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CPAP-Compliance of Aging Individuals with Obstructive Sleep Apnea With or Without Mild Cognitive Impairment

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CPAP-COMPLIANCE OF AGING INDIVIDUALS WITH OBSTRUCTIVE SLEEP

APNEA WITH OR WITHOUT MILD COGNITIVE IMPAIRMENT

by

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A Thesis Submitted in Partial Fulfillment
of the Requirements for a degree with Honors
(Zoology)

The Honors College

University of Maine

May 2020

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ABSTRACT

With approximately 20% of Americans affected by obstructive sleep apnea (OSA), and over 30% of sleep apneic patients non-compliant with the most common form of treatment, CPAP (Continuous Positive Airway Pressure), the proposed study looks to investigate the relationship between OSA, CPAP-compliance, and cognitive decline associated with many aging-related neurodegenerative diseases [1, 2]. Our group has performed in-home sleep studies using a patented, sensor mattress-sheet device, and standard actigraphy. Demographics including a questionnaire on OSA compliance and neurocognitive tests were administered to participants between 62 and 90 years of age. Cognitive decline meeting criteria for MCI (Mild Cognitive Impairment, the prodrome of Alzheimer's Disease) were determined, and groups were made of comparison individuals (n=45) and MCI individuals (n=50). CPAP compliance in relationship to MCI diagnosis was examined. It was hypothesized that there would be a correlation between CPAP-compliance of OSA participants and increased cognitive functioning, compared to the CPAP noncompliant counterparts. The proposed mechanism consists of sleep disruption for the CPAP noncompliant group, which would cause chronic hypoxia and decreased restorative function of sleep in the brain and other organs during sleep. The results show that participants with OSA compared to those where were non-OSA were significantly more likely to have identifiable comorbid conditions: higher BMI (p=0.026), hypertension (p=0.003), hypercholesterolemia (p=0.035), diabetes (p=0.015), and current depressive symptoms (p=0.042). The OSA group was also more likely to be male than the non-OSA group, (p=0.016). Additionally, the OSA group was found to have more

sleep impairments compared to non-OSA: higher PSQI sum composite score (p=0.02), higher PSQI daytime dysfunction score (p=0.02), and decrease in sleep quality duration (p=0.01). Lastly, the OSA group performed significantly worse on the neurocognitive BVMT-R recognition of false alarms compared to the non-OSA group (p=0.002). CPAP-compliance was also found to be significantly associated with less comorbid health conditions and many sleep quality assessments. CPAP noncompliance was associated with hypertension (p=0.006), more current depressive symptoms (p=0.035), and diabetes (p=0.025), compared to the CPAP-complaint group. The CPAP-compliant group was found to have many significant associations with sleep measures compared to the CPAP noncompliant group: increased sleep quality (p=0.03), decreased sleep disturbances (p=0.02), decreased daytime dysfunction (p=0.03), improved PSQI sum composite score (p=0.03), and increased habitual sleep efficiency (p=0.05). There were no conclusive results between CPAP-compliance and neurocognitive assessment.

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INTRODUCTION

<u>Obstructive Sleep Apnea (OSA)</u>

Obstructive sleep apnea (OSA) is defined as a medical condition that has the reoccurring collapse of the airway by relaxation of the upper airway muscles during sleep [3]. The collapse of the airway causes breathing to pause intermittently, decrease air passage, and increase carbon dioxide levels in the blood [4]. Clinically, apnea is defined by the cessation of breathing, with at least 5 cessations per hour, and an increasing number of cessations indicates higher severity [4]. The apnea-hypopnea index (AHI) has been created to categorize the severity of a patient's OSA, from mild, moderate, and severe for 5, 15, and ≥ 30, respectively [5]. The increasing number of apneas means that the body is without air for a greater period of time every hour. This air provides the oxygen needed for the cardiopulmonary system to oxygenate the brain and the periphery. However, the collapse of the airway during sleep diminishes this process. This repeated collapse causes hypoxemia, or deoxygenation of the bodily tissues, during sleep [6]. It is hypothesized that chronic hypoxemia during sleep will cause significant cognitive decline, as hypoxia of the brain is a known factor for cognitive decline and neurodegeneration [7]. Beyond the effects of hypoxia, OSA causes increased arousals during sleep, increased sleep fragmentation, and diminished sleep quality every night [8. This lack of sleep can lead to sleep deprivation, and eventually the risk of MCI [9].

There is increasingly more research into understanding cognitive decline and its lead to MCI and eventual Alzheimer's Disease (AD). Sleep disruption has been an interesting point to highlight in recent years, as it is thought that it may impede the restorative function of sleep. Individuals with OSA have documented sleep disturbances

and suffer from nocturnal intermittent hypoxia, both of which have been hypothesized to cause cognitive impairment [10–12]. Through these proposed mechanisms of sleep disorder associated with OSA-related intermittent hypoxia, it is proposed that individuals with OSA would show signs of cognitive impairment. Other studies have looked to investigate this relationship as well, and while there is yet to be a consensus around a solidified mechanism, persons with OSA have been found to have decreased cognitive assessment scores and more likely to have a cognitive impairment, as seen through MCI and AD [13]. While there is some variation in the proposed mechanisms for these associations, there is an increasing evidence of dual sleep fragmentation and intermittent hypoxia epidemiology [13–15]. Between the detrimental effects on the process of sleep itself, including less sleep overall and a lower quality of sleep with sleep fragmentation, and the fact that the body can be hypoxic for a non-insignificant portion of the night, OSA can be seen to be a truly debilitating disease that can diminish the brain's cognitive abilities.

Continuous Positive Airway Pressure (CPAP)

One of the most common treatments for OSA is continuous positive airway pressure (CPAP). CPAP works by blowing a continuous stream of air into the airway, through the mouth and or nasal passages [16]. There are two major types of CPAP masks, an oral-nasal covering or a nasal mask, and the type of mask is dependent on the patient's preferences and physiology. The air from these masks pushes against the relaxed muscles, increasing the opening of the airway and allowing for more air to reach the remainder in the cardiopulmonary system. This air is often humidified for increased compliance and does not have a direct oxygen input, as from a tank or concentrator, and

simply takes the air from the patient's surroundings. While this is the standard practice for treating OSA, it does not come without its difficulties.

CPAP-compliance is a constant problem with those who use this form of treatment. Some studies have shown that over one-third of patients who are prescribed CPAP are not compliant in its use [17]. While there is a wide spectrum over what is deemed as CPAP-compliant, such as 4-6 hours per night, or for at least 3-5 nights per week, this study's compliance metric was for CPAP use for at least 4 hours a night [17]. While some of these machines do have the functionality to internally record CPAP-compliance metrics, primarily for billing purposes, this information is often not standardly released to each patient. CPAP is well known for its uncomfortable nature, and that the air forced into the body can be quite distressing. This causes many of these patients to either use CPAP for only a few nights per week or a handful of hours per night.

Low CPAP-compliance is most often due to the unwanted side effects of wearing a CPAP mask, such as it being uncomfortable when strapped onto the head and the feeling of the air being blown into the airway. While nasal CPAP machines may be less uncomfortable compared to their oral-nasal counterparts, there are still uncomfortable side effects in most CPAP masks. While there are other treatment options for OSA, such as mouth guards and surgical options, questions on alternative treatment options on the participant survey. What is most interesting about CPAP effectiveness is its effects on intermittent hypoxia and sleep fragmentation. CPAP has shown not only to increase blood oxygen levels but also to decrease the effects of sleep fragmentation [18]. Since these two symptoms of OSA are treated through CPAP, it is reasonable to suspect that

CPAP-compliance may increase cognitive function from the previously mentioned mechanisms. While this project can not study the direct effects of CPAP-compliance on cognitive status, we hope to gain a better understanding of the possible association between OSA, CPAP-compliance and cognitive decline.

<u>Metabolic Syndrome (MS)</u>

Metabolic syndrome (MS) is defined as the common comorbidity of various cardiovascular and endocrine diseases, including hypertension, diabetes, hypercholesterolemia, and obesity [19, 20]. While there are a number of proposed mechanisms for metabolic syndrome, the leading theory states that MS may be from the body's increased lipid levels, and thus leading to insulin resistance over time [20–22]. Beyond the typical mechanism for cardiovascular diseases and hypertension in the body associated with a high BMI, this hyperlipidemia leads to hypertension, thus further propagating negative cardiovascular effects [22, 23].

With these vast, yet intricate systems constantly interworking amongst each other, the effects of OSA can have a crippling double-down effect on both the endocrinological and cardiovascular system. When OSA is added to this already taxed body system, the corresponding effects, known as Syndrome Z, can lead to further distress and complications [24]. About 60% of people with metabolic syndrome have Syndrome Z, and CPAP used to treat the OSA components of Syndrome Z have shown to decrease several of the symptoms of MS [25]. Studies have shown independent effects of OSA on both diabetes or cardiovascular disease. Not only has OSA and diabetes been found to be associated with an increasing prevalence of each other, but some hypotheses claim that they could be linked through the impacts of intermittent hypoxia on the endocrine

systems of the body, leading to symptoms like insulin resistance [26]. Although we have already well established the link between OSA and cardiovascular diseases, other studies have also shown that intermittent hypoxia causes additional stress on the cardiovascular system via increases irregular arousal of the sympathetic nervous system, inflammation, and oxidative stress onto the body [27–29]. Between these two already prevalent interconnected diseases, it appears that OSA could be the connecting point helping to cause further exacerbation of these conditions and increased disease severity. Many of the conditions that make up MS were recorded during the participant demographic questionnaire of this study. By further identifying the comorbid conditions of OSA, we hope to further investigate the role of OSA in turning metabolic syndrome into the more complicated and dangerous, Syndrome Z.

Mild Cognitive Impairment (MCI)

Between the large number of individuals who have OSA and these individuals not being CPAP-compliant, there is an increasing number of people who have decreased oxygen perfusion while sleeping. This study investigated the relationship between OSA, CPAP-compliance, and cognitive decline. Cognitive decline was measured between individuals with Mild Cognitive Impairment (MCI) and those with normal cognition. MCI is defined as cognitive decline that is greater than expected for an individual's age and education level without significantly impairing daily living [30]. This cognitive decline is seen with both crystallized intelligence, knowledge, and skills learned over one's life, and fluid intelligence, complex thinking with problem-solving and reasoning, to some extent [31]. While crystallized intelligence remains strong up to our 60s-70s, on average, fluid intelligence begins to decline after our 30s, and both can be measured and

seen to decline with neurocognitive testing as we age [31]. These forms of intelligence can help serve as markers to judge the form of MCI. MCI can be broadly separated into two groups, amnestic and non-amnestic MCI, memory or cognitive abilities associated with normal functioning such as speaking and mental tasks, respectively [32]. However, these two forms of MCI can make diagnosis and assessment difficult, as they affect different parts of one's cognitive abilities and thus may cause some confusion in trying to fully understand one's MCI diagnosis. Since MCI is so broad, it can relay a spectrum of symptoms that are unique to each patient. These symptoms can range from difficulty remembering basic facts like names, to confusion, or difficulty with complex tasks such as balancing a checkbook or driving. While patients with MCI can have clear and noticeable symptoms, they are still able to function mostly independently and live on their own. It is not until the disease progresses to a more advanced state that a further diagnosis of AD is established, and these patients are unable to live by themselves. After initial MCI diagnosis, cognitive decline can be quite rapid, with up to 15% of MCI patients progressing into an AD diagnosis every year [33]. While MCI can be diagnosed by electronic or paper assessments, AD is diagnosed through a much more significant cognitive decline. This diagnosis requires more advanced diagnostic tools, including MRI and serum analysis, with patients who are often noted with biomarkers including increased beta-amyloid plaques and tau proteins [34]. While the underlying mechanism connecting OSA and AD are not fully understood, nocturnal intermittent hypoxia and sleep disruption seem to be a promising opportunity. CPAP treatment is seen as a plausible route to reducing neurocognitive decline and AD symptoms [35].

Hypotheses

1. Aging individuals with Obstructive Sleep Apnea (OSA) will have:

    a. higher incidence of comorbid health conditions compared to those who do not have OSA (non-OSA).

    b. more sleep problems through subjective sleep measures and show poorer sleep quality in actigraphy, compared to non-OSA.

    c. aging participants with OSA will perform worse on neurocognitive assessments than non-OSA.

2. Amongst the OSA group, those who are CPAP-compliant (CPAP-compliant) compared those who are not (CPAP noncompliant):

    a. CPAP noncompliant are less likely to have comorbid health conditions

    b. CPAP-compliant group will show higher sleep quality, through actigraphy and self-report than OSA CPAP noncompliant groups.

    c. CPAP-compliant group will perform better on neurological assessments compared to the CPAP noncompliant group.

METHODS

Participants

In order to collect the data needed for this research, a standardized set of IRB approved procedures and protocols were followed to recruit participants, set up equipment, record their data and analyze their results amongst our expert panel. Participants, aged 62 and 90 years old, were first recruited in the greater Orono/Bangor, Maine and then areas in southern Maine.

Recruitment

This was done in the local community through methods such as local news reports, flyers, the University of Maine Center on Aging registry, presentations to senior-living facilities, and peers of past participants. This community group made up the original *comparison* group for our study, or those that were not known to have any neurodegenerative disorders (e.g. MCI, AD, etc.). Initially, all participants with cognitive decline and impairment were introduced through neurological consult, Dr. Cliffod Singer, MD, of Northern Light Acadia Hospital in Bangor, Maine, or from the University of New England, Legacy Scholars registry under Dr. Thomas Meuser with scores of 1 or 2 on an AD-8 prescreen. These participants were clinically diagnosed with MCI or pre-screened to likely have MCI. These were participants that made up the *MCI* group.

One of the problems faced during this study was finding enough participants to meet the predetermined threshold for MCI. In order to reach the quota specified in the study, the participant recruitment was expanded from just Bangor, Maine to Southern and central Maine. Additional participants were flagged as potentially MCI participants due to scores on neurocognitive assessments. After a thorough assessment of their data and

consideration by the expert panel, including C. Singer, M.D.; F. Ahmed, Ph.D.; M. Elias, Ph.D.; and J. Aronis, M.A., some control participants were deemed to have cognitive impairment and were transferred into the MCI category.

Assessment Measures

The actigraphy device used for this study was the Philips Respironics Actiwatch 2, the 'gold-standard' in actigraphy assessment. It is a small device worn on the participant's nondominant wrist for 7 consecutive days. This device measured movement of participant sleep/wake and has shown to have significant and meaningful results regarding the movements of aging adults [36].

During the first visit, participants were asked to complete a comprehensive demographics questionnaire, Center for Epidemiological Studies Depression Scale (CES-D), Montreal Cognitive Assessment (MoCA) and self-report sleep questionnaires (Epworth Sleepiness Scale (ESS), the Stanford Sleepiness Scale (SSS), and Consensus Sleep Diary).

The second visit consisted of neurocognitive assessments, testing many facets of participant neurocognitive health, within 30 days. These neurocognitive measures included the Hopkins Verbal Learning Test-Revised (HVLT-R), Trails Making Test A and B, Brief Visuospatial Memory Test-Revised (BVMT-R), and the Boston Naming Test.

Statistical Analyses

An independent-samples t-test (continuous variables) and a chi-square test of association (categorical variables) were conducted to compare physiological demographic

measures of the OSA group, non-OSA group, CPAP-compliant group, and CPAP noncompliant group.

<center>Sleep Study Protocol</center>

The protocol used during this research project was a part of a larger IRB-approved study. The methods used and participant experience was standardized to minimize potential biases. The sleep study protocol was separated into two main components, the first-visit mattress-sheet set-up, and the follow-up neurocognitive assessment. However, before individuals could participate in the study, they were pre-screened through an intake interview that would ensure that they fit the guidelines set by the initial study. The inclusionary criteria included but were not limited to, being within the predetermined age range mentioned above, and having the ability to live independently and perform most of their own tasks. Most of these inclusionary criteria fell within this broader scope of if the patient could live and work independently and did not need a professional caretaker to assist them. The reason for these criteria was to help exclude patients with more serious neurodegenerative disorders from the study. There were numerous other criteria, but they also included basic components that included non-AD individuals, being non-bedridden, and not being able to take care of their daily tasks and activities, independently, as well as having no additional possible causes of MCI (e.g. poorly controlled diabetes, more than one cerebral infarct, REM sleep disorder, etc.). After determining that the individuals were qualified to be a part of the study, participants scheduled their first home visit.

First visits were a crucial step in the study in building relationships with our participants and to further assess participants on their individual situations. After arriving at the participant homes, participants would complete a demographics questionnaire, which included a list of prescribed medications and a detailed examination of their medical history. There were additional questionnaires used to screen for current and historical depression, which included the Center for Epidemiological Studies Depression Scale (CES-D) [37]. After this, a participant interview was conducted including a cognitive prescreen, Montreal Cognitive Assessment (MoCA), and a subjective sleep measure, Pittsburgh Sleep Quality Index [38,39]. Sleep quality and daytime sleepiness were measured using the Epworth Sleepiness Scale (ESS), the Stanford Sleepiness Scale (SSS), and Consensus Sleep Diary, with the latter two being continued over the next seven days [40–42].

After this, the patented mattress-sheet device, *SleepMove*, was then shown to the participants and set up on their bed. The mattress-sheet device is a thin sheet embedded with flat wired sensors that detect movements and respiration during sleep. Participants were instructed to sleep directly on this device for the next two nights as they would normally. Participants were also instructed to wear an Actiwatch on their non-dominant wrist for seven days. The Actiwatch measured patient actigraphy data, including movement and basic motor activity, and was used to help determine wakefulness and sleep patterns.

Within 30 days of the initial visit, the research team returned to the participant homes to conduct an in-depth neurocognitive assessment. This assessment included the Hopkins Verbal Learning Test-Revised (HVLT-R), Trails Making Test A and B, Brief

Visuospatial Memory Test-Revised (BVMT-R), and the Boston Naming Test [43–46].

These tests assessed a wide range of participant cognitive abilities, including item

recognition, brief and long-term recall, and pattern recognition.

Hypothesis 1a

Aging individuals with Obstructive Sleep Apnea (OSA) (OSA group) will have a higher incidence of comorbid health conditions compared to those who do not are non-OSA.

There was a significant sex difference among OSA vs. non-OSA groups; X^2(1, N=95), p=0.016. Males were more likely to have OSA than females. The OSA group was significantly more likely to have comorbid conditions such as high BMI, X^2(1, N=90), p=0.026; hypertension, X^2(1, N=92), p=0.003, hypercholesterolemia, X^2(1, N=93), p=0.035, diabetes, X^2(1, N=93), p=0.015, and current depressive symptoms, X^2(1, N=93), p=0.042. These results are demonstrated in Table 1 below. Table 1 depicts the demographic data of the OSA and non-OSA, and any significant associations found.

Table 1: Demographics of OSA and Non-OSA Groups

Variable (μ±SE or % (n))	OSA (n=22)	Non-OSA (n=73)	p-value
Age, y	72.18±1.29	73.09±0.79	n.s.
Male	50.0% (11)	23.3% (17)	**0.016**
Race (% white)	95.2% (20)	100% (73)	n.s.
Years of education	15.45±0.65	15.48±0.32	n.s.
MoCA	23.41±0.79	24.18±0.44	n.s.
Lifestyle factors			
Drinking alcohol	62.5% (45)	47.6% (10)	n.s.
Current use of sleep medication	42.9% (9)	41.7% (30)	n.s.
Current or former smoker[a]	57.1% (12)	48.6% (35)	n.s.
Body mass index (BMI)	30.42±1.45	27.08±0.67	**0.026**
MCI	63.6% (14)	49.3% (36)	n.s.
Diabetes	33.3% (7)	11.1% (8)	**0.015**
Heart attack or cardiac arrest	23.8% (5)	9.7% (7)	n.s.
Cardiovascular disease	23.8% (5)	13.9% (10)	n.s.
Cerebrovascular disease	9.5% (2)	12.5% (9)	n.s.
Traumatic brain injury (TBI)	19.0% (4)	16.7% (12)	n.s.
Hypercholesterolemia	61.9% (13)	36.1% (26)	**0.035**
Hypertension	70.0% (14)	33.3% (24)	**0.003**
Arthritis	33.3% (14)	52.1% (37)	n.s.
Thyroid disease	14.3 % (3)	33.3% (24)	n.s.
Current depressed mood[b]	42.9% (9)	20.8% (15)	**0.042**

Note: Values are shown as % (n) or mean ± SE, and compared by independent samples t-test (continuous variables) or chi-square test of association (categorical variables).

[a] Current use of sleep medication was described as any self-reported use of over the counter or prescribed sleep medication over the last month

[b] Current depression was indicated by self-report answering the question "Are you currently feeling depressed?"

Table 1. Demographic information table for OSA and non-OSA groups

OSA participants who are in the CPAP-compliant group were less likely to have comorbid health conditions than OSA participants who were in the CPAP noncompliant group.

An independent-samples t-test (continuous variables) and a chi-square test of association (categorical variables) were conducted to compare physiological demographic measures with the CPAP-compliant group and the CPAP noncompliant group. The CPAP compliant group were less likely to have comorbid conditions such as hypertension between OSA groups; X^2(1, N=92), p=0.006, current depressive symptoms; X^2(1, N=93), p=0.035, and diabetes, X^2(1, N=93), p=0.025.

OSA group participants will report having more sleep problems through subjective sleep measures and poorer sleep quality through actigraphy, compared to non-OSA.

An Independent-samples t-test was conducted to compare sleep measures of the OSA group and non-OSA group. For sleep measures, OSA group had a significantly higher composite score for the PSQI (M=8.19, SD= 4.59), compared to non-OSA (M=6.00, SD=3.31); t(91) = -2.43, p = 0.02. This result is displayed in Figure 1, and shows a significant difference in PSQI sum composite scores for the OSA and non-OSA group. For sleep quality measures, higher scores indicate that the individual has poorer sleep quality. In addition, OSA group had significantly higher scores for daytime dysfunction on the PSQI (M=1.04, SD= 1.03), compared to non-OSA (M=0.583, SD=0.746); t(91)=-2.297, p = 0.02. This analysis is demonstrated in Figure 2, as the

PSQI assessment 7 - daytime dysfunction is shown to be significantly different between the OSA and non-OSA groups. Finally, there was also a significant difference in the scores for sleep quality duration for the OSA group (M=1.11, SD= 0.910), compared to non-OSA (M=0.67, SD=0.69); t(91)=-2.58, p = 0.01.
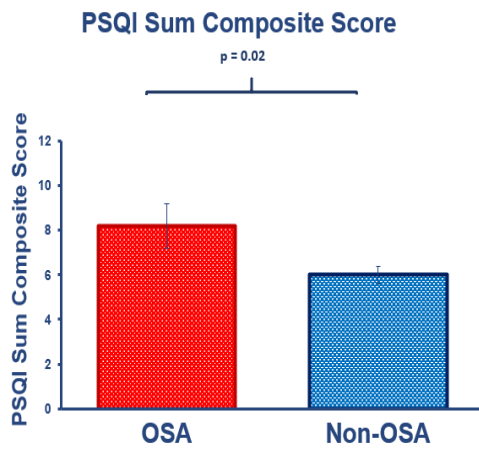
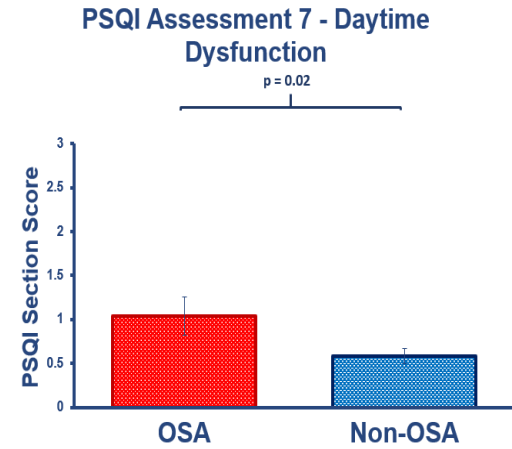

Figure 1. PSQI Sum Composite Score
 by OSA group

Figure 2. PSQI Daytime Dysfunction
 by OSA group

Finally, sleep actigraphy showed no differences in the suite of sleep quality measures listed in Table 2. Table 2 lists measured actigraphy movement data between OSA and non-OSA groups, and zero significance was found for any variable.

Table 2
Actigraphy Variables for OSA vs. non-OSA Groups

Variable	OSA (n=21)	Non-OSA (n=68)	*p*-value
Mean Time in Bed	549.60 ± 18.77	524.54 ± 9.84	0.23
Mean Assumed Sleep	509.12 ± 19.27	487.45 ± 9.82	0.30
Mean Actual Sleep Time	450.87 ± 19.70	431.69 ± 9.94	0.35
Mean Actual Sleep %	88.76 ± 0.92	88.48 ± 0.71	0.84
Mean Actual Wake Time	56.94 ± 4.74	55.95 ± 3.44	0.88
Mean Actual Wake %	11.23 ± 0.93	11.52 ± 0.71	0.84
Mean Sleep Efficiency	82.32 ± 1.93	81.76 ± 1.04	0.80
Mean Sleep Latency	26.39 ± 10.03	24.39 ± 3.32	0.81
Mean Sleep Bouts	23.76 ± 1.56	22.51 ± 0.87	0.49
Mean Wake Bouts	23.29 ± 1.55	22.11 ± 0.88	0.51
Mean Mean Sleep Bout Time	30.98 ± 7.38	29.27 ± 4.21	0.84
Mean Mean Wake Bout Time	2.44 ± 0.11	2.57 ± 0.13	0.58
Mean Number of Minutes Immobile	432.47 ± 19.98	413.91 ± 9.56	0.37
Mean Immobile % Time	84.87 ± 1.24	84.88 ± 0.87	0.99
Mean Number of Minutes Moving	76.46 ± 6.27	73.62 ± 4.37	0.74
Mean Moving % Time	15.13 ± 1.23	15.70 ± 1.00	0.77
Mean Number of Immobile Phases	42.96 ± 2.69	39.12 ± 1.59	0.24
Mean Mean Length Immobility	14.27 ± 3.49	17.45 ± 3.31	0.62
Mean One Minute Immobility	9.19 ± 0.89	9.30 ± 0.74	0.94
Mean One Minute Immobility %	19.76 ± 1.16	20.64 ± 1.18	0.60
Mean Total Activity Score	7748.81 ± 694.55	8341.52 ± 674.43	0.64
Mean Mean Activity Score	14.05 ± 1.31	15.30 ± 1.18	0.58
Mean Mean Score in Active Periods	60.23 ± 8.07	50.53 ± 4.21	0.32
Mean Fragmentation Index	34.89 ± 2.28	35.76 ± 1.92	0.81
Mean Average Wake Movement	51.64 ± 9.37	48.64 ± 6.43	0.83
Frequency of daytime (10 AM-6PM) nap	2.40 ± 0.61	2.02 ± 0.37	0.61
Average duration of daytime (10 AM-6 PM) nap	51.38 ± 9.19	44.81 ± 7.04	0.63

Note. x ± y represents estimated marginal mean (EMM) ± standard error of the mean (SEM), (n) = sample size.

Table 2. Actigraphy results for OSA and non-OSA groups

Hypothesis 2b

The CPAP compliant group compared to the CPAP noncompliant group will record with less impairment in sleep questionnaires (subjective sleep) or actigraphy (objective sleep).

An Independent-samples t-test was conducted to compare sleep measures of the CPAP-compliant group and the CPAP noncompliant group. There was a significant

difference in the scores for subjective sleep quality for the CPAP-compliant group (M=0.56, SD= 0.53), compared to CPAP noncompliant (M=1.33, SD=0.89); t(19)=-2.33, p = 0.03. A higher score is indicative of having a poorer subjective sleep quality. Additionally, there was a significant difference in the scores for sleep disturbances for CPAP-compliant (M=1.11, SD= 0.33), compared to the CPAP noncompliant participants (M=1.58, SD=0.52); t(18.70)=2.55, p = 0.02. A significant difference was also found in the scores for PSQI assessment 7 - daytime dysfunction for CPAP-compliant group (M=0.56, SD= 0.53), compared to the CPAP noncompliant (M=1.42, SD=1.16); t(16.17)=2.27, p = 0.03.

The sum composite PSQI score for CPAP-compliant group(M=5.89, SD= 2.52), was significantly lower compared to the CPAP noncompliant (M=9.92, SD=5.11); t(16.87)=-2.37, p = 0.03. Both of these analyses have been plotted on Figures 3 and 4, to show the significant difference found between the CPAP-compliant and CPAP noncompliant groups for PSQI sum composite score and PSQI assessment - 7 daytime dysfunction, respectively. Finally, the scores for habitual sleep efficiency for CPAP-compliant were trending towards a significant difference (M=0.56, SD= 0.88), compared to the CPAP noncompliant groups (M=1.58, SD=1.38); t(18.65)=2.077, p = 0.052. For the measures listed above, a higher score denotes increased impairment.
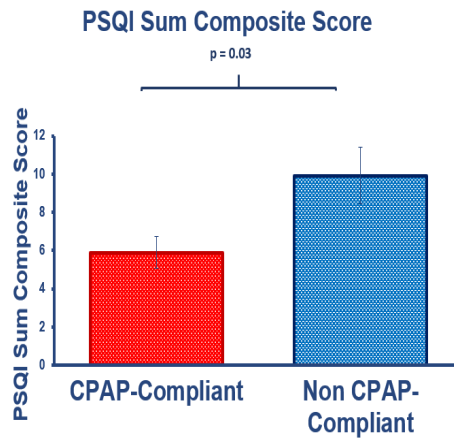
Figure 3. PSQI Sum Composite Score
by CPAP-compliance group
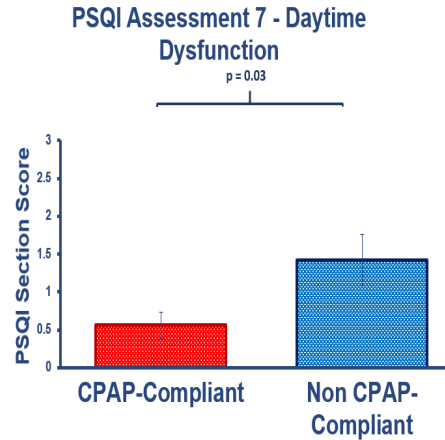
Figure 4. PSQI Daytime Dysfunction
by CPAP-compliance group

Hypothesis 3a

The OSA group will perform more poorly on neurocognitive assessments than the non-OSA group.

An Independent-samples t-test was conducted to compare neurocognitive testing measures between the OSA and non-OSA groups. There was a significant difference in the scores for BVMT-R recognition false alarms for the OSA group (M=0.053, SD= 0.23), compared to the non-OSA group (M=0.42, SD=0.79); t(81.99)=3.27, p = 0.002. A higher score indicated more impairment and that more false alarms on figure recognition occurred. This result is seen in Figure 5, as the non-OSA group has significantly more false alarm recognitions in the BVMT-R than the OSA group. A false alarm is defined as when a participant incorrectly chooses a newly displayed figure as being previously shown earlier in the assessment, even though it has not. The BVMT-R assesses visual

learning and memory, and the false alarms show that the OSA group has some deficits in either visual learning or memory compared to non-OSA. Since the OSA group did not remember and therefore incorrectly identified the displayed figures, it helps to demonstrate that the OSA group has some form of cognitive impairment compared to the non-OSA group.
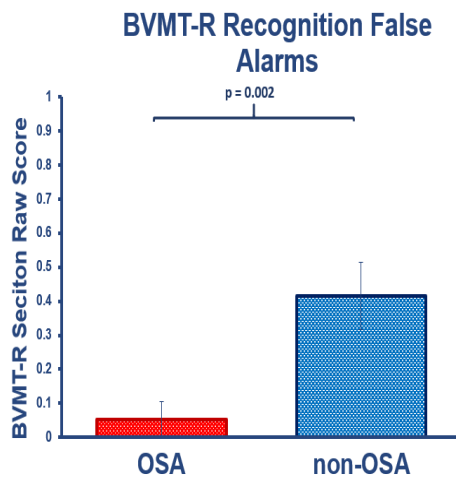
Figure 5. BVMT-R Recognition False Alarms Raw Score
 OSA group

Hypothesis 3b

The CPAP-compliant group will perform with less impairment on neurocognitive testing compared to the CPAP noncompliant group.

An Independent-samples t-test was conducted to compare neurocognitive testing measures for the CPAP-compliant group and the CPAP noncompliant group. There were no statistically significant results to report for CPAP compliance and neurocognitive exam measures.

DISCUSSION

Previous studies have shown that OSA and comorbid health conditions, especially cardiovascular diseases, are significantly associated [36, 37]. Another comorbid condition is metabolic syndrome, which affects the cardiovascular and endocrine systems. This association is especially prevalent in obese individuals [49]. Our results confirm most of what has been previously researched regarding OSA and chronic health conditions. The data shows a significant association between the OSA group and the increased likelihood of a participant having hypertension, hypercholesterolemia, diabetes, higher BMI, and current depressed mood. The results are in line with the metabolic syndrome associated with OSA stated previously, as well as literature on OSA and diabetes [38, 41, 42]. Our data agrees with the previously found results that males are more likely to have OSA than females, which also agrees with current literature [4, 39]. While the direct cause of this is still unknown, perhaps it could be linked to the average distribution of adipose in adults. With men having adipose tissue deposited more centrally around the trunk compared to women, perhaps this could cause for airway obstruction during sleep [51]. While our results were not significant between OSA and thyroid disease, and OSA and diabetes, studies have shown a significant association between OSA and diabetes [52,53].

OSA is known and well studied, to be linked to decreased sleep quality through numerous testing measures. While our data only showed a significant difference for PSQI daytime dysfunction and composite score, OSA has also been linked to measures such as decreased sleep efficiency, increased daytime sleepiness, sleep fragmentation and reduced daytime wakefulness [53].The PSQI is a subjective sleep measure where the participant rates their own sleep quality, with more disturbed sleep earning a higher PSQI

score. Our findings for a higher sum composite PSQI score is not uncommon, as PSQI scores have shown to be significantly higher for OSA individuals in past studies [54]. The proposed cause for decreased sleep quality for OSA individuals is believed to come from sleep disruption from OSA's breathing pauses and hypoxemia during sleep [53].

This nocturnal hypoxia cycle is thought to be the cause of decreased cognitive abilities of OSA individuals [55]. There are a number of studies linking OSA and neurocognitive decline, and most of them reference this intermittent night hypoxia as the plausible mechanism [55,56]. Although there are numerous measures to record cognitive decline, with both subjective and objective options, our study only found significant results with BVMT-R. The BVMT-R is a neurocognitive measure that measures visuospatial memory and tests the participant's ability to remember and identify a series of figures. While our data only found significant differences for BVMT-R recognition false alarms for the OSA group, other studies have shown a significant difference in total recall [56]. For this data set, the OSA group had significantly more false alarms, meaning that the participants incorrectly stated that an example figure was previously displayed, when it actually was not shown.

Although CPAP compliance is still the most successful therapy for OSA, CPAP continues to have low compliance for CPAP. The CPAP-compliant group showed decreased risk for comorbid conditions such as hypertension, current depressive symptoms, and diabetes. While using a CPAP mask may cause a large percentage of users to not adhere to the treatment, those who do, report much higher sleep quality. In this study, OSA individuals who were CPAP compliant recorded significantly higher subjective sleep quality, fewer sleep disturbances, less daytime dysfunction, and a lower

composite PSQI score. Studies have shown that CPAP use improves sleep quality, sleep efficiency, and sleep duration [57]. These findings further support the idea that CPAP-compliance has many positive impacts on sleep quality. While the means for these results show CPAP-compliance as having a lower integer for sleep measures, this still shows that CPAP-compliance increases positive sleep characteristics, as higher scores denote more impairment and worsening sleep measures.

While our data did not display any significant findings between neurocognitive assessment and CPAP-compliance, this could be due to a number of factors that must be considered. First, our sample size for CPAP-compliance was only 22, which can make it difficult to find statistical significance. Current research shows conflicting results regarding the effects of CPAP-compliance on neurocognitive abilities and assessments [58–61]. One of the reasons for this could be due to the complexity and difficulty assessing the vast array of cognitive abilities that the brain possesses, and the numerous cognitive assessments that are used throughout the scientific community.

While actigraphy was a significant component of the data collection and analysis, there were no significant results found for either OSA or CPAP groups. This could be due to several factors, including only having seven days of wrist actigraphy data available. Even when the length of wrist actigraphy was increased in other studies to 2+ weeks, there was still conflicting data regarding OSA and CPAP compliance [62,63]. Some studies have had multiple weeks of data and were unable to find any significance with actigraphy, thus it may be even more difficult to find significance with our 7 days worth of actigraphy data. Also, as actigraphy devices are worn on the wrists of participants, it may not be able to fully detect sleep disruptions occurring in the upper third of the body.

While the chest and neck may be moving during sleep disruption, the wrist may not move

to any significant extent, and thus not record any meaningful results.

CONCLUSION

The goal of this thesis project was to investigate the relationship between OSA and compliance with its most common form of treatment, CPAP, and the possible effects on sleep and neurocognitive status. Through the use of demographics questionnaires, actigraphy, a novel mattress-sheet device, subjective sleep assessment, and neurocognitive examination, data was collected and analyzed. The initial hypothesis suggested that there would be significant decreases in sleep and neurocognitive status compared between OSA and non-OSA participants, as well as CPAP noncompliant vs. CPAP-compliant groups. Our results indicated that individuals were at an increased risk of having OSA if they had a high BMI, hypercholesterolemia, hypertension, diabetes, current depressed mood and if they were a male. This supports the first proposed hypothesis, that the OSA group would have more comorbid conditions than the non-OSA group. OSA group also had significant findings for having poorer subjective sleep quality, through having a higher PSQI sum composite score and having a higher score or PSQI 7 - daytime dysfunction. This increase in score denoted a higher impairment in sleep quality. It was also found that the OSA group were more likely to record false alarms on the BVMT-R, thus signaling a possible neurocognitive deficit. These OSA findings were predicted and supported through previous research studies. While these results do have some support for the OSA hypotheses initially stated in the study, there were only significant findings for a small number of examinations out of the many that were administered.

This study also investigated the relationship between CPAP-compliance and participant health. We found that the CPAP-compliant group were at lower risk for

hypertension, diabetes, and current depressed mood. Additionally, it was found that the CPAP-compliant group had better subjective sleep quality, fewer sleep disturbances, decreased daytime dysfunction, and lower sum composite scores on the PSQI compared to CPAP noncompliant group. All of these results suggest support for the original hypothesis that the CPAP-compliant group would have better sleep health. However, this study did not support its last hypothesis and failed to find any neurocognitive benefits of CPAP-compliance.

While we found mixed results in supporting our initial hypotheses, we had zero significant findings regarding actigraphy with any of our participant data. However, previous studies have shown that it can be difficult to have significant findings with actigraphy, especially with only 7 days worth of data. Our study has other limitations that could have affected our findings. First, we had a relatively low N for OSA and CPAP-compliance groups (N=22). Additionally, the demographics questionnaires administered offered little insight into further patient history of OSA and CPAP-compliance. There was no severity index for participant OSA, such as the well known apnea-hypopnea index (AHI), and the demographics information only included a 'yes/no' option for physician-diagnosed OSA. Similarly, patients were not asked about their CPAP-compliance in depth. CPAP-compliance has a vague and un-agreed upon meaning not only for lay individuals but for the scientific community as a whole.

Future studies would benefit greatly from more precise demographics information, especially regarding OSA and CPAP-compliance. While this study did have its limitations, there were several significant findings that support some of our initial hypotheses and previous research studies. Most importantly, it helps to further bolster the

importance of early detection and diagnosis of OSA and increased use in CPAP mask treatment, by demonstrating the many negative consequences surrounding both OSA and CPAP noncompliance. Furthermore, this study helps support why we should increase resources to public health programs to educate the populace on OSA and the ever-increasing importance of using CPAP treatment. Finally, this study has helped us to learn more about the new novel sleep study mattress-sheet device and the possibility for in-home sleep studies. It is believed that these in-home sleep studies will one day help replace current sleep study methods inside sleep clinics, as participants are able to get a more 'normal' and complete rested sleep within the confines of their own bedrooms.

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AUTHOR'S BIBLIOGRAPHY

Bailey was born and raised in Central Maine and graduated from Winslow High School in 2016. Wanting to stay close to his home, he attended the University of Maine in hope to one day become a physician. During his freshman year Bailey joined the University Volunteer Ambulance Corps (UVAC) and earned his EMT license. In addition to UVAC, Bailey has worked at other local EMS agencies, igniting his passion for public health. While attending the University of Maine, Bailey has been apart of several local health programs including Medical Outreach Maine, an emergency department clinical research intern, CPR instructor, and policy intern at the Maine Medical Association. Additionally, Bailey also found his passion for teaching and mentoring his fellow students and became a Maine Learning Assistant (MLA) in biology, the President of the Health Professions Club, and overseeing the training of new EMTs as the Assistant Chief of Operations at UVAC. After his graduation, Bailey will be attending medical school in July.