateral pharyngeal walls (Mayo Clinic, 2015; Downey III, 2017). Another procedure known as maxillomandibular advancement involves moving the jaw forward to enlarge the space behind the tongue and soft palate; this procedure eliminates the possibility of obstruction (Mayo Clinic, 2015). In more severe, life-threatening sleep apnea cases, a procedure known as tracheostomy involves creating an opening in the neck and inserting a metal or plastic tube to facilitate breathing (Mayo Clinic, 2015). Although this is a nearly 100% effective surgery for OSA, it is a disfiguring procedure and decreases the patient's quality of life (Downey III, 2017). Overall, the efficacy of these surgeries ranges from 30 to 50 percent and usually involve possible complications such as pain and infection (Yoshida, 2010). Several factors that increase the success of these surgical procedures are a lower AHI, lower body mass index (BMI), the location of the collapse, the degree of mandibular protrusion, and fewer comorbidities (Downey III, 2017). For example, surgeries targeted to the collapse of the nasopharynx or oropharynx, as well as those addressing

clear deficiencies in mandibular protrusion have a better outcome (Downey III, 2017). Lastly, standard protocol for all patients undergoing surgery for treatment of OSA involves a follow-up PSG (Downey III, 2017).

Furthermore, bariatric surgery has also been considered a therapy for OSA with some nonrandomized, uncontrolled studies showing a decrease in AHI with weight loss (Downey III, 2017). However, since studies have not examined pre- and post-surgery AHI, included randomization of participants, and followed patients over time, it is difficult to determine if a reduction of OSA symptoms is due to a placebo effect (Downey III, 2017). Further research and ongoing clinical follow-ups are needed to examine these effects.

CPAP Compliance

Consistent CPAP application has been shown to improve quality of sleep, sleep architecture, neurobehavioral performance, reduces daytime sleepiness, lowers blood pressure, reduces the risk for cardiovascular events, and even prevents automobile accidents (Wozniak et al., 2014). CPAP has also been found to improve overall quality of life and to some extent, cognitive dysfunction. A consensus among the literature is the improvement of neuropsychological deficits such as attention, executive functioning, and memory with CPAP usage (Aloia, Arnedt, Davis, Riggs, Bryd, 2004). Crawford-Archour and colleagues revealed that CPAP treatment of at least 6 hours per night allowed maintenance of memory, attention, and executive functioning in the elderly population (Crawford-Archour et al., 2015). However, its effectiveness is limited by poor compliance. Although evidence suggests about 68.5%

of patients prescribed CPAP will accept their treatment, it is uncertain whether they will remain compliant (Pertelle & Fary, 2007). Compliance refers to the length of time a patient uses a CPAP machine on a nightly basis (Pertelle & Fary, 2007). It is measured through subjective patient reports, an hour usage meter that records the average number of hours used nightly, or a modem that reports overall CPAP usage and pressure settings (Pertelle & Fary, 2007). Although there is no universal definition of compliance for CPAP usage, a general clinical and empirical guideline for optimal adherence across several studies is at least 4 hours (Pertelle & Fary, 2007; Wohlgemuth, Chirinos, Domingo, & Wallace, 2015; Sawyer et al., 2011). These studies also suggest a linear relationship between hours of CPAP usage and improvements in functional abilities (Wohlgemuth et al., 2015).

Poor adherence is mainly caused by side effects involving discomfort with CPAP usage, such as pressure sores from the nasal mask, dry, congested, and sore noses and throats, silicon allergies, abrasion to the bridge of the nose, persistent air leakage, chest discomfort, claustrophobia, and aerophagia or air swallowing (Sin, Mayers, Man, & Pawluk, 2002; Pertelle & Fary, 2007). A review of CPAP adherence reported that nasal anatomy such as smaller nasal cavities may impact CPAP adherence by increasing nasal resistance (Sawyer et al., 2011).

There have been other covariates studied to understand difficulties with CPAP adherence, such as age, gender, body mass index (BMI), residual AHI, daytime sleepiness, OSA risk perception, and CPAP outcome expectation (Sin et al., 2002; Wohlgemuth et al., 2015). In a study observing long-term compliance rates, they

discovered several variables that were significantly correlated with increased CPAP use. Among these were the female gender and increasing age (Sin et al., 2002). In another study, residual AHI, CPAP pressure, length of time with CPAP, self-efficacy for using CPAP, and insomnia severity distinguished clusters of patients who were classified as adherers, non-adherers, and attempters (Wohlgemuth et al., 2015). Findings from this study demonstrated that patients who attempted CPAP treatment and had a lower AHI and lower CPAP pressure would likely not appreciate the daily benefits from daily CPAP use and thus would not use the treatment for longer periods of time (Wohlgemuth et al., 2015). Other covariates reported in the literature as an important influence in CPAP adherence are self-efficacy and insomnia. Self-efficacy or the confidence in their ability to use CPAP when faced with difficulties may be more strongly related to frequency of CPAP use rather than duration of use (Lewis et al., 2004; Wohlgemuth et al., 2015). However, insomnia appears to be a more common barrier to adequate CPAP use than level of self-efficacy and is also a common comorbidity with untreated OSA (Wohlgemuth et al., 2015). Patients with severe insomnia either do not try CPAP due to the expected sleep difficulty with treatment or may begin sleeping with CPAP yet remove it later in the night due to difficulty staying or falling asleep (Wohlgemuth et al., 2015). Overall, the group of non-adherers had lower levels of self-efficacy for CPAP use and more severe insomnia (Wohlgemuth et al., 2015). Another study identified outcome expectancies or the patient's expectations for specific responses to CPAP treatment, as well as AHI and self-efficacy are significant contributors to CPAP adherence (Baron et al., 2010). Additionally, they reported active coping styles with challenging situations, including

aggressive efforts to alter situations and planned problem solving were associated with higher rates of CPAP use (Baron et al., 2010).

Another influence on CPAP adherence is a patient's race. Although research on different race and ethnic groups continues to be in its infancy, most studies have reported lower CPAP adherence in African Americans versus Caucasian patients (Platt et al., 2009). This may be due to socioeconomic status (Platt et al., 2009). Therefore, the need for individualized considerations with culturally diverse patients are needed when examining adherence outcomes in CPAP treatment (Platt et al., 2009). Additionally, a study found that patients who experienced some significant life event 6 months prior to CPAP treatment had significantly lower CPAP use than those who did not suffer from a recent life event (Lewis et al., 2004). This study and others also reported findings that patients who lived alone used CPAP significantly less than those who had a bed partner and had spousal involvement with CPAP experience and use (Lewis et al., 2004; Baron et al., 2010).

The health and functional importance of CPAP adherence has led to an extensive amount of research on interventions that would effectively improve CPAP use. In a meta-analysis study that examined three groups of interventions including educational, supportive, and behavioral, they found that all types of interventions had a positive impact on increasing average CPAP machine usage and number of participants compliant with treatment over a short amount of time (Wozniak et al., 2014). However, behavioral interventions resulted in the largest improvement in average hours of CPAP use (Wozniak et al., 2014). The educational interventions used

included written materials, verbal sessions, and/or audio-visually delivered information about OSA and CPAP treatment (Wozniak et al., 2014). Supportive interventions included regular meetings, telephone follow-ups, and/or interactive applications to encourage continued use of CPAP and motivate participants to report problems associated with its usage (Wozniak et al., 2014). The key feature in this type of intervention was the frequent encouragement of feedback on their experience of CPAP treatment (Wozniak et al., 2014). Behavioral interventions involved methods to modify and promote adherence behaviors, such as motivational interviewing techniques and cognitive behavioral therapy (Wozniak et al., 2014; Aloia et al., 2001).

CPAP Compliance and Mood

Although a greater percentage of patients achieve better functioning with longer CPAP use, studies have shown a significant number of patients will not return to normal functioning or experience daytime symptom improvement despite adequate use of CPAP (Antic et al., 2011). Recent studies have examined depression and other mood disturbances and their relationship to CPAP adherence as an explanation for these cases. In one study, a patient's perceptions of sleep apnea symptoms, improvement of symptoms after CPAP treatment, and a patient's perception of their experience with side effects from CPAP usage were different between patients who were diagnosed with and without depression prior to initiating CPAP treatment (Wells, Freedland, Carney, Duntley, Stepanski, 2007). In this study, there was a strong association between self-reports of depressive symptoms and OSA symptoms, which likely reflects the oversensitivity to symptoms and/or over-reporting of

symptoms in self-report measures with depressed patients (Wells et al., 2007). Symptoms of fatigue, low energy, insomnia, and altered sleep patterns are common symptoms in both depression and OSA (Wells et al., 2007). Thus, patients with depressive symptoms who are complaint with CPAP treatment are more likely to report continued fatigue and/or sleepiness (Wells et al., 2007). Similarly, individuals who experienced an improvement with depressive symptoms also reported an improvement in OSA symptoms (Wells et al., 2007). It was also suggested in this study that depressive symptoms may respond differently during CPAP treatment, depending on whether they developed prior to OSA or were secondary to OSA (Wells et al., 2007). Overall, this study emphasized the importance of inquiring about depressive symptoms if an individual does not report an improvement with fatigue or sleepiness after using CPAP appropriately (Wells et al., 2007). Additionally, another study examined patients with personality traits of negative affectivity and social inhibition that perceived a higher severity and frequency of side effects associated with CPAP usage (Brostom et al., 2007). However, there are also studies that have shown a depression diagnosis at the initiation of CPAP treatment has no influence on CPAP usage (Lewis, Seale, Bartle, Watkins, & Ebden, 2004; Stepnowsky, Bardwell, Moore, Ancoli-Israel, Dimsdale, 2002). Nonetheless, it is important to consider other mood disturbances or other medical comorbidities contributing to any neurobehavioral disturbance experienced after CPAP treatment (Antic et al., 2011).

CPAP's Impact on Cognition, Brain Structure and Function

One of the most concerning adverse consequences of OSA is impairment in cognitive functioning. This impairment has implications for social functioning, everyday activity, and occupational performance (Kielb et al., 2012). In their review of the cognitive effects of CPAP compliance, Aloia et al. (2004) described improvements in attention and vigilance in most of the studies reviewed, while global functioning, executive functioning, and memory improved in only some studies. This variability may likely be due to many reasons, such as study design (within-subject and between-subject designs), neuropsychological tests selected that may vary in sensitivity to the effects of treatment, and even practice effects in neuropsychological testing (Ferini-Strambi, Mareli, Galbiati, & Castronovo, 2013). A within-subjects design study reported an improvement in verbal memory in patients using CPAP for an average of six hours a night (Zimmerman, Arnedt, Stanchina, Millman, & Aloia, 2006). Similarly, Aloia and colleagues reported improvements in attention and executive function after 3 months and 6 months of follow-up (Aloia et al., 2003). In comparison, a between-subjects design study reported improvements in attention, spatial ability, and motor speed in patients compliant with CPAP treatment after 15 days of follow-up and after four months (Ferini-Strambi et al., 2003). Other studies considered adherence to CPAP a significant factor when evaluating cognitive effects of CPAP treatment. Zimmerman and colleagues observed that memory performance may be reversible with optimal levels of CPAP treatment and OSA patients with memory deficits initially may need at least six hours of CPAP use per night to experience benefits in memory functions (Zimmerman et al., 2006).

In elderly patients 65 years and older with OSA, long-term CPAP treatment was observed to have a protective effect on cognitive performance (Crawford-Archour et al., 2015). This study allowed the maintenance of several cognitive functions including memory (delayed free recall), attention, and executive functioning (WAIS III Similarities test) and reported adequate self-reported CPAP compliance of at least 6 hours per night (Crawford-Archour et al., 2015). In a randomized, multicenter clinical study of 224 elderly patients 70 years and older with severe sleep apnea, one of the main findings included an overall improvement in all neurocognitive tests in the treatment group, yet more significant changes were observed in tests related to working memory and executive functions (Martinez-Garcia et al., 2015). The extensive neuropsychological battery included executive functioning, visual attention, speed of processing and mental flexibility (Trails Making Test A and B) and working memory (digit symbol and digit span tests; Martinez-Garcia et al., 2015). Furthermore, due to the high prevalence of OSA in patients with dementia, studies have also investigated cognitive effects of CPAP treatment in this population. In a randomized placebo-controlled CPAP trail in mild-moderate AD patients with OSA, composite neuropsychological scores from treatment groups suggested modest statistically significant improvements in cognitive functioning with three weeks of CPAP treatment (Ancoli-Israel et al., 2008). Their neuropsychological battery measured cognitive abilities of learning and memory, frontal/executive skills, attention and vigilance, and mental processing speed (Ancoli-Israel et al., 2008). Exploratory post-hoc examination of change scores for individual neuropsychological tests demonstrated improvements in episodic verbal learning and memory, as well as

improvements in executive functioning tasks such as cognitive flexibility and mental processing speed (Ancoli-Israel et al., 2008). The results of this study support the implication that OSA might be a reversible cause of cognitive impairment in patients with dementia and CPAP treatment when used in the early stages of the dementia may even slow the progression of the disease (Bliwise, 1996).

Canessa and colleagues reported cognitive and structural improvements after 3 months of CPAP treatment (Canessa et al., 2011). Since memory impairments have been observed in patients with OSA, Canessa and colleagues observed hippocampal structures, which are sensitive to hypoxic damage associated with OSA (Gozal, Row, Schurr, 2001). Hippocampal damage may also be associated with the attentional and executive impairment seen in patients with OSA due to the extensive connections between the prefrontal cortex and thalamus (Newbery & Iversen, 2003). Canessa and colleagues observed an increase in volume in the hippocampus (left subiculum and bilateral entorhinal cortex), the medial orbitofrontal cortex, and the rostral portion of the right superior frontal gyrus (Canessa et al., 2011). The increase in volume of the entorhinal cortex was correlated with improvements in verbal and visuospatial short-term memory, attention, and executive functioning (Canessa et al., 2011). This study reported the mechanism of brain change after CPAP treatment is likely vasogenic, which is similar to neuropsychological changes seen with mild cerebrovascular disease or small vessel disease (Canessa et al., 2011).

During the initial diagnostic phase of OSA, it is likely that an individual first visits their primary care physician. If the individual is prescribed a sleep study and is

recommended for CPAP treatment, it is possible they would be apprehensive to adhere to daily CPAP treatment due to reported side effects, such as discomfort with CPAP usage, pressure sores from the nasal mask, dry, congested, and sore noses and throats, silicon allergies, abrasion to the bridge of the nose, persistent air leakage, chest discomfort, claustrophobia, aerophagia or air swallowing, and nasal resistance (Sin et al., 2002; Pertelle & Fary, 2007, Sawyer et al, 2011). Potential cognitive improvements from CPAP treatment are evident in extensive neuropsychological testing. However, this testing is primarily used in research settings and is difficult to perform in the elderly and dementia populations who have a high prevalence of OSA. Therefore, it would benefit physicians to be able to measure this cognitive change in an efficient, yet feasible manner. This evidence of cognitive improvement would be provided to patients and may likely improve compliance. In this present study, the objective was to measure this cognitive change through a time sensitive screener, the MoCA, in an elderly dementia population with OSA and assess its sensitivity in detecting cognitive change following CPAP treatment.

Purpose and Hypotheses

The purpose of this study was to investigate whether the MoCA test is sensitive to the level of cognitive change that occurs in patients who suffer from sleep apnea and undergo CPAP treatment. Being a quick cognitive screener, the MoCA test would be a time sensitive and efficient tool in medical health care settings, such as in memory disorder clinics, when determining the effect of CPAP treatment. Improved cognition in dementia patients could increase independence, thus relieving caregiver burden, and disease-related costs and resources (Ancoli-Israel, 2008). The following was proposed in this study: 1) The MoCA test will be a sensitive indicator of cognitive change following introduction of CPAP in patients with sleep apnea, and 2) Patients who used CPAP will demonstrate significant improvement in MoCA performance compared to non-compliant patients.

Method

Participants

Archival participant data from the Health First Aging Institute and the East Central Florida Memory Disorder Clinic (ECFMDC) was utilized for this study. The participants were patients from ECFMDC with a wide variety of dementia diagnoses including: no cognitive impairment, Alzheimer's disease, mild cognitive impairment, cognitive disorder NOS, and other dementia, who were also diagnosed with sleep apnea and recommended for CPAP treatment. Twenty-six CPAP compliant (61.5% male; 96.2% Caucasian/Non-Hispanic), ages 66-87 years (*M*=76.27(4.90)) and Twenty CPAP non-compliant patients (85% male, 100% Caucasian/Non-Hispanic) ages 66-90 (*M*=77.45 (6.88)) were chosen from a research database. Inclusion criteria involved memory disorder clinic patients who completed a sleep study, were diagnosed with sleep apnea, and were recommended for CPAP treatment. Additionally, pre- and post-CPAP treatment MoCA administrations of no more than 9 months apart were also required for inclusion in the study. All Health First Aging Institute patients consent to the use of their test data and relevant medical records for the purposes of research during their initial appointment. Informed consent is also obtained prior to each patient's neuropsychological testing. Patients are presented with a form explaining the use of de-identified results for research purposes. Lastly, the research has been approved by the Florida Institute of Technology's Institutional Review Board.

Measures and Materials

The MoCA test was used as a pre- and post-treatment measure of cognitive change for CPAP compliant and non-compliant groups. The MoCA is a brief, 10-minute, pen-and-paper screening instrument that is useful in detecting mild cognitive impairment and dementia. Scores may range form 0 – 30 and are equal to or greater than 26 when considered to be within the normal range of functioning. The MoCA test assesses several cognitive domains including attention, concentration, executive functions, memory, language, visuospatial skills, abstraction, calculation and orientation (Julayanont et al., 2012).

Patients suspected of having sleep apnea were referred to sleep clinics to obtain a sleep study and were then prescribed CPAP treatment, if diagnosed with sleep apnea. CPAP contains an airflow generator that provides constant pressurized air to prevent airways from collapsing and becoming blocked. It consists of three main parts: a mask that covers the nose or the nose and mouth; a tube that connects the mask to the motor; and a motor that blows air into a tube. Current models are lightweight, small, quiet, and are designed for daily use (Wozniak et al., 2014).

Procedure

The MoCA test was given prior to CPAP treatment recommendation and at follow-up 4-9 months later for both compliant and non-compliant groups. CPAP compliance was determined through monthly compliance reports sent directly from the CPAP machine smart card to the pulmonologist and/or clinical interview with patient and family members during subsequent medical visits at the East Central

Florida Memory Disorder Clinic. Pre-and post-CPAP treatment MoCA test scores were compared and assessed for change.

The study consisted of an archival investigation. It consisted of patients from the East Central Florida Memory Disorder Clinic who completed a sleep study, were diagnosed with sleep apnea, and received a recommendation for CPAP treatment. Additional inclusion criteria included participants who received a MoCA test in a medical visit prior to CPAP initiation and after.

Statistical Methods

All data were analyzed using SPSS, versions 23 and 24. Pre- and post-treatment MoCA score change as a function of CPAP compliance was analyzed using a mixed model analysis of variance. Specifically, MoCA scores before and after CPAP treatment for CPAP compliant and noncompliant CPAP groups were observed. As such, a control group was not necessary as we were controlling variables by comparing them to themselves. CPAP compliance and non-compliance were the between-subject group, while the pre- and post-CPAP treatment scores were the within-subject groups. The goal was to determine if a statistically significant difference exists in MoCA scores for those patients selected for the pre-and post-treatments. Overall, these analyses provide an answer as to whether the use of MoCA is sensitive enough to detect change in cognitive functioning following CPAP treatment in sleep apnea patients. The interaction between diagnoses and compliance was also observed using a crosstabs analysis.

Results

Prior to tests of hypotheses, the equivalence of group make-up by sex and age was examined. A Mann-Whitney *U*-test indicated no significant difference between sex across compliance groups, $U = 199.00$, $p = .083$, $r = .26$. Groups also did not differ on age as determined with an independent samples *t*-test, $t\ (44) = -0.680$, $p = 0.500$. Figure 1 displays the frequency of patient diagnoses in both compliance groups. Most patients in the compliant group (pre- MoCA $M = 20.38$, post- MoCA $M = 22.27$) had an AD diagnosis, while most of the non-compliant group (MoCA pre- $M = 19.90$, MoCA post- $M = 20.50$) had a dementia or cognitive disorder NOS diagnosis. Cross tabulated frequencies demonstrated no significant relationship between compliance groups and diagnosis, $X^2\ (3, N = 46) = 2.68$, $p = 0.44$. The compliant group had 7 individuals within normal limits (WNL), 6 mild cognitive impairment (MCI), 9 Alzheimer's disease (AD), and 4 individuals with other dementia or cognitive disorder NOS. In comparison, the non-compliant group had 3 individuals WNL, 4 MCI, 6 AD, and 7 individuals with other dementia or cognitive disorder NOS diagnosis. Figure 2 displays the frequency of patient mood disorder diagnoses in both compliance groups. Although most patients in both compliance groups did not have a depression and/or anxiety disorder diagnosis, for those diagnosed with a mood disorder, most had both a depression and anxiety diagnosis. Cross tabulated frequencies demonstrated no significant relationship between compliance groups and mood disorder diagnosis, $X^2\ (3, N = 46) = 0.26$, $p = 0.97$. The compliant group had 3 individuals with a depression diagnosis, 1 with anxiety, 5 with depression and anxiety, and 17 with no mood

disorder diagnosis. Similarly, the non-compliant group had 3 individuals with a depression diagnosis, 1 with anxiety, 3 with depression and anxiety, and 13 with no mood disorder diagnosis.

Figure 1

Frequency of patient diagnosis in CPAP compliance groups

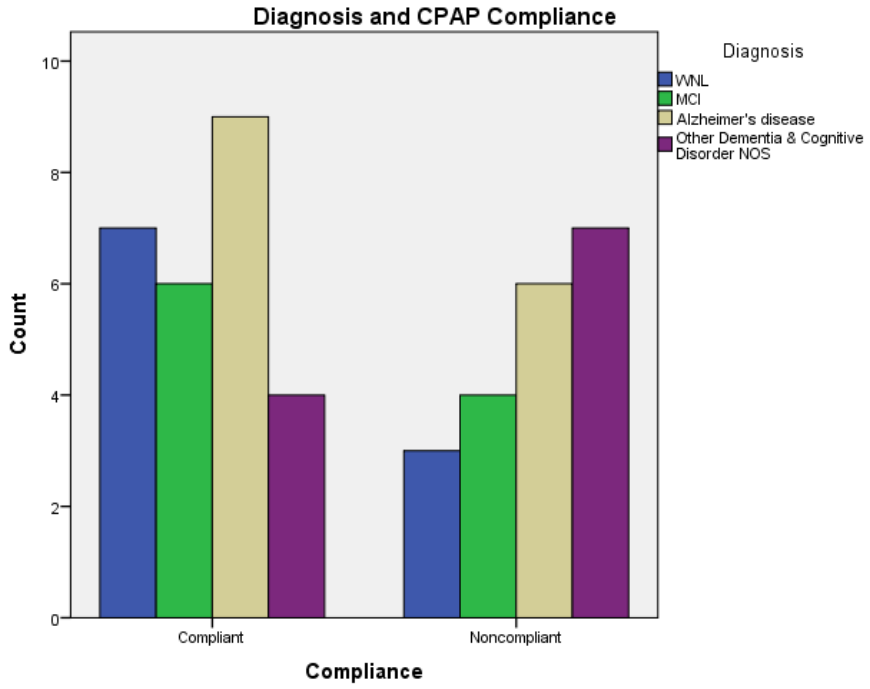
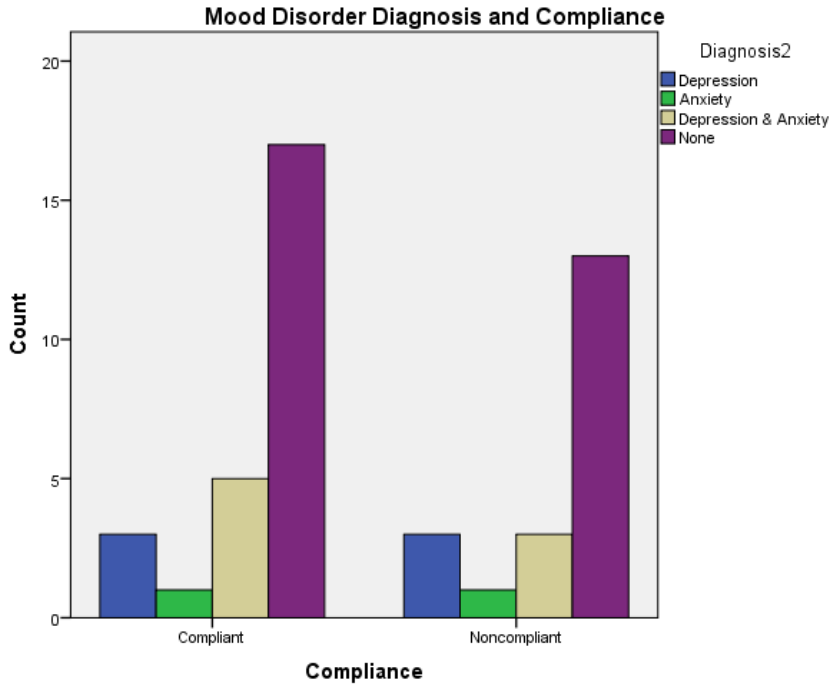


Figure 2

Frequency of patient mood disorder diagnosis in CPAP compliance groups



On another analysis, a Pearson product-moment correlation coefficient was computed to assess the relationship between the interval of time from pre- and post-treatment MoCA scores (days) and MoCA scores (change scores) across both CPAP compliant and non-compliant groups. Results demonstrated no association between the interval of time and MoCA scores in any of the CPAP compliance groups, p = 0.578 (CPAP compliant group), p = 0.681 (CPAP non-compliant group).

Table 1 depicts pre- and post-treatment MoCA score changes as a function of CPAP compliance. Post-treatment MoCA scores for the CPAP compliant group were significantly higher than pre-treatment. Nineteen of the 26 compliant patients evidenced increases in MoCA, three remained the same, and four declined. The non-

compliant group showed no change over time, with seven scores decreasing, 11 increasing, and two remaining the same. Most importantly, 19 of the 26 compliant patients demonstrated improvements in MoCA scores, while only 11 of the 20 non-compliant patients improved.

Table 1

Changes in MoCA scores as a function of CPAP compliance

	Pre-Treatment MoCA Scores		Post-Treatment MoCA Scores		T-test	P-value
	M	SD	M	SD		
Compliance	20.38	4.02	22.27	3.94	-4.992	0.00
Non-Compliance	19.90	4.13	20.50	4.15	-.798	0.44

Table 2

MoCA scores for CPAP compliance and non-compliance groups before and after CPAP treatment

	CPAP Compliance			CPAP Non-Compliance		
	n	M	SD	n	M	SD
Pre-treatment Score	26	20.38	4.02	20	19.90	4.13
Post-treatment Score	26	22.27	3.94	20	20.50	4.15

A mixed model analysis of variance was conducted to assess the interaction of CPAP compliance (CPAP compliant and non-compliant groups) on MoCA scores across the two-time periods, pre-CPAP treatment and post-CPAP treatment (MoCA

change scores). There was no significant interaction between CPAP compliant groups and MoCA change scores, *Wilks' Lambda*= .94, *F* (1, 44) = 2.67, *p*=.109, partial eta squared= .057. There was a substantial main effect for MoCA change scores, *Wilks' Lambda*= .82, *F* (1, 44) = 9.99, *p* = .003, *partial eta squared* = .185. Wilks' Lambda test was selected as the multivariate test due to its greater statistical power. The main effect comparing change in the compliance groups was not significant, *F* (1, 44) = .981, *p* = .327, *partial eta squared* = .022.

Discussion

CPAP treatment has been shown previously to improve performance in neuropsychological measures that might be impacted by sleep apnea (Shranks & Crowe, 2016). However, the extensive neuropsychological testing needed to examine this cognitive change is a difficult task with the elderly and patients with dementia. Since there is a high prevalence of sleep apnea in the elderly and dementia population (Ancoli-Israel et al., 2008), it would be advantageous for patients and physicians to utilize a quick and short screener to assess the usefulness of CPAP treatment. This evaluation would be a more time and cost-efficient procedure to evaluate the effectiveness of CPAP treatment in the elderly.

The results of the current study suggest the MoCA test is sensitive to the level of change that occurs in patients who differ considerably in cognitive ability. First, it is important to note that the estimation of cognitive ability based on the total score of the MoCA is not necessarily linear (Koski, Xie, & Finch, 2009). Thus, a decline is not equally significant at all levels of ability (Koski, Xie, & Finch, 2009). For example, a score of 20/30 does not signify an individual has twice as much cognitive ability as an individual with a score of 10/30 (Koski, Xie, & Finch, 2009). A study by Koski and colleagues, generated a Rasch analysis that allowed a linear estimate of cognitive ability on an interval-like scale for any given MoCA score measured at 2 points in time (Koski, Xie, & Finch, 2009). The study presented a table used to determine the statistical significance of a change in the total MoCA score depending on the baseline score (Koski, Xie, & Finch, 2009). In another study, Krishnan et al. (2016) explored

the utility of the MoCA in the detection of cognitive change in a 3.5-year period in a sample of individuals who were cognitively intact compared to a sample diagnosed with mild cognitive impairment (MCI). After adjusting for age and education, their results demonstrated a change in MoCA scores in the MCI group of -1.70, while the cognitively intact group was -.75 (Krishnan et al., 2016). Thus, individuals who were cognitively intact demonstrated stable MoCA scores over a 3.5-year period, while individuals with MCI demonstrated a significant decline in scores (Krishnan et al., 2016). Overall, a reliable change of 1.73 points in this period represented a clinically meaningful difference (Krishnan et al., 2016). However, the clinical significance of a change in MoCA scores in other levels of ability warrants further investigation.

In this current study, patients with SA who used CPAP demonstrated improved MoCA performance. Nineteen of the 26 compliant patients demonstrated improvements in MoCA scores, while only 11 of the 20 non-compliant patients improved. These findings suggest the MoCA test is sensitive to the level of cognitive change that occurs in patients with sleep apnea. Therefore, it is possible to use the MoCA test when determining CPAP effect. This assessment would be beneficial in general healthcare settings, such as a primary care clinic, as well as specialty clinics, such as a memory disorder clinic, to assess cognitive change after CPAP usage in a time and cost-efficient manner. Most importantly, detecting this cognitive change would increase CPAP compliance and thereby improve cognition in dementia patients. Cognitive improvement from CPAP treatment has the potential to improve quality of

life, relieve caregiver stress, and minimize disease-related costs and resources in the elderly and dementia populations.

When pre-CPAP treatment MoCA scores were compared to post-CPAP treatment MoCA scores in each compliance group, there was no significant difference in MoCA change scores between CPAP compliant and non-compliant patients. The different outcomes of CPAP effects shown by the repeated measures t-tests (improvement for compliant group only) and mixed-model ANOVA (no difference in the change scores between the two compliance groups) could be explained by the t-test reducing within subject variability sufficiently to show a significant outcome despite the relatively low group size of 26. In the mixed-model ANOVA, the change scores of the two groups were compared directly, and relatively large variability in the non-compliant group made finding a significant outcome unlikely.

When examining the distribution of CPAP compliant and non-compliant patients with different diagnoses, diagnosis did not impact the findings of this study. Therefore, compliance and diagnosis are independent from one another and demonstrated no relationship. However, a larger, more representative sample is needed to further explore the relationship or impact of different levels of cognitive ability or diagnoses on CPAP compliance.

Limitations

There are several limitations to the present study. First, a small sample size was used, which likely hindered results. This was due to the limited number of patients who met criteria for the study including a sleep apnea diagnosis, records of a sleep study that

was performed during the time they were an active patient in the memory clinic, a neuropsychological evaluation during the time the patient began their CPAP treatment, and having a MoCA administration prior to CPAP treatment and after CPAP treatment of no more than 9 months apart. The sample size was also lacking in diversity as most patients were white, Caucasians. Nonetheless, the sample is representative of the geographic location where the study took place. It is also important to note most of the patients in the sample had a dementia diagnosis. The neurodegenerative nature of their disease continues to affect their cognitive performance despite the benefit CPAP treatment.

Another limitation was the Electronic Medical Record (EMR) System, which affected data collection and analysis. There were numerous patients who did not have records of their sleep study, no neuropsychological evaluation, were not administered the MoCA at the 6-month follow-up or given the MoCA more than 9 months after the pre-CPAP treatment MoCA score, and providers failed to follow-up on CPAP compliance on some occasions. Additionally, in most cases, there was a lack of records for CPAP compliance reports generated by the CPAP machine and sent electronically to the pulmonologist. In these cases, CPAP compliance was confirmed by self-report in the memory clinic records. Additionally, there was limited resources to recruit patients due to research restrictions of the Brevard County Health First medical system. Authorization for research was only provided to the memory clinic rather than other primary care or specialty providers.

Future Directions

Future research should focus on improving statistical power by increasing sample size, as well as in utilizing a large, more representative sample of various racial and ethnic backgrounds. Another improvement to this study would include assessing its reliability. Since the time interval between the initiation of CPAP treatment and after treatment was highly variable, a prospective study would be helpful to serve as a comparison when the time interval is held constant.

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