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Cognitive-Affective Processing, Sleep Quality, and Mood in Obstructive Sleep Apnea

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by

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and Mood in Obstructive Sleep Apnea

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DECLARATION OF ORIGINALITY

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ABSTRACT

OBJECTIVES : Extant experimental research implicates sleep disturbance as causal to dysregulation of emotional processes and neurocognitive functioning. Clinical research with psychiatric samples suggests that sleep disturbance may be an etiological or sustaining factor in certain conditions, rather than solely a symptom. Recently proposed models have hypothesized cognitive-affective processing (CAP) as a potential mediator for the relationship between sleep disturbance and depressed mood. This study investigated relevant neuropsychological and sleep-physiological variables to explore the applicability of this type of model within a sleep apnea referral sample.

METHODS: 61 participants referred for polysomnogram also completed self-report measures of mood and sleep, as well as a neuropsychological battery consisting of standard neurocognitive measures and novel cognitive-affective processing counterpart measures.

RESULTS: Correlational and ANCOVA analyses suggested cognitive-affective processing measures were potentialy more sensitive toward dysfunction secondary to sleep-disordered breathing than standard neurocognitive measures. Regression analyses were mixed, while most of the a priori model was confirmed, unexpected null findings between sleep physiology and depression suggested poor fit for this sample. Exploratory analyses suggest there may be a more complex model relating the three constructs of interest, incorporating related sleep physiology and affective state constructs.

CONCLUSIONS: Within our sample, findings suggest dysfunctional sleep-breathing physiology impacts the affective valence of previously identified subcortical-frontal retrieval dysfunction. The relative absence of findings within standard measures suggests that cognitive-affective processing measures may be more sensitive to finer gradients of sleep disturbance severity. Additionally, this finding is independent of the incidental findings that the cognitive-affective processing is sensitive to negative mood and psychological distress about lack of sleep, suggesting the neurocognitive measure is sensitive to both physiological and psychological sequelae. This study provides initial support for a neuropsychological measure of how humans process emotionally-laden information, which has significant potential for use in research and clinical fields. Future research will generate normative data for the novel cognitive-affective processing measures, as well as explore the original and expanded model of negative mood within other psychiatric and neurological samples.

Keywords: Sleep, Cognitive Processing, Emotional Processing, Depression, Obstructive Sleep Apnea

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CHAPTER 1

INTRODUCTION

Relevance & Importance

Deficits in sleep quality and associated sleep loss are experienced by nearly all people at some point during life, whether from lifestyle or disorder, and whether chronic or acute. These periods of disturbed sleep are usually limited in their length and incidence, but for many individuals they can last for extended lengths of time, and often re-emerge at various points of a lifetime. Even relatively mild and limited periods of disturbed sleep are associated with a myriad of daytime behavioral impairments. Research has estimated that the overall prevalence rate of adults obtaining insufficient sleep is 20% (Hublin, Kaprio, Partinen, & Koskenvuo, 2001). Additionally, a study of over 1,000 young adults over 5.5 years found that the degree of this partial sleep deprivation was proportional to the amount of daytime sleepiness experienced (Breslau, Roth, Rosenthal, & Andreski, 1997). Neurocognitive functioning is thought to mediate the relationship between sleepiness and behavioral performance decrements, which in turn are directly related to the occurrence of functional accidents in everyday life.

Overall, accidents related to some degree of sleep deprivation have been estimated to have an economic impact ranging between $43 and $56 billion (U.S.; Leger, 1994). Motor vehicle collisions are the most commonly associated cost of sleep deprivation, yet are thought to be highly underestimated (Horne & Reyner, 1999; McCartt, Ribner, Pack, & Hammer, 1996; Mitler, Carskadon, Czeisler, Dement, Dinges, & Graebner, 1988). In addition to motor vehicle collisions, sleep deprivation research has repeatedly found that airline pilots (Bourgeois-Bougrine, Casrbon, Counelle, Mollard, &

Coblentz, 2003; Price & Holley, 1990), truck drivers (Lyznicki, Doege, Davis, & Williams, 1998; McCartt, Rohrbaugh, Hammer, & Fuller, 2000), medical residents (Landrigan, Rothschild, Cronin, Kaushal, Burdick, Katz, et al., 2004; Lockley, Barger, Ayas, Rothschild, & Czeisler, 2007), shift workers (Richardson, Miner, & Czeisler, 1989-1990), and other professions are at high risk for making high-damage accidents due to sleepiness and its related sequelae. Blood alcohol content (BAC) is a useful comparison metric for sleep deprived populations. Driving performance for those deprived of one night of sleep was found to be equivalent to those non-sleep deprived individuals driving with a BAC of 0.07% (Fairclough & Graham, 1999); for comparison, driving in the state of Michigan or Ontario with a BAC of 0.08% or higher is illegal. Multiple other studies have found that as uninterrupted waking periods exceed 16 hours, psychomotor performance impairments progressively increase to levels comparable to BACs ranging between 0.05% and 0.1% (Dawson & Reid, 1997; Williamson & Feyer, 2000).

In addition to functional accidents, disturbed sleep is demonstrated to cause significant quality of life decrements, which strongly drive patients to seek assistance. Reimer and Flemons (2003) conducted a literature review investigating how sleep quality and quantity correlated with a wide range of domains that contribute to quality of life. They found that across all measures and etiologies of disturbed sleep, quality and quantity of sleep were related to some or all measures. For instance, the large Sleep Heart Health Study (n = 5816), in which 90% of participants received an in-home polysomnograph, found that those suffering from excessive daytime sleepiness had significantly poorer quality of health in all subscales measured (Baldwin, Griffith, Nieto, O'Connor, Walsleben, & Redline, 2001). In clinical sleep-disordered breathing

populations (of which obstructive sleep apnea is the predominant diagnosis), symptomatic *fragmented sleep* (meaning many sub-conscious arousals from deep sleep throughout a night) has been associated with increased mortality, abnormal waking electroencephalograms (EEG), metabolic and endocrine dysregulation, decreased immune and inflammatory responsivity, and cardiovascular sequelae (Dinges, Rogers, & Baynard, 2005). In sum, sleepiness secondary to poor sleep is associated with neurocognitive dysfunction, behavioral accidents, and quality of life decrements (both mood and functional).

Relatively recent improvements in the methodology available for sleep research (e.g. polysomnogram, functional imaging) have allowed for more detailed investigation of the relationship between quality and quantity of sleep and daytime behavioral outcomes. The following sections will briefly review the current understanding of sleep physiology, explain how it relates to neurocognitive processing, cognitive-affective processing, and mood, and finally introduce a published cognitive model of sleep-dependent emotional processing in order to guide proposed investigation of neuropsychological functioning in obstructive sleep apnea.

Sleep

The following section is a significantly condensed overview of sleep physiology, emphasizing the introduction and definition of terminology that is relevant to the present study. An expanded version of this section is available in Appendix A.

Sleep Stages and Characteristics

Sleep in mammalian species has been generally categorized into two separate types - rapid eye movement (REM) sleep, and non-rapid eye movement (NREM) sleep, which has predominantly been further subdivided in primates into four, progressively deeper, stages (Rechtschaffen & Kales, 1968). Research in human sleep patterns has identified a 90 minute alternating, ultraradian cycle between NREM and REM sleep. The American Academy of Sleep Medicine (AASM; Iber, 2007) recently updated the terminology used to break sleep down based on electroencephalograph (EEG) readings into REM sleep, and NREM stages labeled N1, N2, N3.

Table 1 summarizes the EEG (AASM, 2007; Steriade & Amzica, 1998), neurochemical (Rosenthal, 1998; Saper, Chou, & Scammell, 2001), and functional anatomic characteristics (Nofzinger, 2005) associated with each stage.

Table 1

Summary of EEG, Neurochemical, and Neurofunctional Characteristics of Sleep Stages

State	EEG	EEG markers	Sleep Characteristics	Neurochemical	Functional
Awake	Desynchronized beta waves (12-30 Hz)			RAS efferents to HT, THAL, BFB Use CA, HTM, ACh, Asp, Glu	
N1	Transition from alpha waves (8-12 Hz) to theta waves (4-7 Hz)		Drowsiness If woken, will report not having been asleep	GABAergic neurons in cortex, THAL, and HT highly active Decreased subcortical cholinergic systems of forebrain and brainstem	Reduced activity of the PFC, TL, BG, THAL, brainstem Reduction level intensifies with progression through N1-N3
N2	11-16 Hz, but predominately 12-14 Hz	Sleep spindles K-complexes	Tranquil state maintained 50% of total sleep time		
N3	0-4 Hz, at least 20% delta waves (0.5-2 Hz)	Slow-wave sleep (SWS)	Mass cortical synchronization (organization processing related to daytime cognition)		
REM	Theta wave reemergence (4-7 Hz) High frequency gamma waves (30-80 Hz)	PGO waves (originating from pons, LGNT, & OC)	Rapid eye movement bursts in rhythm with PGO waveforms 20-25% of total sleep over 4-5 periods Descending muscle atonia & increased variability of heart/breathing rate & temperature	ACh neurons of PT = "REM-on cells," highly active 5HT & NE neurons of Raphe & LC = "REM-off cells," are deactivated	Increased activity of the mbPFC, OC, Thalamic nuclei, PT, ACC, AMYG, HPC Decreased activity of the PCC, PL, dlPFC

Note, top-bottom & left-right: PGO - Ponto-geniculo-occipital, LGNT - lateral geniculate nucleus of the thalamus, OC - occipital cortex, RAS - reticular activating system, HT - hypothalamus, THAL - thalamus, BFB - basal forebrain, CA - catelcholomines, HTM - histamine, ACh - acetylcholine, Asp - asparate, Glu - glutamate, GABA - gamma-aminobutryic acid, PT - pontine tegmentum, 5HT - serotonin, NE - norepinepherine, LC - locus coeruleus, (mb/dl) PFC - (mediobasal/dorsolateral) prefrontal cortex, TL - temporal lobe, BG - basal ganglia, OC - occipital cortex, ACC - anterior cingulate cortex, AMYG - amygdala, HPC - hippocampus, PCC - posterior cingulate cortex, PL - parietal lobe

Sleep-Wake Cycle

Three separate yet networked neuroanatomical systems regulate the sleep-wake cycle in humans (Borbely & Achermann, 1999; Pace-Schott & Hobson, 2002).

A *homeostatic regulation system* is responsible for intensity, length, and quantity of sleep. Adenosine has been identified as a molecular-level somnogen integral to this system at the cellular level. During wakeful periods, it is hypothesized to naturally accumulate to levels that impact sleep/wake related areas of the brain. This nucleoside has an activating effect on ventrolateral preoptic area neurons bordering the basal forebrain and an inhibitory effect on wake-promoting areas of the basal forebrain (Porkka-Heiskanen, Strecker, Thakkar, Bjorkum, Greene, & McCarley, 1997). Thus, during wakeful accumulation of adenosine, a drive towards sleep accrues. Preoptic neural circuitry has been associated with the homeostatic functions.

A *circadian system* manages the timing of sleep and wake periods within the overall day-night cycle, promoting both wakefulness and sleep - at opposite phases. The anterio-hypothalamic elements are associated with circadian functions. The circadian timing system (CTS) is comprised of three components, the central of which is the suprachiasmatic nucleus (SCN) of the anterior hypothalamus, which acts as a circadian pacemaker - coordinating circadian oscillator subcomponents via control over melatonin secretion by the pineal gland (Rossenwasser & Turek, 2005). The SCN is responsible for establishing the sleep-wake circadian rhythm. The SCN is entrained (i.e., synchronized) via physiological and environmental signals. The subcomponent circadian-oscillators in peripheral tissues are in turn entrained by physiological signals from the pacemaker component. Peripheral circadian oscillators are understood also to contain endogenous,

cellular-level pacemaker "clock cells," independent of the circadian system as a whole (Herzog, 2007). The SCN is thus thought to entrain the various peripheral cellular oscillators rather than sustain their rhythmic activity (Okamura, 2004). The third component of the CTS are the efferent projections that serve to regulate otherwise non-rhythmic physiological and behavioral systems (e.g., body temperature, autonomic/endocrine systems, feeding, sleep/wake state, locomotor activity).

The cyclical vacillation between REM and NREM sleep within each sleep period is controlled by an *ultradian system*. Mesencephalic and pontine rostral brainstem areas are associated with REM/NREM regulation; Table 1 offers more details.

Saper, Chou, and Scammell (2001) reviewed recent literature on sleep regulation and identified a substantial amount of evidence that a reciprocal inhibition model of sleep and arousal systems exists; they termed it a *sleep-wake switch*. GABAergic and galaninergic neurons of the ventrolateral preoptic nucleus (VLPO) are active and necessary for normal sleep. In contrast, hypocretin/orexin (exchangeable names) neurons within the posterior lateral hypothalamus (PLHT) are necessary for maintaining normal wakefulness. These two systems are thought to exist in a sustained state of balanced reciprocal inhibition (a bi-stable feedback loop) when not influenced from external pressures. Once either of the systems is excited, it inhibits the other, thereby resulting in further excitation due to decreased inhibitory afferents from its partner. In sum, human sleep physiology can be conceptualized as three gears nested within each other, with the transition between sleep and wakefulness occurring in rapid fashion when the homeostatic and circadian gears align.

Sleep Deprivation

Basal sleep need is defined as habitual sleep duration in the absence of any sleep debt. Sleep debt is conceptualized as "the fundamental duration of sleep below which waking deficits begin to accumulate" (Dinges, Rogers, & Baynard, 2005, p. 68). Both experimental and epidemiologic research has found high interindividual variance in amount of sleep habitually obtained. A large study found that after long-duration sleep designed to eliminate sleep debt, average sleep length stabilized at 8.17 hours (Wehr, Moul, Barbato, Giesen, Seidel, Barker, & Bender, 1993); another large, dose-dependent sleep deprivation study statistically estimated a daily requirement of 8.16 hours of sleep to avoid negative impacts on functioning during the subsequent wake period (Van Dongen, Maislin, Mullington, & Dinges, 2003). The following section will discuss a number of past and present theoretical frameworks for understanding sleep deprivation.

Models

In the 1980's, a two component hypothesis of sleep gained popularity - core and optional sleep (Horne, 1988). The analogy of appetite was cited by its proponents, in which hunger cues consumption of food until satiation, but additional food can be consumed beyond the body's immediate need. Core sleep is composed of primarily slow wave sleep, and it is the quality and length of this period of sleep that determines the degree of daytime cognitive functioning and alertness. Optional sleep is conceptualized as superfluous, or a luxury without confirmed function; one proposed possibility is that optional sleep serves as an evolutionary behavioral carry-over meant to keep the individual withdrawn and safe during the remaining hours of darkness. Proponents redefined the average amount of core sleep required each night from 4-5 hours to 6 hours. However, if this were true, chronic sleep restriction of 6 hours would not be expected to

result in detrimental functional impacts in humans, which is not the case (Van Dongen, Maislin, Mullington, & Dinges, 2003). That study will be addressed in more detail below.

Another hypothesis proposes that at the onset of a chronic restriction of sleep time, acute neurobehavioral functioning decrements occur, but that over time individuals are able to adapt to the new, reduced sleep period. Research has shown that self-reports of sleepiness drop after an initial spike when sleep time is chronically restricted to 4-6 hours per night, up to 8 months (Belenky, Wesensten, Thorne, Thomas, Sing, Redmond, et al., 2003; Lubin, 1967). Abruptness of sleep restriction is an important moderating factor within this hypothesis, with research demonstrating that gradual (versus precipitous) accumulation of a set amount of sleep debt resulted in neurobehavioral performance decrements smaller in magnitude (Van Dongen, Maislin, Mullington, & Dinges, 2003). Other research suggests that adaptation to sleep deprivation may differ depending on which neurobehavioral outcomes are measured. It appears that waking EEG and non-REM slow-wave sleep (SWS) show the most and quickest adaptation, subjective sleepiness shows slower and less adaptation, and that neurocognitive functioning shows the slowest and least adaptation to sleep deprivation (Van Dongen, Rogers, Dinges, 2003; Van Dongen, et al., 2003).

A bio-mathematical two-process model taps the well-researched regulation components of sleep: (1) the homeostatic process that exponentially builds during waking periods and exponentially declines during SWS periods, and (2) a near-24 hour circadian regulation process. The hypothesis proposes that wakeful cognition is primarily based on alertness (A), and that this construct could be mathematically modeled as the quantitative difference between the homeostatic process (S) and the circadian process (C): A=S-C. In

a blind study, this model was found to accurately predict neurobehavioral responses based on total sleep deprivation, but failed to accurately predict cognitive performance and sleepiness across a chronic sleep deprivation paradigm (Borbely & Achermann, 1999).

All of the prior hypotheses and models share a common feature in their conceptualization of chronic sleep deprivation, which is an emphasis on cumulative sleep time lost. The "wake extension" hypothesis approaches alterations of the sleep-wake cycle from a different angle, instead emphasizing cumulative wake-time cost. Proponents attempted to reconcile the neurocognitive results found in complete sleep deprivation and those from chronic sleep deprivation by positing that during periods of wakefulness, neurobiological costs/consequences accumulate (Van Dongen, Maislin, Mullington, & Dinges, 2003).

Researchers used a sleep dose-response experiment (8, 6, or 4 hours in bed across two weeks, and a 0 hours in bed condition across 3 days) to investigate their hypothesized model. Results showed a near-linear accumulation of cognitive performance deficits across all conditions. The rate (slope) of deterioration was inversely related to amount of sleep time; the 0 hour condition demonstrated the highest rate of deterioration. At the two week period, the 4 hours time in bed (TIB) condition was performing with similar cognitive decrements to the 0 hours TIB at the three day mark. Calculating the cumulative sleep loss for each condition reveals that the 4 hour TIB group had lost approximately 55 hours of sleep, whereas the 0 hours TIB group had lost approximately 25 hours. To reconcile this inconsistent observation, the wake-extension time (defined as "continuous wake duration" - "habitual wake duration") was calculated for each group.

This approach resulted in the same values across the restricted sleep conditions as the previous approach. *However*, for the full sleep deprivation condition, each day after the end of the first "habitual wake duration" added a full 24 hours to the wake extension time, thereby bringing the observed deficits into alignment with quantification of sleep/wake disruption (for visual representation of this phenomenon, see Figure 4 within the Van Dongen et al., 2003 paper). This study clearly demonstrates that cumulative wake extension and cumulative sleep loss are different constructs with different quantitative values dependent on how sleep loss occurs. Further, it suggests that the field should conceptualize sleep debt as an accrual of wakefulness beyond roughly 16 hours with an associated neurobiologic cost.

Disturbed Sleep & Neurobehavioral Functioning

Sleep deprivation results in increased sleep propensity, as measured by reduced sleep onset latency and reduced latency between the transition from lighter NREM sleep to SWS on polysomnograms (PSG; Carskadon & Dement, 1987). After one night of complete sleep deprivation, average sleep onset latency drops to less than 1-2 minutes, and the time to progress from sleep onset to deep SWS is halved (Dinges, 1986). Progressive reductions in daytime sleep onset latency has also been demonstrated in a week long, 5 hour sleep restriction paradigm (Carskadon & Dement, 1981). Increased sleep propensity, even when being resisted, results in the occurrence of microsleeps intruding into wakefulness (Akerstedt, 1987). The state instability hypothesis posits that neurocognitive performance becomes progressively more variable as homeostatic pressure accumulates and increasingly disrupts normal neurocognitive processing, which

begins to become more dependent on compensatory mechanisms (Doran, Van Dongen, & Dinges, 2001). Behavioral examples of these compensatory mechanisms include sleep-deprived individuals falling asleep while walking and "semidreaming" while performing verbal cognitive tasks (Kleitman, 1963; Dinges, 1990). Errors of commission are explained as ineffective compensatory efforts initiated during the resistance of sleep (Durmer & Dinges, 2005). Thus, at any given moment, sleep deprived individuals produce widely varied neurocognitive and neurobehavioral performance.

Effects of Disturbed Sleep on Cognitive & Behavioral Functioning

There are several broad findings in the research addressing cognitive performance in sleep deprived and partial sleep deprived healthy individuals that must be considered before reviewing domain-specific findings. Research suggests that sleep deprivation often has unexpectedly measure-specific performance impacts; for example, a study found that after a 5 night, 40% reduction of habitual sleep time, performance decrements on a measure of vigilance and simple reaction time were observed but no deficits were noted on a measure of choice reaction time (Herscovitch & Broughton, 1981). This may be due to psychometric properties of different measures, or perhaps that the impact of sleep deprivation is nuanced and focal rather than broad, even within traditionally internally consistent cognitive domains (Dinges, Rogers, & Baynard, 2005). Cognitive decrements have generally been found to be dose-dependent to the amount and length of sleep restriction (Belenky, Wesensten, Thorne, Thomas, Sing, Redmond, et al., 2003). As previously discussed, extended periods of restricted sleep have an accumulating impairing effect that can eventually become equivalent to acute sleep deprivation (Van Dongen, Maislin, Mullington, & Dinges, 2003). Finally, neurobehavioral performance

deficits associated with sleep deprivation vary significantly between individuals, above and beyond differences in sleep histories. In fact, it appears that vulnerability or resiliency to sleep deprivation is a trait, though no neurobiological correlates have been identified thus far (Van Dongen, Baynard, Maislin, & Dinges, 2004). Though average deficits scores are stable within-subjects, a hallmark of sleep deprivation is a significant increase in variability of test performance, between and within measures; this is thought to reflect the transitory nature of attentional lapses (Waters & Buck, 2011).

To offer a launching point for the following discussion, consider the following. A large meta-analysis has concluded that upon collapsing measures of three areas of functional level (cognition, mood and fatigue, and motor functioning), "any sleep-deprived individual is estimated to be comparable to the 9th percentile of non-sleep-deprived subjects" (p. 120, Durmer & Dinges, 2005). Effect sizes for the impact of sleep loss have generally been classified in the moderate range (Lim & Dinges, 2010). Meta-analysis also found that cognition and mood were affected worse by partial sleep deprivation than total, though the reverse is true for behavior (Pilcher & Huffcutt, 1996). In general, performance on cognitive tasks becomes progressively worse as task engagement time is extended, in an exacerbated "fatigue" effect phenomenon (Kribbs & Dinges, 1994). Conversely, brief measures with an emphasis on speed or time also are sensitive (Dinges, 1992). Finally, early theories on cognitive decrements following disrupted sleep hypothesized that decreased motivation mediated the performance deficits. However, sleep deprived populations have been demonstrated to pass neuropsychological measures of adequate effort, as well as perform poorly on high novelty tasks designed to be intrinsically engaging, suggesting that interest and effort are

not significant etiological factors in explaining cognitive performance declines (Harrison & Horne, 2000; Wilkinson, 1961).

Durmer and Dinges (2005) reviewed the literature on the neuropsychological performance impact of sleep deprivation and identified a number of reliably affected cognitive processes. This section summarizes the majority of their findings, and includes more recent research findings to expand upon their review. First, there will be a discussion of the cognitive findings associated with large amounts of sleep deprivation (i.e. 4 or less hours per night), then these will be related to partial sleep deprivation and fragmented sleep.

Individuals who have been deprived of sleep demonstrate slowing on subject-paced tasks, and make increased errors when a time pressure component is present. Not unexpectedly, this *processing speed* deficit is also reliably demonstrated in reaction time measures. Speed of information processing has been demonstrated to be reliably impacted by any disruption of normal sleep, with a 27 study meta-analysis finding that speed was the most impacted cognitive construct, followed by accuracy (Koslowsky & Babkoff, 1992; Waters & Bucks, 2011). Eye-hand coordination and psychomotor performance consistently show decrements of roughly 30% in speed and accuracy after sleep deprivation (Williamson & Feyer, 2000).

Tasks that require continued *attention and vigilance* are negatively impacted by sleep deprivation, with increases in omission and commission errors. The functional impact of increased attentional fatigue negatively affects performance on sustained attention measures, as well as on other neuropsychological measures that require extended periods of attention. In fact, a meta-analysis of 70 studies concluded that

extended simple attention is more significantly impacted than performance on tasks requiring divided attention (Lim & Dinges, 2010). For example, on cognitive tasks with a learning component, sleep deprived individuals are less efficient at reaching equivalent levels of acquisition, though often can reach normative expected performance levels when given additional time and exposure to the stimuli. *Short-term recall* for successfully encoded information has also been shown to suffer post-sleep deprivation. After 1 night of sleep deprivation, individuals scored worse on measures of visual and verbal short-term memory, and performance was related to the magnitude of abnormally decreased intraparietal sulcus and hippocampal activity (Chee & Chuah, 2007; Chen, Hardy, Zhang, LaHoste, & Bazan, 2006; Van der Werf, Altena, Schoonheim, Sanz-Arigita, Vis, De Rijke, et al., 2009). *Working memory* tasks that require maintenance and manipulation of information from multiple modalities are compromised as well, resulting in difficulty with temporal organization of information, decreased ability to maintain flexible thinking, and decreased ability to filter distractions and maintain focus on relevant information and cues. One study estimated working memory performance drops averaging 37% after large amounts of sleep deprivation (Turner, Drummond, Salamat, & Brown, 2007).

Neuropsychological measures thought to rely on more complex cognitive processes have often been considered insensitive to partial sleep deprivation. It is thought that problem-solving and critical thinking based tasks allow for convergent skills being tapped in parallel, permitting intact performance via compensatory support from less affected systems (Waters & Bucks, 2011). However, consistent with the weaknesses previously noted in more simple working memory tasks, sleep deprived individuals have

impaired performance on certain complex cognitive tasks that require *executive functions* such as mental flexibility and multitasking, perhaps reflecting the increased variability in general cognitive performance following sleep deprivation. More specifically, divergent thinking tasks that require lateral thinking, assimilation and utilization of feedback, and risk assessment all show decrements after sleep deprivation. Executive processing errors such as decreased insight into performance decrements, suppression of inappropriate responses, and increased ineffective response perseveration are also well-documented. Associated with the decrements in executive functioning, sleep deprived individuals rely more heavily on compensatory effort to maintain adequate performance; this comes at the cost of situational awareness, as neglect for activities and stimuli judged to be nonessential increases (Durmer & Dinges, 2005).

The deficits discussed have led researchers to conclude that deprivation of sleep negatively impacts performance on tasks believed to originate from or mediated through the prefrontal cortex (PFC) - for those tasks that are attention-rich, more specifically, the dorsolateral PFC (Kane & Engle, 2002). When sleep restriction is increased to complete deprivation for 36 hours, research found that young participants produced neuropsychological deficit profiles comparable to an elderly habitual sleep group (Harrison & Horne, 2000). This is consistent with current attribution of documented neurocognitive deficits in aging to declines in PFC functioning (Corey-Bloom, Wiederholt, Edelstein, Salmon, Cahn, & Barrett-Connor, 1996). Functional neuroimaging research suggests that two elements of the functional network connected to the PFC are disrupted after sleep deprivation (Harth, 1995; Posner, 1994). The first is an anterior network consisting of the PFC, basal ganglia, and anterior cingulate, which are involved

in selective attention and the mental maintenance of a memory for immediate manipulation (i.e. working memory). The second is a posterior network consisting of the superior parietal lobes, pulvinar, and superior colliculus, which is thought to control attentional switching and divided attention. The anterior cingulate has afferent projections to the superior parietal lobes, and is innervated by the PFC, connecting the three network components.

Significant-to-complete sleep deprivation is a useful paradigm to research the neurocognitive correlates of decreased sleep; however, the ecological application is limited. Sleep decrements *in vivo* generally take the form of partial sleep deprivation or fragmented sleep. Recent research that has improved methodological controls for sleep history and external influencing factors has found that 4 or more days of 7 or less hours of sleep restriction per night results in measureable decrements in neurobehavioral functioning and performance (Belenky, Wesensten, Thorne, Thomas, Sing, Redmond, et al., 2003; Dinges, Pack, Williams, Gillen, Powell, Ott, et al., 1997). Restriction between 6 and 3 hours per night results in increased sleep propensity, working memory deficits, and impaired sustained attention and vigilance (Carskadon & Dement, 1981; Drake, Roehrs, Burduvali, Bonahoom, Rosekind, & Roth, 2001). The most extensive study on sleep deprivation and restriction to date, conducted by Van Dongen and colleagues (2003), was previously discussed, confirming that sleep restriction induced neurocognitive performance decrements accumulate to levels equivalent to acute complete sleep deprivation. While occupational research on partial sleep deprivation is relatively common (e.g., for air traffic control, heavy machinery operators, etc.), a relatively under-researched area is the impact of sleep deprivation on everyday complex tasks with high

potential risk, such as driving. An epidemiological study found an elevated occurrence of sleep-related vehicle crashes in those individuals who reported an average of less than 7 hours of sleep per night (Strutts, Wilkins, Osberg, Vaughn, 2003). Driving simulator research has found that 1 night of restricted sleep (5 hours) results in decrements of performance in simulated normal driving conditions and situations requiring emergency maneuvers (Horne & Baulk, 2003). Another two studies found that chronic restriction of sleep (time in bed between 4 and 6 hours) is associated with a significant increase in number of accidents, and rates increase further after 2 nights of this degree of sleep restriction (Dorrian, Dinges, Rider, Price, & Rogers, 2003; Rupp, Arnedt, & Carskadon, 2003).

Fragmented sleep refers to repeated arousals (3+ seconds of disrupted EEG frequency in NREM or increased electromyographic frequency during REM) occurring throughout a sleep period. Arousals do not result in awakenings. However, multiple studies have demonstrated that persistent fragmentation of sleep results in the same effects on daytime somnolence, mood alteration, and cognitive performance decrements as partial sleep deprivation (Bonnet, 1985; Bonnet, 1986; Bonnet, 1989; Martin, Engleman, Deary, & Douglas, 1996). In fact, arousals occurring at an average rate of once per minute throughout a sleep period of normal duration result in neurocognitive performance decrements equivalent in pattern and magnitude to that of 1 night of complete sleep deprivation (Bonnet, 1986; Downey & Bonnet, 1987). This is not an unusual fragmentation pattern for those suffering from intrinsic sleep disorders such as obstructive sleep apnea (Durmer & Dinges, 2005). These findings hold true in quasi-experimental studies measuring cognitive performance of those with endogenous

fragmentation of sleep, as well as experimentally fragmented sleep using aural stimulation (Martin, Wraith, Deary, & Douglas, 1997). A detailed discussion of cognitive, behavioral, and mood decrements in the obstructive sleep apnea (OSA) population is provided later in this review. Finally, of considerable importance is the finding that across all domains, cognitive deficits are reversible following a period of normal sleep, which means that cognitive dysfunction attributed to disrupted sleep should be framed in remediable terms and highlights the clinical importance of sleep intervention (Waters & Buck, 2011).

Sleep & Affect

Affective Processing

The ability to effectively and efficiently process affective-based stimuli is crucial for human functioning from a socio-evolutionary perspective, as suggested first by Charles Darwin in 1872 (Norris & Cacioppo, 2007). The generation and regulation of emotions and the guidance provided by emotional content and cues is fundamental to individual mental health, interpersonal functioning, and societal structure. In the past decade, cognitive neuroscience and clinical neuropsychology have rapidly embraced and investigated the domain of emotional or affective processing as a critical element of normal and abnormal cognition, and recognized the relationship between affective processing and clinical mental health (Labar & Cabeza, 2006). The following will provide a brief outline of a systems-level framework of affective informational processing.

To discuss affective processing, a few terms and constructs should be clarified. For the purposes of this review, the term *emotion* is meant to represent a complex physiological, behavioral, and cognitive experience associated with the onset and maintenance of mood/s. *Affective* is a descriptor meant to refer to characteristics that conveys emotionally-relevant information, and *affect* is meant to refer to the process or state of consciously labeling and experiencing internal emotional states (generally resulting in phenotypic expression of the emotion, as often commentated on clinically). Thus, affective processing is a form of information processing whereby emotionally-relevant information is gleaned from a stimulus, analyzed, and then utilized in order to facilitate correct/adaptive/appropriate reaction. Suchy (2011) posits that there are three theoretical properties that are necessary for an affective processing system (APS). First, the brain's APS needs the ability to detect emotionally-germane stimuli and judge the affective qualities and characteristics (e.g., valence and intensity) quickly (likely incorporating aspects of preconscious detection) in order to facilitate an immediate, adaptive reaction. Second, an APS must also be able to initiate and maintain physiological, behavioral, and cognitive events that comprise the response. Third, an association and memory component is required to learn emotionally relevant characteristics of a stimulus that was initially emotionally-neutral. Two related neural circuits are involved in triggering emotional responses to stimuli - the amygdala processes and responds to external stimuli, and the hypothalamus processes and responds to disruption to internal homeostasis. The following will focus on the amygdala, as this process involves the reviewed and proposed research methodologies.

Two information processing routes exist, with both sharing an input pathway and the amygdala acting as a mediator for behavioral and physiological responses (Suchy, 2011). The "fast route" (≈10-12 msec.) of affective information processing begins with the sensory organ input projecting to the thalamus and primary visual cortex, where crude, basic information (i.e., valence and intensity) regarding the stimuli is perceived. The fast route next consists of this affective information being received by the basolateral amygdala which projects to the orbitofrontal cortex and striatum involved with emotional learning circuitry, and also to the central nucleus of the amygdala which in turn projects to the hypothalamus and brainstem nuclei to generate physiological and behavioral responses. The "slow route" (≈30-40 msec.) involves primary association cortices that supply information about the perceived stimuli and supramodal association cortices that supply more abstract and contextual meanings about the stimuli. These include the secondary sensory cortex, tertiary sensory cortex, and hippocampus.

The integration of affective processing and cognitive research has resulted in some domain-specific findings. Attentional blink paradigms have shown that responding to a target during rapid stimuli presentation causes momentary depletion of attentional resources, resulting in missed targets that immediately follow a first target. Strong affective valence of the second target ameliorates this depletion. However, individuals with amygdala damage cannot benefit from this phenomenon (Anderson & Phelps, 2001). Significantly faster psychomotor response speed has also been found for negative/threatening valenced stimuli, above and beyond that which can be explained by increased provision of attentional resources to the stimuli (Flykt & Caldara, 2006; LoBue & DeLoache, 2008). The amygdala has also been found to facilitate episodic memory for

affectively salient stimuli (Frank & Tomaz, 2000). This occurs due to improved encoding via amygdala modulation of the perceptual cortical areas and improved consolidation of affective stimuli in proportion to the relative survival importance of the associated outcome (Phelps, 2004). Individuals with damaged or dysfunctional amygdala do not benefit from the memory facilitation by affective characteristics of emotional stimuli as found in healthy controls (Dolan & Fullam, 2010).

The Role of Sleep in Affective-cognitive Processing

The domain of learning and memory is a useful cognitive domain to research as it relates to the affective processing system (APS), as it is understood to tap elements of attention, working memory, and executive functions such as organization. Impact of sleep quality on memory recall has focused on two stages, the initial formation of new memories (encoding), and then the subsequent solidification of the memories (consolidation). Both will be addressed with an emphasis on encoding as it is more germane to this dissertation (Marshall & Born, 2009; Walker, 2009).

Affective Memory Encoding and Sleep

The elicitation of emotional states can strongly modulate the initial stages of learning (i.e., encoding). Stimuli with emotionally arousing affective traits are recalled better than those considered neutral (Buchanan & Lovallo, 2001; Heuer & Reisberg, 1990; Phelps, 2004). The modulation effect of emotionally arousing stimuli on encoding occurs in different ways depending on the affective stimuli's valence (positive, neutral, negative) and arousal level (calm to excitement). High arousal affective characteristics enhance memory encoding through the adrenergic system. Introduction of propanolol (a beta-adrenoceptor antagonist) to individuals prior to exposure to a gradient of different

emotionally arousing stimuli (narratives, individual words) results in a disappearance of the enhancing effects of affect on learning found in control groups (Cahill, Prins, Weber, & McGaugh, 1994; Strange, Hurlemann, & Dolan, 2003). Lesion and functional neuroimaging has identified the amygdala, anterior hippocampus, ipsilateral parahippocampus, and ventrolateral prefrontal cortex as being involved with the formation of memory for affectively-valenced information (Cahill, Haier, Fallon, Alkire, Tang, & Keator, 1996; Dolcos, Labar, Cabeza, 2004; Kilpatrick & Cahill, 2003). In the absence of high arousal, valence of stimuli (versus neutrality) still positively modulates encoding, though this is primarily governed by frontally-mediated strategic and semantic processes outside of the amygdala and paralimbic system (Labar & Cabez, 2006). High arousing stimuli with a negative valence have been found to have the strongest enhancing effect on encoding compared to positive and neutral stimuli (Kensinger & Corkin, 2003).

The above findings relate to individuals under normal sleeping conditions. Beginning at a cellular level, in rodent studies REM sleep deprivation (24-72 hours) has been found to reduce hippocampal neuron excitability and significantly impair long-term potentiation (LTP), a process demonstrated to be a critical mechanism for memory formation (Davis, Harding, & Wright, 2003). The LTP observed after REM sleep deprivation decays within 1.5 hours, suggesting significant impairment in hippocampal plasticity. Behaviorally, avoidance learning, passive avoidance learning, and taste aversion processes are all significantly impaired in rodents following both general sleep deprivation and specific REM deprivation (McGrath & Cohen, 1978; Smith, 1985). Deficits in performance are present even when the deprivation is limited to 5 hours, and

continued practice trials do not result in performance improvements (Gruart-Masso, Nadal-Alemany, Coll-Andreu, Portell-Cortes, & Marti-Nicolovius, 1995).

In one thorough human study, participants were either deprived of sleep for 36 hours or allowed a habitual sleep period, then exposed to emotionally arousing and neutral stimuli (Walker, unpublished results, most recently cited in Saletin & Walker, 2012). All participants then were allowed two habitual sleep periods before recall was tested, thereby controlling for impaired recall due to sleep deprivation confounds; retention of material was thus deemed to represent encoding processes. Control group individuals demonstrated significantly superior retention for positive and neutral stimuli relative to the experimental group. Sleep deprived individuals had significantly impaired retention for neutral stimuli, but even worse retention of positively valenced stimuli (59% reduction relative to control group for positive stimuli) compared to controls. Retention of negative stimuli was not significantly different from that of the control group. In effect, sleep deprivation led to skewed encoding sessions, with the experimental group ending the session with a prevailing dominance of memory for negative material, and far fewer neutral and positive memories. Explanations for this sleep deprivation and affective valence interaction range from suggestions that the arousal levels differ significantly at the neural level of the stimuli (rather than the reported level) which interact with the post-sleep deprivation hypo-activation of the prefrontal cortex and hyper-activation of the amygdala to bias toward successful encoding of negative stimuli versus neutral/positive stimuli (Chee & Chuah, 2008; Kensinger & Corkin, 2004; Yoo, Gujar, Hu, Jolesz, & Walker, 2007). Additionally, as discussed later, the negative affective state in sleep-

deprived individuals could lead to a mood-congruent encoding bias (Lewis, Critchley, Smith, & Dolan, 2005).

Affective Memory Consolidation & Sleep

Currently, research suggests that emotion and affective characteristics of stimuli have a modulating impact on subsequent memory consolidation. Behavioral human studies have found decreased forgetting of affectively valenced material versus neutral material. This retrieval benefit emerges more strongly as the delay between encoding and retrieval attempt increases, as demonstrated in a variety of different delay contrast methodologies: immediate versus 1 hour or 24 hours (LaBar & Phelps, 1998; Sharot & Phelps, 2004, respectively), 20 minutes versus 1 week (Kleinsmith & Kaplan, 1963), and 15 minutes versus 2 weeks (Anderson, Yamaguchi, Grabski, & Lacka, 2006). Research has demonstrated that using pain manipulation and stress hormone introduction (adrenaline and corticosterone) post-learning trials increases amygdala activity and selectively improves long-term memory for affectively valenced stimuli (Cahill & Alkire, 2003; Cahill, Gorski, & Le, 2003). Neurotransmitter research in this area has identified adrenergic transmitters and acetylcholine as co-regulators of the consolidation of memory for affective stimuli. Acetylcholine augments amygdala-reliant memory consolidation; antagonist and agonist introduction into the amygdala of rodents impairs and enhances (respectively) memory for previously learned, valenced material (e.g., fear-conditioning and alteration of reward magnitude paradigms; Power & McGaugh, 2002; Schroeder & Packard, 2002).

In humans, REM sleep characteristics have been noted to be altered after shock-avoidance tasks and contextual fear learning tasks, suggesting that consolidation

mechanisms impact sleep-stage characteristics (Sanford, Silvestri, Ross, & Morrison, 2001; Sanford, Tang, Ross, & Morrison, 2003). Next-day memory retention has been demonstrated to be impaired after sleep deprivation between learning and testing, which is thought to reflect a disruption of memory consolidation (Walker & Stickgold, 2004). Sensitivity to fear-conditioning consolidation deficits appears to be limited to paradigms that disrupt/deprive sleep 0-6 hours after the learning task, suggesting that negatively valenced memory consolidation occurs shortly following learning (Graves, Heller, Pack, & Abel, 2003; Ji, Wang, & Li, 2003). Emerging research suggests a REM-sleep-dependent hypothesis of affective human memory consolidation, elements of which were proposed by both Cahill (2000) and McGaugh (2004). Consolidation of affectively arousing stimuli across a 12 hour day, or a 12 hour period including a habitual sleep period, results in a benefit in consolidation of the affective information only when sleep occurs between learning and testing (Hu, Stylos-Allan, & Walker, 2006). Total sleep deprivation for only the first night after exposure to neutral and valenced visual stimuli resulted in significant decrements in retention for all stimuli at testing 1 week later, however, the greatest decrement was for neutral stimuli (Atienza & Cantero, 2008). The authors hypothesized that the consolidation process for emotionally-relevant memories may be intrinsically more resilient to sleep disruption. Speed of recognition for affectively valenced facial stimuli is increased after a period of sleep, in proportion to the amount of REM sleep experienced. In a separate study the power of right-dominant prefrontal theta activity during REM sleep in a nap following a learning task for neutral/negatively valenced stimuli was also proportionally related to emotional memory increase (Nishida, Pearsall, Buckner, & Walker, 2009; Wagner, Kashyab, Diekelmann, &

Born, 2007). This supports the conclusion of neurophysiological reviews that posit REM sleep representing a brain environment especially amenable to consolidation of memory for affective material, based on its pro-cholinergic (forebrain ACh levels up to four times higher when compared to NREM) characteristics (Marrosu, Portas, Mascia, Casu, Fa, Giagheddu, et al., 1995; Pare, Collins, & Pelletier, 2002; Walker, 2009). One limitation of this area of research is the absence of human investigation using positively valenced stimuli (van der Helm & Walker, 2009).

Emotional Experience, Regulation, & Sleep

Research on the impact of sleep deprivation, or loss, on emotion is limited, despite the fact that nearly all psychiatric and neurological condition involving disturbed mood also have documented, co-occurring sleep disruption. Affective volatility, lability, and irritability are subjectively increased following sleep deprivation (Horne, 1985). Emotional disturbance due to chronic restricted sleep (5 hours per night across 1 week) has been demonstrated to have an accruing impact (Dinges, Pack, Williams, Gillen, Powell, Ott, et al., 1997). Furthermore, restricted sleep has been found to blunt intrinsic positive reactions to rewarding/goal-oriented activities and increase negative emotional reactions toward experiences that disrupt the achievement of goals or rewards (Zohar, Tzischinsky, Epstein, & Lavie, 2005).

Only recently have researchers investigated the interaction between sleep and psychophysiological/emotional reactivity. One functional MRI study exposed controls and sleep deprived (1 night) individuals to images spanning a gradient between negative, neutral, and positive valences (Yoo, Gujar, Hu, Jolesz, & Walker, 2007). Both groups demonstrated increased amygdala activation in proportion to the gradient of the negative

images, but the sleep deprived group showed a 60% increase in extent of activation and three times the volume of amygdala recruitment compared to the control group. Researchers noted decreased functional connectivity between the medial prefrontal cortex and the amygdala, a pathway normally thought to represent frontal inhibition of amygdala reactivity. This finding suggests that sleep is crucial to appropriate top-down inhibitory functioning within the mPFC-amygdala circuit, and that this circuit significantly governs appropriate emotional responses to affectively loaded stimuli. Functional imaging research on populations with mood disorders that commonly have co-occurring disturbed sleep patterns have also identified abnormalities in this circuit (Davidson, Pizzagalli, Nitschke, & Putna, 2002). Little conclusive research findings exist for positively valenced material (van der Helm & Walker, 2009).

Current conceptualization of mood disorders almost universally includes sleep disturbance as a common feature or formal symptom (American Psychiatric Association, 2013), with reviews of the research into the relationship generally concluding mood and sleep disturbances are bi-directional (Bliwise, 2004; Harvey, 2001). However, a massive (N = 18,631) longitudinal twin-study offered strong evidence that poor sleep predates onset of depression, though the methodology could not confirm a mechanistic causal relationship (Paunio et al., 2009). Depression is a clinical condition that is highly relevant to the intersect between abnormal affective processing and disturbed sleep. Depression has comorbidity rates of disturbed sleep as high as 90%, with polysomnogram (PSG) profiles indicating increased sleep latency and arousals, along with decreased REM sleep latency and increased REM time and density (American Psychiatric Association, 2013; Waller, Hardy, Pole, Giles, Gullion, Rush, 1989; Armitage, 2007; Gottesmann &

Gottesmann, 2007). Depressed individuals exhibit heightened activity in the anterior paralimbic cortex and midbrain reticular formation while awake, which researchers have suggested may reflect a predisposition to encode negatively valenced experiences and consolidate them more easily (Nofzinger, Price, Meltzer, Buysse, Villemagne, Miewald, et al., 2000).

Walker and Van der Helm (2009) proposed a *clinical model of sleep-dependent emotional processing*, based upon their literature review, concluding that under conditions of sleep loss, the brain has a tendency toward encoding negatively valenced stimuli and emotional memories, hyper-active limbic reactivity toward negatively valenced events, and that negative memory consolidation is increased during REM sleep (which tends to be higher density post-sleep deprivation). Their model proposes a "sleep to forget and sleep to remember (SFSR)" hypothesis to explain the consistent finding that emotional memory initially is comprised of both affective (generally amygdala-associated activity) and informational (hippocampal-associated activity) components, but that over time (many months) the affective component is stripped from the informational component of the memory (Dolcos, LaBar, Cabeza, 2004, 2005). The SFSR hypothesis posits that this decoupling predominately takes place during sleep, with the end result being sleeping to *forget* the affective/emotional component but sleeping to *remember* the informational component. Failure to strip the affective component due to disturbed sleep results in potential mood impacts during wakeful hours. Further, their model argues that REM sleep offers a distinctly advantageous neurobiological environment for the information-association facilitation of core memories and the depotentiation and elimination of an affective charge associated with memories. The authors also point out

that the findings that affective valence impacts cognitive processing and memory across waking periods absent of sleep suggest that sleep may be a preferential period for consolidation but that a mechanism similar to REM sleep or completely independent occurs during waking periods. How this segment of affective-processing relates to sleep in both healthy controls and mood disorder populations requires further elucidation. However, in effect, these authors suggest that there may be an alternate or complementary conceptualization of how depression relates to sleep and neurocognitive processes (see Figure 1).

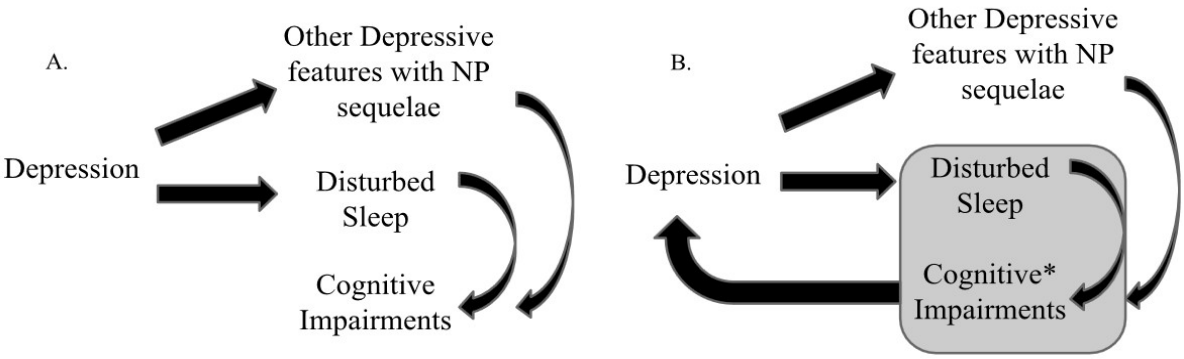

Figure 1. Two Conceptualizations of the Interaction between Depression, Sleep, and Cognitive Impairments.
Note, NP: Neuropsychological. A) Common neuropsychological conceptualization of cognitive difficulties for a chronic depressive patient. B) Modified neuropsychological conceptualization, *cognitive processing dysfunction includes a negative bias in processing emotionally-valenced information (i.e., cognitive-affective processing).

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is a common sleep disorder, estimated to affect roughly 2 to 4% of the adult population (Bresnitz, Goldberg, & Kosinski, 1994; Kripke, Ancoli-Israel, Klauber, Wingard, Mason, & Mullaney, 1997; Olson, King, Hensley, & Saunders,

1995). Base rates vary slightly based on demographics; 4% of middle-aged men versus 2% of middle-aged women are thought to suffer, with a large spike after the age of 65 resulting in estimates of up to 42% of this age group suffering (Ancoli-Israel, Kripke, Klauber, Mason, Fell, & Kaplan, 1991; Young, Dempsey, Skatrud, Weber, & Badr, 1993). The pathophysiology of OSA is characterized by repeated episodes of momentary (10+ seconds) incomplete (hyponea event, 50+%) or complete (apnea event, 100% reduction) cessation of airflow. In OSA, the decreases in airflow are attributable to obstruction or restriction of the breathing airway by the tongue and/or soft palate. The near complete attenuation of skeletal muscle tone that occurs in N2 (intermittently) and REM sleep is true for neck musculature as well, making these stages a common period for the breathing events to occur. During apnea/hyponea events, blood oxygen saturation (SaO_2) can fall to dangerous levels and physical exertion to breathe by the diaphragm and chest muscles increases. These trigger neurological mechanisms that cause a neurological arousal to resume muscle tone and breathing almost never completely awakens an individual, but does result in fragmented sleep and disturbed sleep architecture (Bassiri & Guilleminault, 2000). Diagnosis of OSA is usually done with a polysomnography (PSG), which also allows for an apnea-hyponea index (AHI; based on average number of apnea or hyponea events occurring each hour) to be assigned as an indicator of severity; a score of <5 is considered normal, a score of 30+ is severe.

OSA is associated with a cluster of cardiovascular health complications such as hypertension, heart disease and stroke (Guilleminault & Robinson, 1997). Individuals diagnosed with OSA are estimated to have annual health care costs twice as high as age/sex-matched controls (Kapur, Blough, Sandblom, Hert, de Maine, Sullivan, et al.,

1999). Finally, this population also has a higher accident morbidity rate, thought to in part be related to attentional performance comparable to mildly to moderately intoxicated controls (George & Smiley, 1999; Powell, Riley, Schechtman, Blumen, Dinges, & Guilleminault, 1999). Unfortunately, the compliance rates for the primary treatment option for OSA (Continuous Positive Airway Pressure; CPAP) is low; non-compliance (less than 4 hours per night) rates range from 46-83% (Weaver & Grunstein, 2008). The same study found that patient perception of symptoms is a significant factor in non-compliance. The sub-awakening arousals and fragmented sleep found in OSA patients are inherently difficult for the patients to perceive. Alternative routes of educating identified OSA patients about the health and functioning impacts of their condition is a prime area for the clinical neuropsychologist to contribute to treatment.

Neurocognitive Deficit Correlates

One meta-analysis of peer reviewed OSA articles with neuropsychological findings between the years of 1985 and 2002 identified 37 peer-reviewed articles related to neuropsychological performance in OSA populations (excluding non-clinically diagnosed, cognition-related comborbid, non-adult, and central apnea populations or studies using non-validated measures), which were subsequently divided into non-mutually exclusive pre-treatment, treatment efficacy, and correlational study groups (Aloia, Arnedt, Davis, Riggs, & Byrd, 2004). Pre-treatment results suggest spared global cognition and language functioning, consistent with sleep deprivation findings that crystallized knowledge remains intact and compensatory recruitment allows for well-preserved general cognitive functioning. Attention (especially vigilance), memory, and executive functioning performance was found to be significantly lower in over two-thirds

of the studies reviewed. While motor speed was found to be intact, fine motor control suffered in 80% of measures. Residual impairment after continuous positive air pressure (CPAP) treatment revealed that only fine motor control did not improve with treatment. Severity rating based on hypoxemia (i.e. amount of sleep time where SaO_2 <80%) was related to global cognition, whereas a rating based on sleep fragmentation (AHI) was associated with attention/vigilance performance. One area that the present study hopes to address were methodological concerns that Aloia and colleagues (2004) developed during the process of article collection, which included clarifying the exact diagnostic criteria used, quantifying and specifying degree of treatment compliance (and treatment compliance history), and finally ideally including a contrast group when possible (i.e., a group examined by polysomnogram and not diagnosed with OSA).

Another thorough meta-analysis by Fulda and Schulz (2001) identified 24 articles, with 28 patient groups (total N = 893) related to cognitive functioning in sleep-related breathing disorders (unfortunately without inclusion criteria). The authors found moderate to large effect sizes for decrements in sustained attention performance, delayed visual memory, working memory, and driving simulation tasks. Small to moderate effect sizes were noted in tests of verbal fluency, vigilance, and delayed recall for verbal stimuli. Reasoning and concept formation showed no significant difference. Executive functioning measures were too diverse and limited to make a quantifiable estimate.

Beebe and colleagues (Beebe, Groesz, Wells, Nichols, & McGee, 2002) found 25 studies that met their meta-analysis review criteria, and set out to investigate neuropsychological performance in OSA populations compared to normative data as well as OSA population performance compared to control groups (two sets of effect sizes).

The authors' analysis accumulated reviews that represented 1,092 OSA patients and 899 healthy controls. Both the norm-referenced and the case-controlled data indicated that untreated OSA had a non-significant impact on verbal and intellectual functioning, but a substantial impact on vigilance and executive functions. Motor and visual functions produced mixed results, with post-hoc analysis indicating that fine-motor control and drawing measures were significantly sensitive to OSA, whereas motor speed and visual perception were not. Memory functions were the most variable, which the authors attributed to the wide variability in methodologies and measures used. It should be noted that the previous meta-analyses had nine overlapping studies.

Mood Correlates

Obstructive sleep apnea patients have been demonstrated to have increased rates of diagnosed depression. The degree of increase and the relationship between the two diagnostic constructs is less clear, but a few large scale and meta-analytic findings will be reviewed here to offer the generally accepted comorbidity parameters. A recent epidemiologic study investigating comorbidity between sleep-related breathing disorders and major depressive disorder estimated that of the 18,980 individuals reviewed, 17.6% of those presenting with one diagnosis also presented with the other; the odds of having a sleep-related breathing disorder was 5.26 for those diagnosed with a major depressive disorder. Furthermore, this relationship was not significantly changed when obesity and hypertension were controlled (Ohayon, 2003). A longitudinal study of men and women (n = 1, 408) that repeatedly collected polysomnogram diagnostic data and self-reported depressive symptoms found that an increase in 1 degree of sleep-related breathing disorder severity (e.g., mild to moderate) was associated with a 1.8-fold increase in

adjusted odds for presenting with depression (Peppard, Szklo-Coxe, Hla, & Young, 2006). Combining the longitudinal data with cross-sectional data resulted in 1.6, 2.0, and 2.6 fold increased odds of developing depression compared to controls for minimal, mild, and moderate or worse sleep-related breathing disorder severity ratings respectively.

Research has proposed and investigated multiple potential mechanisms underlying the relationship between OSA and depression. As discussed, two hallmark symptoms of OSA are sleep fragmentation and hypoxemia. Research has found that within OSA populations, amount of sleep fragmentation correlates proportionally with excessive daytime sleepiness and self-report of depressive symptoms, with some researchers proposing that the impact to quality of life and functioning that EDS has is responsible for the depression (Sforza, de Saint Hilaire, Pelissolo, Rochat, Ibanez, 2002). Severity of hypoxic event occurrence has been found to correlate with cognitive performance impairments with effect sizes ranging from .3 standard deviations in mild AHI to 2-3 for moderate to severe AHI ratings, (Engleman, Kingshott, Martin, & Douglas, 2000). Additionally, imaging studies have observed cerebral metabolic disruption during periods of nocturnal hypoxemia in OSA patients, both findings suggesting a disrupting effect to normal neural functioning (Kamba, Inoue, Higami, Suto, Ogawa,& Chen, 2001). Depressive symptoms have been independently associated with white matter hyperintensities in those with affect disorders (Taylor, MacFall, Steffens, Payne, Provenzale, & Krishnan, 2003; Thomas, O'Brien, Barber, McMeekin, & Perry, 2003). Unfortunately, only one study with a small sample size could be reviewed that combined these intersecting findings, and concluded that amongst older OSA patients, more subcortical white matter hyperintensities were found in those with severe OSA

versus mild, and that there existed a positive correlation between white matter hyperintensities and reported depressive symptoms (Aloia, Arnedt, Davis, Riggs, & Byrd, 2004).

It is possible that the relationship between OSA and depression exists but that methodologically lax investigations have resulted in literature reviews overstating the strength of this relationship. For instance, one review of 16 studies that examined this relationship strength found that 9 found a strong relationship, five suggested that depression is secondary to OSA (or that depression resolved after OSA treatment), and two indicated the comorbidity rate of OSA and depression does not significantly exceed that of other diagnoses with similar base rates (Andrews & Oei, 2004). Additionally, though it logically makes sense that rises in depression would follow OSA symptomatology, clinical researchers have pointed out that some sedating medication prescribed to depressed individuals (e.g., benzodiazepines for sleep or comorbid anxiety) may adversely affect oral skeletal muscle tone, increasing risk for the onset of OSA (Guilleminault, 1990).

CHAPTER 2

THE PRESENT STUDY

Rationale, Objectives, & Hypotheses

Walker and Van der Helm posit that their model of sleep-dependent emotional processing may be clinically useful when applied to understanding the etiology of psychiatric disorders and comorbid sleep complaints through a cognitive conceptualization. Obstructive sleep apnea is a medical condition with (1) a better understood mechanism than psychiatric disorders, (2) well documented cognitive deficits as demonstrated on standard neuropsychological measures of attention, memory, and executive function domains, and (3) fairly well established research supporting increased risk and rate of depressed mood. Walker and Van der Helm's model thus provides a framework to investigate this medical condition as it relates to cognitive-affective processing which could possibly add insight into the relationship the disorder has with depressed mood.

To that goal, this study hopes to accomplish a number of objectives of varying inter-relation. They can be summarized under four major themes, listed below, with specific hypotheses and justification following each theme.

1. To determine whether results from past investigations into the interrelationships between sleep physiological indicators, subjective sleep measures, cognitive performance, and mood could be replicated; (a) objective indicators of sleep quality (i.e., polysomnogram), self-reported sleep quality, mood, and standard measures of neuropsychological performance that have been shown to be related to sleep and mood will be correlated with one another; (b) using clinical cutoffs, more severe OSA severity groups will perform significantly worse than less severe OSA groups on a learning and

memory task as well as on executive measures of verbal divergent production; (c) using objective clinical cutoffs, more severe OSA severity groups will report significantly more negative mood than less severe OSA groups on both depression and positive/negative-affect self-report inventories.

2. To document the psychometric properties of two novel measures of cognitive-affective processing; (a) created measures of cognitive-affective processing will demonstrate acceptable psychometric properties.

3. To investigate how the sleep and mood measures relate to the novel cognitive-affective measures; (a) cognitive-affective processing measures designed to parallel standard neuropsychological measures will be significantly related to objective indicators of sleep quality (i.e., polysomnogram), self-reported sleep quality, and mood; (b) more severe OSA severity groups will perform significantly worse than less severe OSA groups on cognitive-affective processing measures; (c) more severe OSA severity groups will demonstrate significantly more negative (or less positive) processing independent of quantitative production within the cognitive-affective processing memory measure.

4. To investigate whether the novel cognitive-affective measures help explain the relationship between sleep disturbance and mood; (a) the relationships between objective sleep disruption and negative mood will be partially explained by this cognitive-affective processing valence bias.

The selected traditional neuropsychological measures were selected largely based upon published performance decrements in OSA populations. Additionally, these measures, sleep indicators, and mood indicators have been demonstrated to relate individually and in subgroups to each other multiple times within samples similar to the

present study's, as well as with other clinical and non-clinical samples. There is strong evidence for physiological sleep disruption impacting neurocognitive functioning, and subjective report of sleep quality being related to mood.

One cognitive-affective measure has already been piloted and demonstrated appropriate psychometric properties; it is expected to do the same in this population. Another cognitive-affective measure is new, but has been created with statistically analogous properties to a well researched and validated memory measure for neutral words. Thus, it is expected to demonstrate appropriate properties as well.

The described cognitive, sleep, and mood constructs have all been found to relate to each other to varying degrees in the literature, though no research has looked at all of this project's variables within one sample. It is expected that these individual and smaller subsets of relationships will all be found within the present sample. There are mixed findings on how strong of a relationship polysomnogram indicators (e.g., fragmented sleep, hypoxemia) have with a variety of cognitive performance measures and mood. Similar findings exist for self-reported sleep. The neuropsychological domains and aspects of mood this study measures were selected with the goal of maximizing statistical power for demonstrating predictive utility of the sleep indicators.

Portions of this study are exploratory in nature. As such, the relationships between the newly constructed measures, cognition, self-report/physiological sleep quality, and mood will be investigated. These analyses will guide future research focusing on OSA populations, affective-cognitive processing, and sleep quality.

The exploratory analyses will be used to explore whether the aforementioned clinical model appears to explain observations in the obtained sample. Affective

characteristics of stimuli should interact with OSA severity, and have an enhancing effect on tasks tapping memory for negatively valenced stimuli independent of memory production, and an interfering impact with tasks of fluency. Additionally, qualitatively negative valence of affective-processing should predict depressive symptoms and possibly mediate the relationship between OSA and/or sleep disturbance severity and depressive symptoms.

CHAPTER 3

DESIGN AND METHODOLOGY

Participants

Participants were recruited from a database of outpatients referred for evaluation of possible obstructive sleep apnea at the Windsor Regional Hospital. A power analysis was conducted, and set a sample-size goal of N = 59, see below for statistical details. Inclusion criteria included: a referral for polysomnograph (PSG) sleep study (with or without CPAP titration), and 18 years of age or older. Exclusionary criteria included: history of traumatic brain injury or stroke, history of/current neurological conditions affecting functioning (aside from other sleep disorders), presence of moderate-severe chronic pain, a psychiatric condition aside from depression, current recreatinoal substance use, or alcohol use reaching "hazardous levels" (21+ drinks per week for men, 14+ drinks per week for women, per gender-specific cutoffs accepted by the National Institute of Alcohol Abuse and Alcoholism and reported in Reid, Fiellin, O'Connor, 1999). Recruitment of pre-diagnosis/pre-treatment referrals, along with patients with confirmed OSA who used their CPAP during the polysomnogram, allowed for the maximal range of sleep fragmentation dysfunction. This strategy also allowed for treated versus untreated comparisons.

Approval from the Research Ethics Board of the Windsor Regional Hospital was obtained in addition to the Research Ethics Board of the University of Windsor prior to data collection. Participants were incentivized to participate by the offer of a gift certificate for a small Tim Horton's item and validated hospital parking. Recruiters also explained that by participating in the research, the individual will be assisting in

contributing to the body of clinical research related to their disorder, which will hopefully assist in future treatments and symptom management for the clinical group as a whole.

Additionally, participants were informed of an opt-in offer for the neurocognitive test results to be compared to a priori conservative cut-offs, with the understanding that if the profile contained a significant number of significantly low enough test scores, the participant would be contacted and provided instructions regarding the general referral process required (i.e., discussing cognitive health options with their primary care physician or their sleep/respiratory physician), as well as referral source groups associated within the Windsor Regional Hospital, and local independent groups. The cut-off for an abnormal profile was set at two scores of the ten battery items falling at or below two standard deviations below zero. Research on the frequency of abnormal test scores in healthy adults, as a function of battery size and normative adjustments, has demonstrated that only 3.4 to 4.6% of healthy adults are observed scoring at the described conservative cut-off (Schretlen, Testa, Winicki, Pearlson, & Gordon, 2008). The advantage of this approach included removing clinical judgment from the decision making process, and instead relied solely on a statistically validated and a conservative decision tree.

The opt-in procedure meant that by default, the participant was not contacted with the feedback. Opt-in participants who produced profiles within normal limits were contacted and informed of that fact. All opt-in participants were also reminded that their participation in this study was not the same as a clinical neuropsychological assessment, and that their opting-in to the screen did not equate entering into a patient-clinician

relationship. Participants who remained in the opt-out category were still offered referral information if they wished.

The risks of participating were minimal, but explained in full to potential participants. Depressed mood and some general psychiatric screening questions were used during data collection. Discussing symptoms associated with depressed mood can sometimes draw attention to them, resulting in psychological distress. If a participant endorsed clinically significant levels of depression, suicidal ideation, or other psychiatric symptoms, similar referral process information and options were provided (along with encouragement for contacting emergency services if suicidal ideation arose).

As with all clinical research, there was the ethical question of the researcher incidentally gaining healthcare provider responsibilities. The extensive explanation provided to potential participants regarding the purpose and limitations of the neurocognitive profile review, along with encouragement to contact two of their already established healthcare providers in addition to a referral to clinical psychological service providers, prevented the research team entering a healthcare provider role with the participant. As such, information gained from the data collection phase of this project was not and will not be provided to any of the aforementioned healthcare providers, as it was not gathered for that purpose.

Measures

Sample Characteristics and Self-report Measures

Demographic and self-report data was collected through administration of a series of questionnaires and measures. The assembled measures were chosen with the goal of

assessing three constructs: 1) the sample's medical history and demographic characteristics, 2) subjective reports of sleep quality, and 3) mood and emotional state.

Demographics and General Medical Background

A self-report form was created and included questions related to: gender, date of birth, country of birth, first language, education, average household income, military service, list of medications, CPAP use and compliance, sleep habit information, and medical/psychiatric history questions. It also inquired as to presence and degree of any pain, along with questions about the participants' previous night of sleep. Medical conditions and age were translated into a Charlson Comorbidity Index score per published formulas (Charlson, Pompei, Ales, & Mackenzie, 1987; Charlson, Szatrowski, Peterson, & Gold, 1994). See Appendix B for this form.

Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989)

The PSQI is a self-report questionnaire designed to assess sleep quality and disturbances, and currently is the most widely used general measure of sleep quality. It measures a broad array of domains associated with sleep quality. It consists of 19 questions regarding sleep characteristics over the past month. These scores form seven equally-weighted components, 1) Subjective Sleep Quality, 2) Sleep Latency, 3) Sleep Duration, 4) Habitual Sleep Efficiency, 5) Sleep Disturbances, 6) Use of Sleeping Medication, and 7) Daytime Dysfunction. These in turn provide a global score ranging from 0-21 (0 = no reported sleep disturbance, 21 = maximum amount of sleep disturbance).

The creators validated the measure over an 18 month period with a group of healthy controls ("good sleepers"), a group of patients with depression and a group of

patients with sleep disorders ("poor sleepers"). A global score over five (6+/21) had high sensitivity (89.6%) and specificity (86.5%) for distinguishing good versus poor sleepers (kappa = 0.75, $p < .001$). Traditional norms are not available, but research has been published on a variety of groups. These include, healthy controls (n = 52, 2.67 ± 1.70), OSA (n = 127, 7.5 ± 3.9), major depression (n = 34, 11.09 ± 4.31), disorders of initiating and maintaining sleep (n = 45, 10.38 ± 4.57), and disorders of excessive daytime somnolence (n = 17, 6.53 ± 2.98). Scores increase with age, even in healthy controls over the age of 80 (n = 44, age = 4.75 ± 3) (Buysse, Reynolds, & Monk, 1991; Park et al., 2007). It is suggested that the PSQI be supplemented with a measure of daytime fatigue and sleepiness.

Test-retest reliability demonstrated no significant changes in global score and internal homogeneity was acceptable (Cronbach's alpha = .83). The PSQI significantly correlates with some polysomnogram (PSG) data (e.g., sleep onset latency, total sleep time, sleep efficiency, and % of stage 2 sleep), but was found to overestimate PSG estimates of usual sleep duration and sleep efficiency (Buysse, Hall, Strollo, Kamarck, Owens, Lee, et al., 2008). See Appendix C for this form.

Epworth Sleepiness Scale (ESS; Johns, 1991)

The ESS is a self-report questionnaire designed to measure the likelihood an individual has of falling asleep in various situations, and has been widely validated in the sleep disorder literature. It consists of 8 questions requiring the individual estimate how likely they might doze or fall asleep in different daily living situations (e.g., sitting and reading, while stopped at a traffic light, etc.). Each question is rated on a scale of 0-3 (0 = would

never doze, 3 = high chance of dozing), and a total score above 10 suggests significant sleepiness.

Test-retest reliability was found to be high (r = .82), and internal consistency was also found to be appropriate (Cronbach's alpha = .88), when given to a group of medical students. Validation research has found that ESS scores are correlated with number of obstructive sleep apnea (OSA) events but not to degree of hypoxemia in OSA patients. After 3-9 months treatment with CPAP, the OSA group's ESS scores significantly decreased. Factor analysis of both groups found one factor. More recent research suggests that the ESS and PSQI measure orthogonal dimensions of sleep/wake symptoms. Both have also been found to differ from some polysomnogram measured constructs, and thus an emphasis should be placed on these tools as a measure of subjective elements of the various sleep constructs (Buysse et al., 2008). See Appendix D for this form.

Center for Epidemiologic Studies Depression Scale (CESD; Radloff, 1977)

The CESD is a self-report questionnaire designed to measure symptoms associated with depression. Previously validated depression scales were used as the source for 300 items, which was narrowed to 20 items, each inquiring about the frequency an individual has experienced a symptom over the past week. All items use a 4-point scale (0 = rarely or none of the time [<1 day] to 3 = most or all of the time [5-7 days]; four items are reverse-scored), with total scores ranging from 0-60. These items comprise six scales, each associated with a major dimension of depression: Depressed Mood, Feelings of Guilt and Worthlessness, Feelings of Helplessness and Hopelessness, Psychomotor Retardation, Loss of Appetite, and Sleep Disturbance. Scores ranging from 15-21 suggest mild to moderate amounts of depressive symptoms and scores over 21 suggest the possibility of

major depression. A score of 16 or higher is commonly used as a cut-off for clinical depression, with 85% of those diagnosed with a depressive disorder by a clinician scoring between 16 and 60. However, 21% who scored within this range had rapid resolution of their symptoms and/or did not fit criteria for a depression diagnosis. Other researchers have suggested using a higher cut-off if the goal is the identification of a clinically depressed population or individual (Zich, Attkisson, & Greenfield, 1990). The CESD is useful with chronically ill groups who complain of fatigue (e.g. cancer, HIV), including OSA populations (Bardwell, Moore, Ancoli-Israel, & Dimsdale, 2003; Cockram, Judd, Mijch, & Norman, 1999; Hann, Winter, & Jacobsen, 1999).

High internal consistency scores were reported, with Cronbach's alpha coefficients ranging from .85 to .90 across studies. Good reliability scores have been reported across multiple groups of varied ethnicity and geographic location, age, and gender (Knight, Williams, McGee & Olaman, 1997; Radloff, 1977; Roberts, Vernon, & Rhoades, 1989). Test-retest correlations are generally moderate, ranging from .45 to .70; this is attributed to scores reflecting the past week and therefore being more liable to shift depending on intervening events. The CESD is not intended as a diagnostic tool, but was constructed based upon symptoms reported in clinical cases. Furthermore, the CESD correlates with severity ratings made by clinicians (correlation coefficient = .56), and with Hamilton Clinician Rating scale scores (.44 to .75), which are based on self-report of symptoms (Radloff, 1977). Past research using the CESD has found high rates of depressed symptoms in those diagnosed with OSA, both for community and clinical samples (17% and 21-41%, respectively). Scores on the CESD scores have been found to account for a large amount of the fatigue OSA patients experience (24.5% above and

beyond the 13.4% that OSA severity does; Thomas, Bardwell, Ancoli-Israel, & Dimsdale, 2006). High CESD scores are also associated with higher percentage of time spent in REM sleep in OSA patients compared to OSA patients who scored low on the CESD (Bardwell, Moore, Ancoli-Israel, & Dimsdale, 2000). In women, but not men, high CESD scores were associated with increased observed apneas (Harris, Glozier, Ratnavadivel, & Grunstein, 2009). In a different study, controlling for gender, age, and ethnicity, CESD scores were positively correlated with the number of instances blood saturation levels dropped by greater than 4% (r = .14, p = .011; Kripke, Ancoli-Israel, Klauber, Wingard, Mason, & Mullaney, 1997). Across multiple studies on OSA populations, mood disorder incidence was 33%, with a mean CESD score of 12.6 (SD = 11.3; Bardwell, Ancoli-Israel, Dimsdale, 2001; Bardwell, Moore, Ancoli-Israel, Dimsdale, 2000 & 2003). Longitudinal research is limited. With regard to the use of this measure and the OSA construct, one prospective study found that OSA onset/increased severity was associated with higher CESD scores, but more research needs to be done in order to investigate the reverse possibility (Harris, Glozier, Ratnavadivel, & Grunstein, 2009). See Appendix E for this form.

Positive and Negative Affective Schedule - Expanded (PANAS - X; Watson & Clark, 1994)

The PANAS-X is a self-report questionnaire designed to measure affect at the present moment, or over the past days to weeks to months, depending upon the instructions. It consists of 60 items, each asking the individual to rate the extent to which they have felt that emotion over the decided upon time-frame using a 5-point scale (1 = very slightly or not at all, 5 = extremely). The measure is an expanded version of the original PANAS,

which was limited to positive emotionality and negative emotionality scales (Watson, Clark, Tellegen, 1988). These items comprise two broad scales, one positive, the other negative (PA and NA), each is comprised of multiple, correlated, yet distinguishable affective states. The PA and NA scales represent valence of emotion, whereas the specifier states represent the content of affect. These dimensions are thought to be orthogonal. High NA is representative of unpleasant engagement and subjective distress, whereas low NA is the absence of these experiences. High PA is epitomized by alertness and enthusiasm, with low PA representing sadness and lethargy. The specific emotional states measured include Fear, Sadness, Guilt, Hostility, Shyness, Fatigue, Surprise, Joviality, Self-Assurance, Attentiveness, and Serenity. The measure was selected to supplement the CES-D mood information, as the PANAS-X captures a larger variety of moods (including positive affect), which might be of interest for aspects of the exploratory analyses.

The expanded measure was developed on a variety of undergraduate and adult samples ranging in size from 114 to 3,622 (Watson & Clark, 1994). Internal reliabilities (Cronbach's alpha values) were high for both higher order scales (PA = .83-.90; NA = .85 - .90). The correlations between the PA and NA scale appear to be quasi-independent, ranging from -.05 to -.35, an advantage for analysis purposes. Looking at the largest community sample, mean daily scores for the higher order scales are 28.3 (*SD* = 2.9) for the PA and 16.4 (*SD* = 4.1) for the NA. Factor analysis revealed a two factor solution, with both scales correlating strongly with each respective factor (from .89 to .95), and correlating weakly with the other (-.02 to -.18). Self-rating is strongly associated with peer-rating on the measure, with correlations ranging from .35 to .48 for the PA and .21

to .36 for the NA. Multifactorial design analysis revealed clear and clean contributors to each of the specific emotional states measured, with almost all items loading exclusively on their respective emotional state at strengths generally ranging from .50 - .75. Internal consistency reliabilities for the 11 lower order scales ranged from .70 to .94, across all temporal phrasing conditions. The PA and NA scales correlate moderately to strongly with measures of both trait and state affect, with appropriate temporal phrasing given. Little research has been conducted using the PANAS in OSA populations, with no comparative norms available. See Appendix F for this form.

General Cognitive Measures

A series of well-established neuropsychological measures was assembled. The decision to include each depended on a number of criteria: (1) performance of sleep apnea populations on the measure in prior research, (2) breadth of domains, and (3) depth of domains (i.e. multiple measures for domains, measures that tap multiple aspects of a domain). Additionally, the advice that Dorrian, Rogers, and Dinges (2005) published concerning neurocognitive battery assemblage that is sensitive to sleep deprivation was considered. Of their recommendations, most relevant for the present study were that measures included (1) reflect fundamental features of neurocognitive functions (e.g., attention over time), (2) are straightforward and are only minimally affected by aptitude, (3) have relatively short durations, to avoid extraneous variables (e.g., decreased interest), (4) consist of a high signal load, to increase opportunity for behavioral sampling within the limited assessment time, (5) demonstrate good reliability and validity, and (6) have readily interpretable results (e.g., functional or related to sleep cycle physiology). However, only those measures discussed in detail below were the focus of the present

dissertation. Please note the summary of additional measures and justification for their inclusion at the end of this section.

North American Adult Reading Test (NAART; Blair & Spreen, 1989)

The NAART is a measure used to estimate premorbid verbal intelligence. Participants are given a sheet containing 61 words of varying pronunciation difficulty. Total words pronounced correctly can be entered into a predictive equation for Wechsler Adult Intelligence Scale - Revised Full Scale, Verbal, and Performance IQ scores (SE_E's = 7.63, 6.56, 10.67, respectively; Blair & Spreen, 1989). The NAART is one of the most reliable measures in clinical use, with a test-retest reliability coefficient of .92, and an interrater reliability coefficient of .99 (Blair & Spreen, 1989; Raguet, Campell, Berry, Schmitt, & Smith, 1996). The authors also found moderate to high correlations (.40 - .80) between the NAART and other measures of general intellectual performance. Additionally, it has been found to be robust against changes following neurological insults, disease, and decline related to old age, making it a good measure of premorbid IQ (Anstey, Luszcz, Giles, & Andrews, 2001). Thus, it is not surprising that the NAART scores in OSA research are average unless the researchers were seeking out impaired subpopulations (e.g., Naismith, Winter, Hickie, & Cistulli, 2005). See Appendix G for this form.

California Verbal Learning Test - Second Edition (CVLT-2 Delis, Kaplan, Kramer, & Ober, 2000)

The CVLT-2 is a measure of learning and memory for verbal stimuli. A 16 word list is read aloud five times, with the individual attempting to recall all the words after each presentation. This target list is made up of four animals, four vegetables, four items of furniture, and four modes of traveling. Next, a distractor list is read aloud with the same

recall task following. This list is composed of four animals, four vegetables, four parts of a house, and four instruments; it therefore shares two semantic categories (though made up of different words) with the target list. Immediately after the recall attempt of the distractor list is complete, the individual is prompted to recall the target list without a presentation. After this short-delay free recall, the individual is again asked to recall target words, but prompted with the four target list's semantic categories. After a 20 minute delay, this free and cued recall process is repeated. Following the long delay recall, the individual is read a list of 48 words and asked to positively identify those words that were on the target list. The recognition list is composed of the 16 target words, the 16 distractor list words, eight novel distractors that fit into a target list semantic category, and eight novel distractors that do not fit into target list or distractor list semantic categories. Finally, after another 10 minute delay, individuals are presented with 16 forced-choice items, where a target word is paired with a distractor word unrelated to any semantic categories used in the test.

Strauss, Sherman, and Spreen (2006) suggest that the CVLT-2 is overall a strong neuropsychological measure in their psychometric review, which the following information discusses. For instance, this measure has very high split-half reliability in the normative sample ($r = 0.94$) and a clinical sample ($r = 0.96$). Word category recall across learning trials were similarly high for the two samples ($r = 0.82, 0.83$, respectively). Test-retest reliability is high ($r's = 0.80$ to 0.89) for overall measures of achievement (e.g., Trials 1-5 Correct, Short Delay Free Recall Correct, Long Delay Free Recall Correct, and Total Recognition Discrimination). Validity, as measured by correlation coefficients between the CVLT and the CVLT-2 are generally adequate to high (e.g., $r = 0.76$ for

Trials 1-5 Correct); the CVLT normative data were likely too stringent, with the CVLT-2 sample being more representative of the educational population of the U.S. A five-factor model was found for the CVLT-2, with all 16 of the selected variables used falling into appropriately representational factors (i.e., general verbal learning, response discrimination, recall efficiency, organization, and primacy-recency reliance). In clinical samples, temporal lesion populations have demonstrated learning deficits across Trials 1-5 and short/long delay recall (Alexander, Stuss, & Fansabedian, 2003). Additionally, focal frontal lesions have been demonstrated to be significantly related to self-monitoring (repetitions, intrusions) and organizational strategies of encoding.

Research investigating OSA population performance on the CVLT-2 is limited, and research conclusions regarding this clinical group's learning and memory performance is mixed. One study compared 28 OSA patients with 24 healthy controls using the original California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987; Salorio, White, Piccirillo, Duntley, & Uhles, 2002). Though an older version, the two tests differ only in stimulus words/categories and the newer inclusion of a forced-choice paradigm. Also, the study was methodologically strong (i.e. included women and men; heterogeneous AHI; PSG diagnosis used; exclusion of medical and learning disorder comborbidities). The researchers found the OSA group to score significantly worse on trial 1 recall, trial 5 recall, and trial B recall, but not on delayed recall or recognition. They interpreted these results to be indicative of encoding deficits rather than maintenance decrements existing in this population. The researchers also found that OSA groups used less semantic grouping in free recall and benefited less from semantic cues than controls. This demonstrated an impaired use of either internally or externally

sourced executive organization strategies. Finally, they note that though the difference in performance was statistically significant, OSA performance decrements generally fell within 1 SD below the control group. This suggests that, from a clinical perspective, the deficits are subtle. However, the authors also note that even with treatment, the deficits are persistent, suggesting that OSA's impact on cognition is more significant when viewed as a contributor to a multi-etiology decline. A meta-analysis found significantly worse long term verbal memory (including the CVLT and other measures with similar paradigms) for OSA populations when compared to a normative-reference set (Cohen's d = 0.52, p = .010), but only a trend for a control-reference set (Cohen's d = 0.27, p = .085; Beebe, Groesz, Wells, Nichols, & McGee, 2003). A more recent study by Lau, Eskes, Morrison, Rajda, and Spurr (2010) using the CVLT-2 only found a trend in the OSA population to demonstrate worse performance across total learning (trials 1-5), (Cohen's d = 0.45, p = 0.086). See Appendix H for this form.

FAS/Animal Naming verbal fluency tasks (FAS/Animals; Spreen & Benton, 1977; Rosen, 1980)

Verbal fluency was measured using two related tasks. The FAS task is a measure of phonemic fluency, requiring an individual to generate as many words as possible that begin with a specific letter, within 60 seconds. Using the instructions first published by Spreen and Benton (1977) and detailed in Spreen and Strauss (1991), participants are also instructed that they should not provide proper nouns or multiple words using a stem with varying suffixes (e.g. eat, eats, eating). A similar measure, that taps semantic fluency, is the Animal Naming task. The instructions published by Rosen (1980) were used, requiring the individual to list as many types of animals as they can, within 60 seconds.

According to Strauss, Sherman, and Spreen (2006), the FAS task has good internal consistency between letters (Cronbach's alpha = .83) and test-retest reliability ($r = .74$, $p < .01$). Furthermore, the Animal Naming task did not differ significantly in test-retest reliability, and correlated with FAS scores significantly ($r = .52$, $p < .01$). Age and education account for small to moderate amounts of variation in both measures, and thus appropriate norms should be used when comparing between individuals (see Tombaugh, Kozak, & Rees, 1999). Verbal fluency has been found to be sensitive to injury to temporal and frontal lobes, as well as the caudate nucleus (for review of articles see, Tombaugh, Kozak, & Rees, 1999). Additionally, phonemic fluency deficits are related to cognitive decrements in nondemented individuals, whereas semantic fluency appears to be more related to a dementia process (e.g. Alzheimer's) (Steenhuis & Ostbye, 1995). Verbal fluency deficits are not clearly evident in meta-analysis, aside from severely affected OSA populations (e.g., Bédard, Montplaisir, Richer, Rouleau, & Malo, 1991; Fulda & Schulz, 2001). However, there is evidence that suggests phonemic fluency decrements with intact semantic fluency within the OSA research, which may have confounded meta-analyses that use a unified fluency construct (Salorio et al., 2002). Despite the potential insensitivity of this measure within an OSA referral sample, it was included as a measure of interest due to its analogous status compared to a cognitive-affective processing measure described below. See Appendix I for these forms.

Other Measures

Participants were given other well researched and validated measures of cognitive performance in traditionally investigated domains of neurocognitive functioning. However, these were not the focus of the present dissertation. Instead, the data will be

used for other research projects associated with the primary investigator, his supervisor, and the lab. The data will also be used in the previously discussed cognitive screen decision. The full battery was be approved by both University and Hospital ethics boards. Other battery measures include: Stroop Color-Word Test (Stroop; Golden, 1978), Trail Making Test A & B (TMT A& B; Reiten, 1955), Symbol Digit Modalities Test-Written (SDMT-W; Smith, 1982), Digit Span Forward & Backward (DSF & DSB; Wechsler, 1981), Digit Vigilance Test (DVT; Lewis, 1995), and the Grooved Pegboard (GPT; Matthews & Klove, 1964).

Neurocognitive Measures of Emotional Processing

As previously discussed in the literature review, there has been extensive research conducted regarding traditional neurocognitive domain deficits associated with obstructive sleep apnea. Far less research has been conducted on the emotional processing deficits associated with poor sleep, even less so with regards to a specific, though common, sleep disorder such as obstructive sleep apnea.

The extant neuropsychological literature on emotional processing as a domain of neurocognitive functioning is limited with regards to published tests and measures. Often, the researchers use a self-constructed measure, including a general description of its characteristics, but limited protocol and psychometric information (for an example of some current emotional processing measures see Suchy, 2011). Further complicating the evaluation of this construct (though not unique to emotion) is the presumed broad impact affective-processing has across all traditional cognitive domains. These characteristics unfortunately result in problems with wide-spread measurement of emotional processing

in research (for replication studies) and clinical settings (assisting in diagnosis and functional intervention).

With this in mind, a counterpart measurement approach was used to supplement the more traditional neurocognitive measures described above. Thus, tasks were selected or constructed with the goal of contrasting the traditional domains (e.g., memory for neutral verbal stimuli versus memory for affect-based stimuli). In this way, the researchers hope to distinguish between potential performance differences unique to either non-emotional or emotional stimuli and processing. The previously described considerations recommended by Dorrian and colleagues (2005) were again consulted during the construction of measures. Again, only those measures discussed in detail below will be the focus of the present dissertation, but there is a summary of additional measures and justification for their inclusion in the battery at the end of this section.

Cognitive-Affective Verbal Learning Test (CAVLT)

Instructions and construction of this measure were based upon the CVLT-2, which was described previously. The protocol for this task is exactly the same as the CVLT-2, with only the stimuli words changing and removal of the forced-choice aspect of the task (which was not conducted during CVLT-2 testing). Sixteen positively valenced emotion words, sixteen negatively valenced emotion words, and sixteen neutral words were selected from the Affective Norms for English Words (ANEW) database (Bradley & Lang, 1999). Of the sixteen neutral words, half were concrete, the other half abstract. Mean distances from neutral were averaged for the positive and negative valence groups and a t-test was conducted to ensure no significant difference. ANOVAs were conducted across the positive, negative, and neutral groups to ensure that average word length and

word frequency did not differ. An ANOVA with contrasts was also conducted to ensure the average valence of each group was significantly different from each other group. Four words from the positively valenced group, negatively valenced group, abstract-neutral group, and concrete-neutral group were selected to form a target list. Each neutral group had a semantic organizational rule. Another four words from each group were selected for the distractor list. The remaining 16 words were mixed with target and distractor words to form the 48-word recognition task, meaning eight novel words that fit into either of the emotion semantic categories and eight novel distractors that do not. Order of all words in each list was randomized. ANOVAs were conducted across the target list, distractor list, and supplemental recognition list to ensure no significant difference between word length and word frequency. Finally, t-tests were conducted to ensure no significant differences existed in word length or frequency between CAVLT lists and their corresponding CVLT-2 lists. See Appendix J for this form.

Emotion Word Fluency Test (EWFT; Abeare, Chauvin, Kaploun, Chu, Dumitrescu, & Pascual-Leone, 2009)

Instructions and construction of this measure were based upon the FAS phonemic fluency task, which was described previously. Examinees are asked to list as many emotion words as they can within one minute. Number of emotion words, perseverations, and rule-breaks (i.e. non-emotion words), are calculated. Emotion versus non-emotion word determination is done by clinical judgment and consensus judgment for words that scorers determine to not clearly be addressed by the following rules. Scoring criteria is inclusive, with any word unambiguously referring to an emotional state (e.g. happy,

smiling) being counted as a correct response. Words that refer to cognitive states (e.g. confusion) or somatic states (e.g. tired) are not counted.

Abeare and colleagues (2009) reported that EWFT inter-rater reliability is strong (Pearson's r = .91), and intra-class correlation coeffcient for agreement was similarly strong (r_{ICC} = 0.806). The measure demonstrates good test-retest reliability across multiple intervals (r = .74 for five hours, r = .676 for one week). Reliability values for this measure are comparable to those values found with other measures of verbal fluency. This measure is in the process of being examined with clinical samples, but has not been used with OSA populations. See Appendix K for this form.

Other Measures

Participants were also given other newly constructed measures hypothesized to measure affective-cognitive processing. However, these were not the focus of the present dissertation. Instead, that data will be used for other research projects associated with the primary investigator, his supervisor, and the lab. The full battery was approved by both University and Hospital ethics boards. Other measures will include the Emotion Stroop Test (EST; emotion-stimuli matched to the Stroop Color-Word Test; Gardizi & Abeare, not yet published), Emotion-Digit Coding Test (EDCT; emotion-stimuli matched to the Symbol-Digit Modalities Test), and the Emotion Vigilance Test (EVT; emotion-stimuli matched to the Digit Vigilance Test).

Physiological Measures

As part of the sleep disorder referral process, the participants underwent polysomnography (also known as PSG), a hospital lab-based, polymetric measurement of the biophysiological characteristics of an individual's sleep session. The polysomnogram

data was collected and analyzed by hospital staff, then provided to the research team. Both pre-diagnosis/pre-treatment and post-diagnosis/CPAP polysomnograms were collected, depending on the patient's progress through the referral and treatment procedure. The polysomnogram data from the study immediately prior to, or subsequent to, the neuropsychological evaluation was used, in order to match the data as close temporally to the cognitive/mood data as possible. The polysomnogram is widely used in sleep research and sleep disorder diagnosis. This data was accessed from participants' health records after consent was gained. A subset of polysomnogram indicators was selected for investigation, per the American Academy of Sleep Medicine scoring manual (AASM, 2007). All of the below physiological indicators have been found to be aberrant in a variety of OSA samples, as well as associated with cognitive performance variance to varying degrees (reviewed by Aloia, Arnedt, Davis, Riggs, & Byrd, 2004). See Appendix L for an example of a polysomnogram report.

Percentage of time spent in each sleep stage (%N1, %N2, %N3, %REM)

Time spent in, non-REM stage 1, 2, 3 (N1, N2, N3), and REM sleep, divided over total sleep time.

Sleep efficiency

Total time asleep divided by time in bed.

Sleep apneas/hypneas

Number of apneas (>= 10 second cessation of air-flow) and hypneas (>= 10 second reduction of air-flow of >= 50%).

AHI

The sleep apnea and hypnea counts are used to create an Apnea/hypnea Index (AHI), an indicator of apnea severity.

REM-AHI

This is an index of AHI frequency during REM stage sleep.

Oxygen Saturation

Arterial O2 saturation (%) is measured throughout sleep. Less than 85% O2 saturation is considered of clinical significance

Procedure

Recruitment

Patients who had already undergone a recent OHIP-covered polysomnogram, along with patients who were scheduled for an upcoming one, were contacted via telephone or in person at the Hospital's clinic. Each individual was provided with information about the purpose, benefits, and risks of participating in the study, and then scheduled for assessment if they voiced interest in volunteering. A script was used for most of the interaction (Appendix M). Additionally, brochures describing the study and providing contact information were provided to the physician collaborators, to be given out to those patients they deemed potentially eligible for the study (Appendix N). Both the graduate principal investigator (PI) and trained undergraduate research assistants (RA) conducted recruitment.

Evaluation

Each participant underwent a single evaluation session taking place at Windsor Regional Hospital, lasting roughly two hours. Each session began with the researcher once again

covering the consent form with the participant, explaining the purpose, content, and benefits associated with the study. Additionally, the participant was informed of their right to discontinue testing at any time. After signing, the participant filled out the demographic questionnaire (for reassurance that the participant did not meet exclusionary criteria). Afterward, the participant filled out the PSQI, ESS, CESD, and PANAS, in that order. Next the researcher administered the battery of neuropsychological measures in the following order (measures that are the focus of this dissertation project are underlined; brackets indicate two sections of the battery that were counter-balanced to control for potential practice effects from parallel measures): 1) NAART, {{2) CVLT-2, 3) TMT A&B, 4) SDMT -W, 5) DVT, 6) DigSpn, 7) FAS/Animals/EWFT 8) Stroop,}} {{9) CAVLT, 10) EDCT, 11) EVT, 12) GPT 13) EST}}.

At the conclusion of testing, the researcher asked the participant whether he or she had any questions or concerns with the evaluation. If the participant made any statements regarding suicidal ideation, or scored above a 15 on the CES-D, referral information for psychological counseling was provided on the spot (see Appendix O for both versions). The researcher explained that the participant would be contacted with cutoff score feedback in the near future if the participant opted into the cognitive-screen feedback at the onset of the testing. When necessary (e.g., offered to those not opting-in to the cognitive screen protocol or those with a positive result on the cognitive screen), referral information for these services was also provided, as previously discussed. Refer to Figure 2 for details on recruitment, evaluation, and selection for analysis.

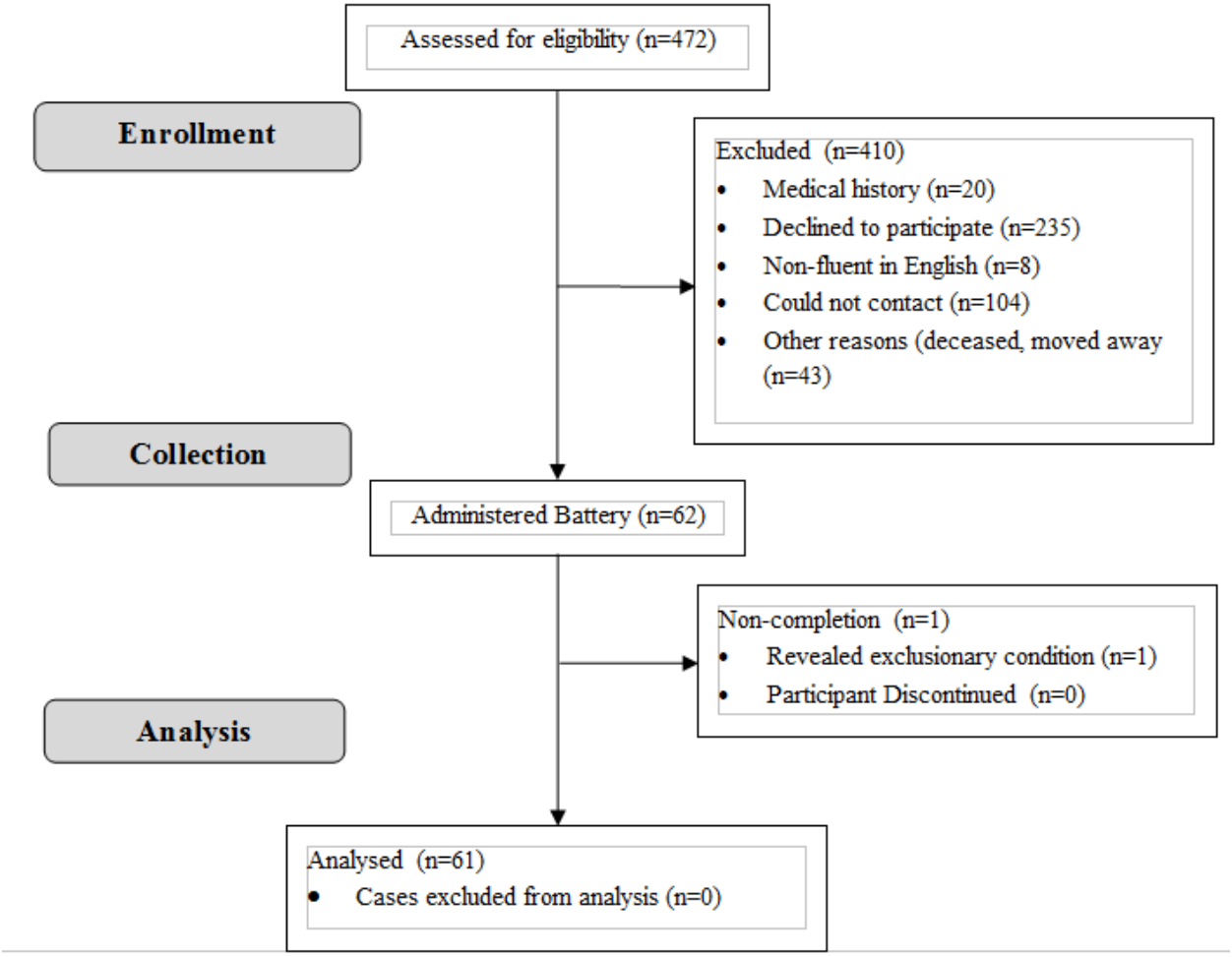

Figure 2. Flow-chart detailing the recruitment process.

Measures, Scoring, Data Storage

Participants were assigned a participant number upon arrival at the evaluation; this number was only linked to their name and phone number on a password protected key-list, stored on a password protected folder, in order to keep track of those who had completed the study and those that required follow-up contact. At no point were any participant names placed on any measure.

The measures were scored and placed within the locked research lab's storage. The hard copies will be kept for a minimum of one year after dissertation defense. Raw scores and demographically matched normative data were entered into an electronic database. This database and password protected key-list will be kept for a minimum of seven years after dissertation defense or five years after study publication.

CHAPTER 4

ANALYSIS OF RESULTS

Statistical Analyses

Analyses of the data were conducted using IBM SPSS Statistics Version 22. There were four overarching objectives for the analyses; (1) to determine whether results from past investigations into the interrelationships between sleep physiological indicators, subjective sleep measures, cognitive performance, and mood could be replicated; (2) to document the psychometric properties of two novel measures of cognitive-affective processing; (3) to investigate how the sleep and mood measures relate to the novel cognitive-affective measures; (4) to investigate whether the novel cognitive-affective measures help explain the relationship between sleep disturbance and mood.

SPSS software analyses were used to investigate the first three objectives (i.e., correlation, ANOVA and repeated measures ANOVA, and regression, respectively). However, for the fourth objective, a macro developed by Preacher and Hayes (2008) was also incorporated, as an alternative to hierarchical regression to analyze the path coefficients in the multiple mediator model. The macros uses a bootstrapping methodology to produce confidence intervals for the specific indirect, and total, effects of an independent variable on a dependent variable via multiple potential mediators. The authors outline multiple advantages to this method. First, the analysis is exploratory in both its operationalization of a theoretical model (i.e., van der Helm & Walker, 2009), as well as the novel measures created, while hierarchical regression is difficult to use without clear theoretically based, a priori, variable-block-entry order. The Preacher and Hayes (2008) method is specifically useful in this situation, as the bootstrapping

approach controls for error and maximizes power. Second, the method is argued to be superior to the common method of using a SOBEL test after individual mediation analyses. The SOBEL method is too liberal with small samples, and thus interpretation would be limited within the present study. Third, the macro is capable of handling groups of mediators as well as covariates, allowing for a more efficient number of analyses and minimization of a compounding familywise error rate. In the following analyses, 1000 iterations and a 95% confidence interval were selected, per recommendation of the authors.

Given the number of hypotheses and planned analyses, consideration was given to concern of familywise error (i.e., type 1 error due to multiple comparisons). With regard to correlations, all construct interrelationships had specified a priori directionality within the hypotheses. Furthermore, this type of approach (i.e., multiple correlation matrices) is a logical first step toward identifying a priori hypotheses that do not warrant follow up analyses. With regard to the multiple means comparisons, MANCOVA is conducted first, prior to subgroup comparisons. Finally, the model testing via regression is exploratory (though based on extant research and framed with a priori hypotheses), therefore there were no additional measures taken to decease the probability of type 1 error for these analyses.

Assumptions

Before data collection, a power analysis was conducted using G*Power, a free software program that allows for a priori sample size estimation for specific statistical tests (Erdfelder, Faul, & Buchner, 2007). Almost all the cognitive and affective-cognitive

measures included in this study tap some form of working memory, mental flexibility, inhibition, or associated executive processes. Extant sleep research does not have reliably obtained cognitive-affective effect sizes, thus, a collection of review studies that reported effect sizes for cognitive domains such as complex attention, mental flexibility, working memory, executive functioning, and frontal processing in OSA samples compared to healthy controls were collected, and these effect sizes (*d*'s = .70, .75, .79) were then averaged, resulting in *d* = .747, or *f2* = .140 (Beebe & Gozal, 2002; Fulda & Schulz, 2001; Naegele, Thouvard, Pépin, Lévy, Bonnet, Perret, Pellat, & Feuerstein, 1995). User settings for hierarchical regression were as follows (since planned F statistic tests would require the largest sample), a power value of 0.8, an alpha value of 0.05, a total possible maximum of 7 predictors (age, gender, education, polysomnogram, subjective sleep, cognitive measure, cognitive-affective measure), and a numerator df of 1 (representing the experimental variable of interest in each analysis). Of note, the liberal predictor value was selected in an effort to protect against concerns of an underpowered sample in the case of the model requiring more predictors and covariates than hypothesized. This results in an estimated required total sample size of 59.

To investigate normality of data, Shapiro-Wilk tests, skewness and kurtosis cut-offs (-2/2 and -3/3, respectively), Q-Q plots, and boxplots were investigated. All of the analyzed variables demonstrated a normal distribution, with a few exceptions. Splitting the sample by OSA cut-offs resulted in non-normal Shapiro Wilk results for the PSQI, CESD, and PNA measures within the non-OSA group and the PSQI for the severe OSA group. However, visual inspection of the plots strongly suggested equivalent normality compared to the other groups. Additionally, the Shapiro-Wilk test is statistically

conservative with small groups (i.e., subgroups of the present sample). Finally, all planned analyses are considered robust against violations of normality. Given these factors, no transformations were conducted. Multiple extreme outlier scores were identified (>3*inter-quartile range), including two CESD data points and one Sleep Efficiency % data point, were removed from analyses. Homogeneity of variance was confirmed for all variables via use of Levene's test. Variance sphericity was safely assumed for all relevant measures, with the exception of the CVLT learning trials (1-5); thus, for this analysis, epsilon tests output was interpreted. Twelve (12) cases contained at least one missing value, spanning 4 variables, which represented 2.31% of the overall data. Thus, no statistical procedures to further evaluate or address the missing values was deemed necessary.

For multivariate regression analyses, a 5:1 (n:predictors) ratio is considered a minimum standard (Tabachnick & Fidell, 2001). As covariates could be accounted for via the regression macro selected, and not entered into a control-variable block, the maximum expected number of predictors (4) resulted in a 15:1 ratio, surpassing this standard. Standardized residual plot inspection indicated appropriate linearity between variables of interest, as well as an appropriate homoscedastic distribution. The data passed a Durbin cut-off (>1), a multicollinearity check (Tolerance < 0.9), Cook's value cut-off (>1), and a Leverage Value determined by using a sample-specific cut-off ([2 x number of predictors]/N = 0.13). Lastly, a Mahalanobis' distance cut-off using df = 4, p = .01, with a chi-squared table cut-off of 13.277, identified no multivariate outliers.

Neurocognitive data collected for research contains similar validity concerns as within clinical contexts. While there were no alterior motives for disengenious

performance with these participants (in fact, most were highly motivated to engage, as all were attracted to participation due to subjective cognitive complaints), it was thought advisable to check two embedded performance validity indicators within the database. Using empirically-derived digit span (7+; Greiffenstein, Baker, & Gola, 1994), verbal fluency regression (Sugarman & Axelrod, 2015), and 3-variable CVLT regression (Wolfe et al., 2010) cut-offs, no sub-optimal performance participants were identified (i.e., above cut-off on 2+ of the three indnicators).

Demographic and Descriptive Data

The demographic descriptives of the whole sample, as well as the AHI severity subgroups, are summarized in Table 2. Chi-squared analyses found no significant gender distribution differences, χ^2 (3, N = 61) = 6.40, p = 0.09. The same non-significance was found for reported household income, χ^2 (24, N = 61) = 13.70, p = 0.95. Over a third of the sample (n = 22) reported the highest bracket of income ($75,100+), followed by "prefer not say" (n = 10), $50,100-$75,000 and $40,100-$50,000 (both n's = 7), $20,100-$30,000 (n = 5), $30,100-$40,000 (n = 4), $15,100-$20,000 (n = 3), $0-$10,000 (n = 2), and $10,100-$15,000 (n = 1). No significant differences were identified between groups for age, education, or estimated IQ, p's > 0.10. No analyses were run for ethnicity due to the limited number of non-white participants (n = 3).

Table 2

Sample Demographic Descriptives by OSA Clinical Severity Group

	Gender	Age Mean (*SD*)	Education Mean (*SD*)	NAART IQ Mean (*SD*)	Ethnicity
Whole Sample (N=61)	29 females 47.5%	52.74 (*14.40*)	13.86 (*3.07*)	103.63 (*8.04*)	58 White 2 Black 1 Asian
No OSA (n=22)	15 females 68.2%	49.64 (*15.18*)	15.18 (*3.46*)	106.46 (*6.60*)	22 White
Mild (n=11)	4 females 36.4%	58.64 (*13.55*)	13.27 (*4.20*)	106.67 (*8.31*)	11 White
Moderate (n=11)	3 females 27.3%	54.00 (*12.51*)	13.65 (*2.76*)	106.1 (*8.05*)	10 White 1 Black
Severe (n=17)	7 females 41.2%	52.74 (*14.40*)	13.65 (*2.76*)	105.38 (*7.78*)	15 White 1 Black 1 Asian

Note: NAART IQ: North American Adult Reading Test Estimated Premorbid IQ

Correlational Analyses

Demographic Investigation

As only a minority of the variables of interest provided demographically-corrected normative scores, a bivariate correlation analysis was used to determine potential covariates for the planned analyses. Participant age was found to significantly correlate with the following measures, p's < 0.01: CVLT Learning, r = -0.41; CVLT Short Delay Recall, r = -0.39; Animals Fluency, r = -0.37; CAVLT Learning, r = -0.44; CAVLT Short Delay Recall, r = -0.53; CAVLT Long Delay Recall, r = -0.55; Sleep Efficiency, r = -0.27. Gender and Education did not significantly correlate with any self-report, cognitive, cognitive-affective processing (CAP), or sleep study (PSG) variables. Thus, the decision was made to use raw scores across all measures and to control for age in all subsequent analyses, unless otherwise noted.

Variables of Interest Investigation

Six partial correlations, controlling for age, were conducted to both investigate a number of hypotheses as well as assist in guidance for subsequent regression analyses. Results of each are summarized below. Additional variables were calculated for CAVLT subtests, in order to quantify response bias with regard to the emotional words versus non-emotional words, as well as positive-versus-negative valence response bias within emotional word recall responses. These factors were designed to represent response bias controlling for the actual learning or memory production performance itself. With regard to the former, an Emotionality Factor (EF) was calculated by using positive emotion word responses (PE), negative emotion word responses (NE), and non-emotion word responses (NEF, i.e., the two remaining word groups), where EF = ((PE+NE)-NEF)/(Total Words))*100. However, due to the non-emotion word response categories containing a concrete non-emotion word category (i.e., body parts) and an abstract non-emotion word category (i.e., units of time), a corrected EF was calculated in order to parse out recall variance impacted by the abstractness-versus-concreteness of the words. This resulted in Emotionality Factor = ((Positive Emotion Words+Negative Emotion Words)-(2*Abstract Non-Emotion Words)/(Positive Emotion Words+Negative Emotion Words+(2*Abstract Non-Emotion Words)))*100. For the CAVLT Emotionality Factor, values can range between -100 and 100, with positive values representing a tendency towards emotional-word response, a negative value representing a tendency toward non-emotional word response.

With regards to positive-versus-negative valence response bias, the following was used to calculate a Valence Factor (VF) = ((Positive Emotion Words-Negative Emotion Words)/(Positive Emotion Words+Negative Emotion Words))*100. For VF, positive or negative values (-100 to 100) represent the corresponding valence tendency in responses given, designed to represent response bias controlling for the actual learning or memory production performance itself. For purposes of reporting, VF differences are phrased as "bidirectionally diverged" if the group difference's midpoint is near 0 and "more negative/positive" if one group's factor score is near 0 and the contrasting group is significantly higher/lower.

Sleep & Mood

Self-report sleep measures, polysomnogram sleep measures, and self-reported mood interrelationships were analyzed (see Table 3 for details related to correlation strengths and significance values). Overall, subjective sleep disturbance measures were more widely and strongly associated with mood reports compared to objective sleep measures. Specifically, sleepiness and sleep disturbance were associated with increased depressive symptoms and negative affect, along with less positive affect. Objective sleep disturbance measures demonstrated more limited results. Higher sleep efficiency was associated with less negative affect and less depressive symptoms, and fragmented REM sleep also was associated with less negative affect.

Table 3

Partial Correlation Matrix (controlling for age) of Mood, Subjective Sleep Measures, and Sleep Study Indicators

	1	2	3	4	5	6	7	8	9
1.CESD	--								
2. PPA	**-0.69**	--							
3. PNA	**0.68**	**-0.39**	--						
4. ESS	**0.39**	**-0.38**	**0.30**	--					
5. PSQI	0.20	-0.13	0.23	0.18	--				
6. AHI	0.21	-0.27	0.01	0.01	-0.4	--			
7. R-AHI	-0.10	-0.07	-0.25	-0.02	0.04	**0.45**	--		
8. SE%	-0.20	0.08	-0.37	0.15	0.07	-0.25	-0.04	--	
9. lowO2%	0.19	-0.15	0.06	-0.03	0.12	**0.41**	-0.08	-0.07	--
10. REM%	-0.04	0.11	0.20	0.14	0.02	-0.27	0.23	0.04	-0.28

$p < 0.05$, ***p* <0.01**, ***p* <0.001**

Note: CESD: Center for Epidemiological Study – Depression Scale, PPA: PANAS Positive Affect Scale, PNA: PANAS Negative Affect Scale, ESS: Epworth Sleepiness Scale, PSQI: Pittsburgh Sleep Quality Index (high scores = high sleep disturbance), AHI: Apnea-Hypnea Index, R-AHI: REM Sleep Apnea-Hypnea Index, SE%: Sleep Efficiency, Low O2%: Proportion of sleep time spent in hypoxia, REM%: proportion of sleep spent in REM.

Sleep and Cognition

Self-report sleep measures, polysomnogram sleep measures, and cognitive performance interrelationships were analyzed; see Table 4 for details related to correlation strengths and significance values. Self-reported sleepiness (ESS) and sleep quality (PSQI) had no significant correlational findings with the cognitive measures. Sleep apnea severity (AHI) had small (based on Cohen, 1988) negative correlations with the CVLT's Long Delayed Recall and Recognition trials (*r*'s = -0.23, -0.25, respectively). There were moderate-to-strong negative correlations between hypoxia (low O2%) and Long Delayed Recall and

Recognition (*r*'s = -0.42, -0.29 respectively), and hypoxia was moderately correlated with worse category-fluency for Animals (*r* = -0.31). In sum, objective measures of sleep disturbance demonstrated wider and stronger correlations with impaired cognitive performance measures than subjective sleep disturbance reports.

Table 4

Partial Correlation Matrix (controlling for age) of Subjective Sleep Self-Report Measures, Sleep Study Indicators, and Standard Cognitive Measure Performance

	CVLT Learning	**CVLT Short Delay Recall**	**CVLT Long Delay Recall**	**CVLT Recognition**	**Verbal Fluency: FAS**	**Verbal Fluency: Animals**
ESS	-0.01	-0.09	-0.18	-0.14	0.04	0.13
PSQI	-0.11	-0.21	-0.11	-0.11	-0.09	-0.12
AHI	-0.07	-0.05	-0.23	-0.25	-0.01	-0.03
R-AHI	0.11	0.20	0.12	0.12	0.09	0.09
REM%	-0.09	-0.14	0.01	0.01	-0.11	-0.16
SE%	0.04	0.04	0.07	0.07	0.12	0.06
Low O2%	-0.02	-0.10	**-0.42**	-0.29	-0.15	**-0.31**

$p < 0.05$, $\mathbf{p < 0.01}$

Note: ESS: Epworth Sleepiness Scale, PSQI: Pittsburgh Sleep Quality Index (high scores = high sleep disturbance), AHI: Apnea-Hypnea Index, R-AHI: REM Sleep Apnea-Hypnea Index, SE%: Sleep Efficiency, Low O2%: Proportion of sleep time spent in hypoxia, REM%: proportion of sleep spent in REM, CVLT: California Verbal Learning Test-2

Sleep and Cognitive-Affective Processing

Self-report sleep measures, sleep study (polysomnogram) measures, and cognitive-affective processing (CAP) performance interrelationships were analyzed; see Table 5 for details related to correlation strengths and significance values. Self-reported sleep disturbance (PSQI) correlated moderately with increased negatively biased (VF) CAVLT Long Delayed Recall (*r* = -0.32) and to a lesser degree with a bias away from emotional

words in the CAVLT Recognition trial (Emotionality Factor, *r* = -0.24). Self-reported sleepiness (ESS) demonstrated no significant correlations with cognitive-affective processing measures.

For sleep study measures, sleep fragmentation severity (AHI) negatively correlated with CAVLT Short and Long Delay Recall (*r*'s = -0.23, -0.28, respectively). Furthermore, AHI was correlated with a bias toward recall for negative words in Short Delay Recall (Positive Emotion Words, *r* = -0.30) and in Long Delay Recall (Positive Emotion Words, *r* = -0.29; Valence Factor, r = -0.26). Sleep fragmentation in REM (R-AHI) was not associated with reduced word recall, but was associated with a bias toward negative valence (VF) within the CAVLT Learning (*r* = -0.23), Short Delay Recall (*r* = -0.32), and Long Delay Recall (*r* = -0.28) trials. Percentage of REM sleep (REM%) correlated with lower CAVLT Short Delay Recall (*r* = -0.23), and a bias away from negative emotion word production in that subtest (SDR NE, *r* = -0.24). Time asleep spent in a hypoxic state (Low O2%) impacted long delay recall (CA-LDR) qualitatively, in a pattern similar to the AHI findings increased amount of negative emotion words (NE, *r* = -0.23) and negative valence for those recalled (VF, r = -0.28). Hypoxia was also correlated with reduced CAVLT Recognition (*r* = -0.24). Higher sleep efficiency (SE%; i.e., sleep time regardless of fragmentation) was associated with more emotionality of those words recalled after short and long delay (Emotionality Factor, *r*'s = 0.38, 0.22, respectively), as well as increased initiation and fluency for emotion words (EWFT, *r* = 0.27).

Overall, the analysis reveals a pattern whereby objective sleep study measures (and to a lesser extent, subjective measures) of sleep disturbance were associated with 1)

lower short and long delayed recall, recognition, but not initial learning performance, and 2) recall responses (and to a lesser extent learning) biased away from positive words and emotion-related words.

Table 5

Partial Correlation Matrix (controlling for age) of Subjective Sleep Self-Report Measures, Sleep Study Indicators, and Cognitive-Affective Processing Performance Measures

	ESS	PSQI	AHI	R-AHI	REM%	SE%	lowO2%
EWFT	0.07	-0.01	0.02	-0.08	0.05	0.27	0.08
CAVLT							
Learning	-0.08	0.01	0.01	0.01	-0.15	-0.01	0.02
(+) Words	-0.17	0.05	-0.17	-0.12	0.01	0.09	-0.10
(-) Words	-0.12	0.09	0.04	0.05	-0.16	-0.09	0.07
Valence Factor	0.05	0.07	-0.18	-0.23	0.12	0.20	-0.22
Emotionality Factor	0.07	-0.03	-0.01	-0.01	0.01	0.25	0.17
Short Delay Recall	-0.08	-0.07	-0.23	0.01	-0.23	-0.05	-0.19
(+) Words	-0.20	-0.10	**-0.30**	-0.19	-0.17	0.18	-0.06
(-) Words	0.05	0.18	0.06	0.29	-0.24	0.15	-0.12
Valence Factor	-0.16	-0.2	-0.20	**-0.32**	-0.09	-0.12	0.04
Emotionality Factor	0.10	0.08	-0.06	0.10	-0.09	**0.38**	0.19
Long Delay Recall	-0.17	0.13	**-0.28**	0.07	-0.02	0.08	-0.17
(+) Words	-0.17	0.16	**-0.29**	-0.06	0.04	0.22	-0.23
(-) Words	-0.02	0.22	0.08	-0.19	-0.16	0.09	-.080
Valence Factor	-0.22	**-0.32**	-0.26	**-0.28**	0.09	-0.02	**-0.28**
Emotionality Factor	0.14	0.14	0.11	0.28	-0.16	0.22	0.01
Recognition	-0.11	0.03	-0.18	-0.06	-0.12	-0.20	-0.24
(+) Words	0.01	-0.02	-0.13	-0.15	0.08	-0.07	-0.11
(-) Words	-0.21	0.01	0.16	0.17	-0.26	-0.08	0.19
Valence Factor	0.19	-0.01	-0.20	-0.25	0.32	-0.06	-0.22
Emotionality Factor	0.07	-0.24	-0.20	-0.16	0.06	-0.15	0.21

$p < 0.05$, ***p* <0.01**, ***p* <0.001**

Note: ESS: Epworth Sleepiness Scale, PSQI: Pittsburgh Sleep Quality Index (high scores = high sleep disturbance), AHI: Apnea-Hypnea Index, R-AHI: REM Sleep Apnea-Hypnea Index, SE%: Sleep Efficiency, Low O2%: Proportion of sleep time spent in hypoxia, REM%: proportion of sleep spent in REM, EWFT: Emotion Word Fluency Test, CAVLT: Cognitive-Affective Verbal Learning Test, (+) Words: Positive Emotion Words, (-) Words: Negative Emotion Words

Mood and Cognition

Self-report mood measures and cognitive performance were analyzed; see Table 6 for details related to correlation strengths and significance values. Overall, depressive symptom report was associated with small-to-moderate range decrements in delayed recall and verbal fluency measures. Neither positive nor negative affect report scores were correlated with cognitive performance.

Table 6

Mood and Cognitive Performance Partial Correlation Matrix (controlling for age)

	CVLT Learning	CVLT SDR	CVLT LDR	CVLT Recognition	Verbal Fluency: FAS	Verbal Fluency: Anm
CESD	-0.14	-0.16	**-0.39**	0.07	-0.23	-0.23
PPA	0.01	0.02	0.14	0.01	-0.03	0.01
PNA	-0.03	-0.08	-0.15	-0.03	-0.11	-0.12

$p < 0.05$, $\mathbf{p < 0.001}$

Note: CESD: Center for Epidemiological Study – Depression Scale, PPA: PANAS Positive Affect Scale, PNA: PANAS Negative Affect Scale, CVLT: California Verbal Learning Test-2.

Mood and Cognitive-Affective Processing

Self-report mood measures and cognitive-affective performance were analyzed; see Table 7 for details related to correlation strengths and significance values. Depressive symptom report (CESD) correlated with CAVLT Learning for Negative Emotion Words ($r = 0.26$), lower Short Delay Recall for Positive Words ($r = -0.34$) and Valence Factor ($r = -0.25$), lower overall Long Delay Recall ($r = -0.20$), and a negative bias for the Recognition Valence Factor ($r = -0.23$). Positive Affect scores were conceptually similar, correlating with lower CAVLT Learning for Negative Emotion Words ($r = -0.21$), higher Short

Delay Recall for Positive Words (r = 0.38), and a positive bias for the Short Delay Recall Valence Factor (r = 0.34) and Recognition Valence Factor (r = 0.24) trial. Contrary to the pattern, higher Positive Affect had a small correlation with negatively biased Learning trial Valence Factor (r = -0.25). Negative Affect had no significant correlations with cognitive-affective processing measures.

Overall, the depression scale (CESD) demonstrated a correlational pattern consistent with more negative Valence Factors/Negative Emotion Word production across Learning, Short Delay Recall, and Long Delay Recall trials of the CAVLT. The PANAS Positive and Negative Affect scales demonstrated less consistent and less strong pattern of correlations with the CAVLT subtests and qualitative factors. None of the mood variables correlated with Emotion Word Fluency Test scores.

Table 7

Partial Correlation Matrix (controlling for age) for Self-Reported Mood Scores and Cognitive-Affective Processing Performance

	CESD	**PPA**	**PNA**
EWFT	-0.18	-0.09	0.11
CAVLT			
Learning	-0.14	-0.09	-0.07
(+) Words	-0.03	-0.13	0.08
(-) Words	0.26	-0.21	-0.07
Valence Factor	0.09	-0.25	0.11
Emotionality Factor	0.20	-0.03	0.10
Short Delay Recall	-0.14	0.06	-0.01
(+) Words	**-0.34**	**0.38**	-0.10
(-) Words	-0.34	0.37	-0.01
Valence Factor	-0.25	0.24	0.07
Emotionality Factor	-0.09	0.10	-0.06
Long Delay Recall	-0.20	0.05	-0.18
(+) Words	-0.15	0.11	-0.03
(-) Words	-0.11	-0.04	-0.13
Valence Factor	-0.04	0.16	0.14
Emotionality Factor	-0.01	-0.03	0.03
Recognition	-0.02	0.06	0.06
(+) Words	0.14	-0.06	0.10
(-) Words	-0.10	0.27	-0.11
Valence Factor	-0.23	-0.25	0.20
Emotionality Factor	0.14	0.08	0.05

$p < 0.05$, ***p* <0.01**

Note: ESS: Epworth Sleepiness Scale, PSQI: Pittsburgh Sleep Quality Index (high scores = high sleep disturbance), AHI: Apnea-Hypnea Index, R-AHI: REM Sleep Apnea-Hypnea Index, SE%: Sleep Efficiency, Low O2%: Proportion of sleep time spent in hypoxia, REM%: proportion of sleep spent in REM, EWFT: Emotion Word Fluency Test, CAVLT: Cognitive-Affective Verbal Learning Test, (+) Words: Positive Emotion Words, (-) Words: Negative Emotion Words

Cognition and Cognitive-Affective Processing Performance

Standard cognitive performance and cognitive-affective processing performance intercorrelations were analyzed, see Table 8 for details related to correlation strengths and significance values. All standard cognitive measures and subtests demonstrated significant positive correlations with the counterpart cognitive-affective processing measures and subtests. Correlations for the Learning measures were generally in the strong range, and correlations for the Short/Long Delay Recall measures were in the moderate-to-strong range. The standard measure of semantic fluency (Animals) correlated strongly with the cognitive-affective processing fluency task (EWFT), compared to the phonemic fluency measure (FAS), which was significant but statistically less strong (Fisher's $z = 2.76$, $p < 0.01$). The small-to-moderate range positive correlations found between the CVLT and the standard verbal fluency measures were slightly less strong (i.e., small range exclusively), and less broad, for the CAVLT and the EWFT. The NAART intelligence estimate did not significantly correlate with the CAVLT or EWFT, p's > 0.10.

Table 8

Cognitive and Cognitive-Affective Processing Performance Partial Correlation Matrix (controlling for age)

	1	2	3	4	5	6	7	8	9	10
CVLT										
1. Learning	.									
2. SDR	**0.87**	.								
3. LDR	**0.72**	**0.75**	.							
4. Recognition	**0.39**	**0.42**	**0.43**	.						
CAVLT										
5. Learning	**0.63**	**0.53**	**0.42**	0.26	.					
6. SDR	**0.64**	**0.61**	**0.49**	**0.33**	**0.76**	.				
7. LDR	**0.57**	**0.51**	**0.48**	**0.35**	**0.72**	**0.75**	.			
8. Recognition	**0.46**	**0.47**	0.26	**0.37**	**0.54**	**0.49**	**0.57**	.		
Fluency										
9. FAS	0.18	0.20	0.25	-0.03	0.23	0.22	0.15		.	
10. Animals	**0.34**	**0.35**	**0.46**	**0.32**	0.26	0.27	0.20	0.25	**0.25**	.
11. EWFT	0.20	0.22	**0.34**	0.10	0.24	0.11	0.29	0.08	**0.12**	**0.56**

p <0.05, ***p* <0.01**, ***p* <0.001**

Note: CAVLT: Cognitive-Affective Verbal Learning Test, CVLT: California Verbal Learning Test-2, SDR: Short Delay Recall, LDR: Long Delay Recall, EWFT: Emotion Word Fluency Test

Mean Comparisons for Sleep Apnea Severity Subgroups

A one-way MANCOVA using OSA severity group (AHI) as the IV, and cognitive (CVLT: Learning, SDR, LDR, Recognition; FAS, Animals), cognitive-affective processing (CAVLT: Learning, SDR, LDR, Recognition, VF for each previous subscore; EWFT), and mood dependent variables (CESD, PNA, PPA) as DV's, with age as a covariate, was significant, Wilk's lambda = 0.52, $F(45, 107.73) = 1.52$, $p = 0.04$. Though a conservative approach would use the MANCOVA contrasts to determine differences

for specific measures, the small amount of missing values combined with list-wise deletion significantly reduced the available n for each contrast, which was judged to be too restrictive on power for such an exploratorially driven study. Thus, the previously listed dependent variables were entered into an ANCOVA, controlling for age, in order to compare OSA severity group profiles. The following tables (10-13) contain *unadjusted* means and standard deviations, as these are more easily interpretable. Tukey's contrasts were used to investigate pattern of subgroup differences, and those *p*-values were reported where applicable. Additionally, below each table, the pattern of contrast differences will be specified where applicable. Limitations on the interpretations that follow this course of analysis are appropriately addressed in the discussion.

Polysomnogram Indicator Comparisons

Apnea-hypnea Index (AHI) scores significantly differed between groups (see Table 9 for details), in the expected direction given that this indicator is the clinical classifying criteria, $F(3, 61) = 167.24$, $p < 0.001$, $ES = 0.90$, with contrasts indicating all groups significantly differing amongst each other, p's < 0.001. AHI severity during REM sleep (R-AHI) significantly differed between groups, $F(3, 57) = 6.29$, $p = 0.001$, $ES = 0.27$. A Post-hoc contrast indicated that AHI severity during REM sleep was significantly lower for the No OSA groups compared to the Moderate and Severe OSA groups, p's < 0.01. Sleep Efficiency (SE%) also differed significantly, $F(3, 60) = 3.58$, $p = 0.03$, $ES = 0.10$, with higher efficiency in the No OSA group compared to the Severe group, $p = 0.05$. Percentage of sleep time spent in REM (REM%) significantly differed amongst groups, $F(3, 61) = 3.68$, $p = 0.02$, $ES = 0.17$. Specifically, it was significantly lower for the No OSA and Severe groups compared to the Moderate group, an unexpected finding without

obvious explanation, *p*'s < 0.05 . Finally, hypoxia during sleep (Low O2%) differed amongst the severity groups, $F(3, 60) = 7.38$, $p < 0.001$, $ES = 0.29$. Clinically low oxygen blood saturation time was significantly higher for the Severe OSA group compared to the other groups, which did not differ amongst themselves, *p*'s < 0.01. Overall, a general pattern of significant polysomnogram abnormality was demonstrated across indicators for the Severe OSA group compared to the others, with Moderate OSA less frequently distinguished as significantly more abnormal than the lower-severity groups, and the Mild group not differing from the No OSA group across any, aside from AHI (a finding expected as AHI was used to create clinical groups).

Table 9

ANCOVA (controlling for age) Comparison of Polysomnogram Sleep Quality Indicators by AHI Diagnostic Category

	AHI* Mean (*SD*)	**R-AHI^** Mean (*SD*)	**SE%#** Mean (*SD*)	**REM%&** Mean (*SD*)	**Low O2%+** Mean (*SD*)
No OSA (n=22)	2.45 *(1.38)*	8.91 *(11.20)*	85.20 *(12.07)*	14.58 *(8.30)*	0.39 *(1.20)*
Mild (n=11)	10.03 *(3.24)*	23.36 *(14.13)*	81.28 *(8.27)*	15.52 *(3.66)*	5.15 *(13.69)*
Moderate (n=11)	23.48 *(3.75)*	37.18 *(19.35)*	84.46 *(7.74)*	21.44 *(3.56)*	2.78 *(3.14)*
Severe (n=17)	66.76 *(16.93)*	37.74 *(34.34)*	76.10 *(19.04)*	11.21 *(11.01)*	18.50 *(14.21)*

*: No < Mild < Moderate < Severe;
^: No < Moderate & Severe;
+: No, Mild, & Moderate < Severe
#: No > Severe;
&: No & Severe < Moderate
Note: AHI: Apnea-Hypnea Index, R-AHI: REM Sleep Apnea-Hypnea Index, SE%: Sleep Efficiency, Low O2%: Proportion of sleep time spent in hypoxia, REM%: proportion of sleep spent in REM

Self-Reported Mood and Sleep Quality Score Comparisons

No significant group differences emerged upon comparison of self-reported mood or sleep quality measures, *p*'s > 0.10 (see Table 10 for details).

Table 10

ANCOVA (controlling for age) Comparison of Self-Reported Mood and Sleep Quality Scores by AHI Diagnostic Category

	CESD	**PNA**	**PPA**	**ESS**	**PSQI**
No OSA (n=22)	10.28 *(6.91)*	16.55 *(7.76)*	30.42 *(8.51)*	9.14 *(4.74)*	8.16 *(5.69)*
Mild (n=11)	13.77 *(8.83)*	16.36 *(5.95)*	30.73 *(8.06)*	8.09 *(3.83)*	8.91 *(4.25)*
Moderate (n=11)	13.36 *(9.50)*	15.73 *(2.80)*	32.82 *(9.63)*	9.45 *(4.50)*	8.64 *(4.13)*
Severe (n=17)	16.00 *(13.14)*	15.59 *(4.71)*	26.88 *(8.18)*	9.12 *(4.50)*	9.09 *(5.37)*

Note: CESD: Center for Epidemiological Study – Depression Scale, PNA: PANAS Negative Affect Scale, PPA: PANAS Positive Affect Scale, ESS: Epworth Sleepiness Scale, PSQI: Pittsburgh Sleep Quality Index (higher scores = more reported sleep disturbance).

Cognitive Performance (Raw Scores) Comparisons

No significant group performance differences emerged upon analysis for any of the standard cognitive test measures (*p*'s > 0.10; see Table 11). No significant differences were found when repeated measure ANCOVAs were used to evaluate whether significant patterns of performance differences existed (*p*'s >0.10) within the CVLT learning trials (i.e., Trials 1, 2, 3, 4, 5) or across time-increments within the verbal fluency tasks (i.e., total output at 15 seconds, 30s, 45s, 60s; output during increments 1-15 seconds, 16-30s, 31-45s, 46-60s).

Table 11

ANCOVA (controlling for age) Comparison of Cognitive Raw Score by OSA Diagnostic Severity Category

	No OSA n=22 Mean (*SD*)	**Mild** n=11 Mean (*SD*)	**Moderate** n=11 Mean (*SD*)	**Severe** n=17 Mean (*SD*)
CVLT				
Learning	49.05 *(12.70)*	47.00 *(13.73)*	45.91 *(8.83)*	45.53 *(10.42)*
Short Delay Recall	10.29 *(3.57)*	10.18 *(5.33)*	9.18 *(2.79)*	9.35 *(3.39)*
Long Delay Recall	10.19 *(2.99)*	10.36 *(5.26)*	9.00 *(2.65)*	8.29 *(4.04)*
Recognition	14.33 *(1.80)*	14.45 *(2.02)*	14.50 *(1.35)*	14.00 *(1.66)*
Verbal Fluency				
FAS	35.73 *(9.36)*	40.00 *(11.23)*	36.36 *(17.97)*	38.69 *(7.61)*
Animals	17.91 *(4.00)*	18.27 *(5.33)*	19.09 *(4.06)*	18.56 *(3.60)*

Note: CVLT: California Verbal Learning Test-2

Cognitive-Affective Performance (Raw Scores) Comparisons

For the CAVLT, total number of words recalled across learning trials was significantly different across OSA severity groups, $F(3, 60) = 2.98$, $p = 0.04$, $ES = 0.14$. Specifically, the number of words recalled was higher for the No OSA group compared to the three diagnostic groups, p's < 0.05, which did not differ amongst themselves (see Table 12). No significant performance differences were found for total recall after short delay, but positive-emotion word recall was different, $F(3, 59) = 3.25$, $p = 0.03$, $ES = 0.15$ with the No OSA group demonstrating greater Short Delay Recall for Positive Words than the Moderate and Severe groups, p's < 0.05. Similarly, the Valence Factor for Short Delay

Recall (i.e., controlling for overall amount of recall) was significantly different, $F(3, 59) = 3.35$, $p = 0.03$, $ES = 0.16$, with more positive affective bias for the No OSA and Mild groups compared to the more negative bias for the Moderate and Severe groups, p's < 0.05.

Long Delay Recall on the CAVLT differed significantly across OSA severity groups, $F(3, 59) = 2.97$, $p = 0.04$, $ES = 0.14$. Specifically, the No OSA group recalled significantly more words after a long delay than the Moderate and Severe groups, p's < 0.05. For the Long Delay Recall subtest, significant group differences were found for Positive Emotion Words, $F(3, 59) = 3.02$, $p = 0.04$, $ES = 0.14$, and the valence factor, $F(3, 59) = 3.62$, $p = 0.02$, $ES = 0.17$. The No OSA group recalled more Positive Emotion Words than the Severe group, $p = 0.004$, and the Valence Factor was significantly lower (more negatively biased, controlling for amount of recall) for the Severe group compared to all other groups, p's < 0.05. No recognition subtest differences were found (p's > 0.10). No significant differences were noted across any of the submeasures for the Emotionality Factor, which was designed to measure bias toward recall of emotional words versus non-emotional words (p's > 0.10). Similar to the standard verbal fluency tests, no EWFT performances differed significantly. Repeated measure ANCOVAs did not reveal significant differences between AHI severity groups in CAVLT learning trial performance, nor EWFT quartile-sum and quartile-production performances (p's > 0.10).

Table 12

ANCOVA (controlling for age) Comparison of Cognitive-Affective Raw Scores by OSA Diagnostic Category

	No OSA n=22 Mean (*SD*)	**Mild** n=11 Mean (*SD*)	**Moderate** n=11 Mean (*SD*)	**Severe** n=17 Mean (*SD*)
CAVLT				
Learning*	52.27 (10.49)	43.30 (13.01)	40.91 (8.80)	45.35 (10.50)
(+) Words	12.14 (3.80)	9.40 (2.76)	9.64 (3.85)	9.88 (3.87)
(-) Words	11.95 (3.19)	10.60 (2.50)	10.55 (3.59)	10.41 (3.08)
Valence Factor	-0.40 (16.01)	-7.18 (8.36)	-6.14 (31.01)	-9.94 (19.66)
Emotionality Factor	13.48 (31.83)	39.60 (12.52)	36.77 (11.09)	41.23 (10.00)
Short Delay Recall	10.86 (3.18)	8.10 (4.04)	7.91 (2.21)	8.18 (3.01)
*(+) Words^*	2.38 (1.16)	1.70 (1.16)	1.36 (1.03)	1.35 (0.93)
(-) Words	2.10 (0.89)	1.30 (1.16)	1.82 (0.75)	1.82 (1.02)
Valence Factor#	4.53 (27.81)	24.33 (47.97)	-27.27 (49.84)	-24.18 (44.40)
Emotionality Factor	11.06 (47.11)	12.19 (64.56)	26.88 (64.26)	28.02 (76.38
Long Delay Recall^	10.52 (3.43)	8.00 (4.52)	7.82 (2.56)	7.41 (3.03)
(+) Words@	2.19 (1.33)	1.50 (1.27)	1.55 (0.93)	1.00 (1.06)
(-) Words	1.90 (1.18)	1.30 (1.25)	1.55 (1.04)	1.59 (1.00)
Valence Factor&	5.44 (29.52)	6.00 (24.59)	1.52 (49.70)	-35.69 (57.10)
Emotionality Factor	-7.03 (42.42)	-11.25 (50.67)	18.18 (58.64)	13.08 (73.09)
Recognition	14.67 (1.71)	14.60 (1.78)	13.90 (1.29)	13.60 (1.77)
(+) Words	3.33 (1.02)	3.50 (1.08)	3.40 (0.70)	3.20 (0.68)
(-) Words	3.43 (0.75)	3.50 (0.85)	3.20 (0.63)	3.33 (0.72)

Valence Factor	-3.24 (16.91)	-1.90 (19.72)	2.76 (15.08)	-1.90 (14.07)
Emotionality Factor	-45.47 (16.17)	-24.00 (28.56)	-31.68 (22.26)	-33.22 (33.47)
EWFT	10.00 (2.93)	11.27 (3.47)	9.36 (3.96)	10.44 (3.03)

*: No > Mild, Moderate, & Severe

^: No > Moderate & Severe
@: No > Severe
#: No & Mild > Moderate & Severe
&: No, Mild, & Moderate > Severe
Note: CAVLT: Cognitive-Affective Verbal Learning Test, EWFT: Emotion Word Fluency Test, (+) Words: Positive Emotion Words, (-) Words: Negative Emotion Words

Mean Comparisons for Subjective Sleep Report Clinical Groups

Both subjective sleep self-report measures (ESS and PSQI) significantly and strongly correlated with depressive symptom report (CESD), and demonstrated more sporadic and weaker correlations with cognitive and cognitive-affective performance, suggesting there may be important subjective sleep quality group differences. Clinical cut-offs supported within the literature were used to create "good" versus "bad" reported sleep quality (PSQI > 5 and 7; Buysse et al., 2008) and sleepiness (ESS > 7 and 9; Rosenthal & Dolan, 2008) groups. These four variables (i.e., two sets of bivariate cut-offs for each of the two subjective sleep self-report measures) were used as independent variables in a four-way MANCOVA, with the same cognitive, cognitive-affective processing, and mood variables used previously as dependent variables, with age as a covariate. The analysis was non-significant, Wilk's lambda = 0.20, $F(54, 87.25) = 1.16$, $p = 0.26$. However, Roy's Largest Root, a liberal estimate of lower bound significance, was significant, p = 0.03. Given the liberal significance indicator, exploratory ANCOVA's were used to explore whether there were any underlying contrast findings that might partially direct study

interpretations. Only the use of the ESS cut off of over 7 showed significant differences for performance measures, though they were all in one measure, the CAVLT. Those judged to be excessively sleepy at the described cutoff recalled fewer words over the course of the Learning Trials, $F(1, 57) = 4.42$, $p = 0.04$, $ES = 0.07$, after Short Delay, $F(1, 56) = 4.43$, $p = 0.04$, $ES = 0.07$, and after Long Delay, $F(1, 56) = 8.13$, $p = 0.004$, $ES = 0.14$. With regard to the CESD, more depressive symptoms were reported in the excessively sleepy group using both a cut off score of over 7, $F(1, 56) = 10.68$, $p = 0.002$, $ES = 0.16$, and over 9, $F(1, 56) = 86.64$, $p = 0.013$, $ES = 0.11$.

Regression Pathway Analysis

The planned Preacher and Hayes (2008) regression pathway analysis was designed to investigate whether a proportion of the variance between polysomnogram factors and mood could be explained through the degree of valence bias in cognitive-affective processing performance content (see Figure 3). Note, Figure 3's unidirectional arrows are meant to represent the a priori model based upon van der Helm and Walker (2009). While these regression analyses on cross-sectional data cannot address the causal elements, the results will be reported as being at least consistent or inconsistent with said model. The authors suggest placing all potential pathway variables into the analysis, and if significant or near-significant findings result, post-hoc removal of non-significant pathway variables can be conducted in an exploratory fashion. To test this a priori hypothesis, the AHI was entered as the predictor variable for CESD score, with inclusion of the four CAVLT Valence Factors (affective-valence bias indicators) as potential mediation pathway variables, controlling for age. The resulting model was non-significant, with the underlying problem being no significant relationship between AHI and CESD ($p > 0.10$).

Based upon the regression findings, REM, AHI, and Sleep Efficiency % were considered as alternate predictor variables, with consideration of both PANAS affect subscales (PPA and PNA) as a dependent variable of mood. Each combination of these alternative predictor and dependent variables resulted in the same non-significant model obstacle, i.e., the relationship between the polysomnogram indicator and the mood variable (*p*'s > 0.10). Alternative exploratory analyses were generated to explore alternative relationship patterns, and are discussed below.

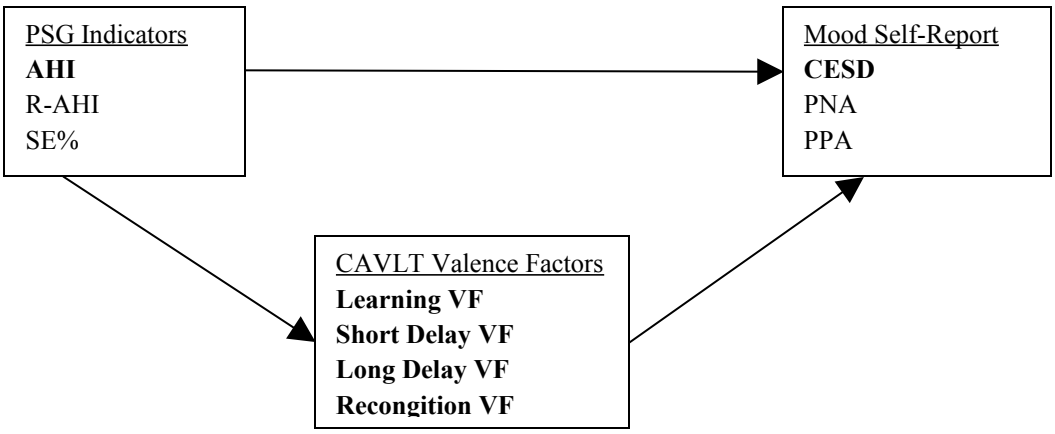

Figure 3. Proposed Mediation of Relationship between Sleep Study Indicators and Mood Measures via Cognitive-Affective Processing Valence Bias
Note: Controlling for Age. Original measures proposed for the model are **bolded**

Exploratory

The proposed model was not supported by the data analyses conducted. However, despite the documented weakness in relation between AHI severity and depressive symptoms (CESD), the sleep study and mood constructs did demonstrate other correlations. Furthermore, the CAVLT Valence Factors demonstrated significant correlations with the sleep study and mood constructs, as well as significant differences within the ANOVA

analyses. Taken together, this suggested that further exploratory analyses were warranted, in order to explore alternative relationships between sleep study indicators (PSG), mood (CESD, PNA, PPA), and cognitive-affective processing bias in emotional-valence processing (i.e., Valence Factors)

Alternative Pathway Analysis – Subjective Sleep

As self-reported depression significantly and strongly correlated with self-reported subjective sleep measures, the potential for a model adjustment to substitute subjective for objective sleep disturbance was explored. While the relationship between the selected predictor (ESS or PSQI) and the dependent variable (CESD or PPA) was significant, *p*'s < 0.01, as seen in the previous correlation analyses, the predictor → mediators and mediators → dependent variable pathway coefficients were non-significant, *p*'s > 0.10. Thus, while this pathway analysis redemonstrated a significant relationship between the self-reported sleep measures and the self-reported mood measures, there were not findings suggestive of a mediation pathway through any Valence Factors (i.e., negative/positive bias in processing of emotional information) in the CAVLT subscores.

Regression: Predicting CAP-emotion/VF with Mood and Polysomnogram

Null findings for the a priori mediation pathway model, using AHI, CESD, and CAVLT VFs, were unexpected for reasons based in theoretical expectations but also due to the significant correlation and mean-comparison results (specifically, with regard to the CAVLT VF variables) of the present study. The latter suggest that the affective bias in recall performances are significantly associated with both physiological sleep disturbance, as well as self-reported mood. The unexpected null findings relating

polysomnogram and mood variables will be commented on in the discussion. For the purpose of exploring alternative conceptualizations of these relationships, stepwise hierarchical regression was used as it allowed for interpretation of the best set of predictors, an important factor given that our theoretical a priori hypothesis was non-significant.

The regression structure consisted of two blocks: 1) forced entry for Age, and 2) stepwise entry for CESD (reported depressed mood), PPA (positive affect), AHI, R-AHI, and lowO2%. This analysis was run for each CAVLT affective bias indicator (VFs). Significant models were found for short delay VF, $F(3, 53) = 3.82$, $p = 0.02$, *adj R2* = 0.19, and long delay VF, $F(3,53) = 3.58$, $p = 0.02$, *adj R2* = 0.18. See Tables 13 and 14 for regression details. Amount of AHI during REM was significantly predictive of more negative bias in short and long delay recall. Self-reported depressive symptom score was uniquely predictive of more negative bias in short delay recall, but not for long delay. In contrast, hypoxia during sleep accounted for prediction of more negative bias in long delay recall but was not significant for the short delay model. No significant models were found for CAVLT total learning trial or Recognition trial affective bias indicators (VF's).

Table 13

Regression Statistics: Significant Sleep Study Indicators and Self-reported Mood Scores that Predict CAVLT Short Delay Recall Valence Factor

Model #	Component	B	*SE*	*Standardized B*	*t*	*p-value*
1	Constant	-13.04	24.79		-0.53	0.60
	Age	0.19	0.46	0.06	0.41	0.68
2	Constant	-5.97	23.86		-0.25	0.80
	Age	0.34	0.44	0.10	0.77	0.45
	R-AHI	-0.58	0.24	-0.33	-2.43	0.02
3	Constant	18.97	25.62		0.74	0.46
	Age	0.23	0.43	0.07	0.54	0.59
	R-AHI	-0.66	0.23	-0.37	-2.83	0.01
	CESD	-1.29	0.58	-0.29	-2.21	0.03

$p < 0.05$

Note: R-AHI: REM Apnea-Hypnea Index, CESD: Center for Epidemiological Study Depression Scale

Table 14

Regression Statistics: Significant Sleep Study Indicators and Self-reported Mood Scores that Predict CAVLT Long Delay Recall Valence Factor

Model #	Component	B	*SE*	*Standardized B*	*t*	*p-value*
1	Constant	-22.43	25.67		-0.87	0.39
	Age	0.32	0.47	0.09	0.67	0.51
2	Constant	-26.13	24.76		-1.06	0.30
	Age	0.52	0.46	0.15	1.12	0.27
	Low O2%	-0.97	0.43	-0.31	-2.27	0.03
3	Constant	-19.61	24.09		-0.81	0.42
	Age	0.64	0.45	0.19	1.43	0.16
	Low O2%	-0.93	0.41	-0.29	-2.24	0.03
	R-AHI	-0.52	0.24	-0.28	-2.17	0.04

$p < 0.05$

Note: R-AHI: REM Apnea-Hypnea Index, Low O2%: proportion of time spent in hypoxic state

Alternate ANCOVA Investigations

Another statistical approach to investigate potential interaction effects of disturbed polysomnogram and depressed mood was conducted through two different sets of analyses. The first was to add CES-D as a covariate to the four previously conducted ANCOVAs (using AHI severity group as the independent variable and CAVLT VFs as dependent variables). Self-reported depression scores on the CESD were not a significant covariate for any of those analyses (p's > 0.10). Another approach was conducted via the creation of a bivariate CESD variable (non-depressed versus probable depression) to incorporate into the 4x2 ANCOVA (AHI severity x CESD status). No main or interaction effects were found for depression status (p's > 0.10).

Alternate Clinical-vs.-Nonclinical Subgroup Comparisons:

An exploratory effort using MANCOVA was conducted in order to investigate whether CAVLT VFs differed significantly amongst other potential clinical subgroups. A MANCOVA (controlling for age) was conducted using clinical cut-off splits for the following independent variables: REM-AHI, SE%, lowO2, PSQI, ESS. All four CAVLT VFs were entered as dependent variables. No significant main or interaction effects were found, p's > 0.10, and the decision was made not to investigate post-hoc contrasts due to concerns about avoiding a "fishing-expedition" approach.

CHAPTER 5

DISCUSSION, CONCLUSIONS, AND RECOMMENDATIONS

The present study was designed to further investigate the interrelationships between sleep processes, neurocognition, and mood. Extant research outlines the breadth and severity of impact that disturbed sleep causes to the effectiveness of processing information and the experience of depressive symptoms. More recent research has examined the relationship between disturbed sleep and negative affective biases. This dysfunctional process has theoretical support as a mechanism underlying the cause and/or maintenance of psychiatric conditions that involve negative mood (e.g., depressive and anxiety disorders). We constructed a battery designed to measure these constructs and evaluated 61 patients referred for polysomnogram for diagnostic differential of obstructive sleep apnea, a condition associated with both sleep physiology disruption and chronic nighttime hypoxia. Notable inclusions in the battery were two novel cognitive-affective processing measures, which were counterparts of standard neurocognitive measures of memory and verbal fluency.

The results will be summarized briefly as they apply to specific hypotheses (matching the organization of numbered and lettered hypotheses found in Chapter 2), organized under the previously outlined four overarching study objectives. Discussion will then focus on: 1) the theoretical implications and clinical utility of the findings; 2) how the results of this study reflect on the state of current research within the cognitive-affective processing field, specifically related to the improvements that the present measures offer upon previous paradigms, and 3) limitations and directions for additional research will be outlined.

The study offered mixed support for replicating the interrelationships documented in the research between sleep physiological indicators, subjective sleep measures, cognitive performance, and mood: (1a) correlations were significant between objective indicators of sleep quality (i.e., polysomnogram), self-reported sleep quality, mood, and standard measures of neuropsychological performance; (1b & 1c) using objective sleep pathology clinical cutoffs, significant differences between severity groups were not detected on two standard cognitive measures (i.e., CVLT-2 and FAS/Animals fluency), and three measures of mood (i.e., CESD, PPA, PNA) were not detected.

Results documented and provided support for the validity of the two novel measures of cognitive-affective processing; (2a) convergent and divergent validity were demonstrated, as well as support for aspects of the measures being sensitive to sleep-breathing disorder pathology in our sample.

The interrelationship between sleep, mood, and the novel cognitive-affective measures were supported; (3a) the cognitive-affective processing measures were significantly related to objective indicators of sleep quality (i.e., polysomnogram), self-reported sleep quality and mood; (3b) the more severe OSA severity groups performed significantly worse than less severe OSA groups on the CAVLT, though not the EWFT; (3c) the more severe OSA severity groups demonstrated a negative bias in learning and recall on the CAVLT, independent of overall production.

Finally, the study provided mixed support for the proposed model; (4 a) a lack of relationship between objective measures of sleep disturbance and mood meant that negative bias in the CAVLT could not be explored as a mediating pathway between the

two. However, further exploratory analyses suggest a more complex relationship between the constructs exists.

The Relationship of Sleep with Cognition and Mood

The first broad hypothesis was the replicative expectation of a significant interrelationship between the constructs of interest. Overall, this hypothesis was supported, with significant correlations existing amongst sleep study indicators, self-reported subjective sleep measures, self-reported mood measures, standard cognitive performance, and cognitive-affective processing performance. As expected, objective indicators of sleep disturbance were significantly correlated with both fluency and memory performance decrements. Of note, amount of sleep time spent in hypoxia appeared to be a stronger and broader indicator of cognitive performance than number of disturbed-breathing related arousals. This finding is important given the fact that all a priori hypotheses relied on AHI as the independent variable subgroup construct. Depressive symptom report also correlated with cognitive performance measures, though to a less broad and strong degree. The relationship between objective sleep indicators and negative mood existed, but was narrower and weaker than expected. While subjective sleep report demonstrated significant relationship with negative mood indicators, it did not relate to cognitive performance. Previous research findings suggest that cognitive processing deficits found within different sleep deprivation samples (clinical and experimental) are not due to lack of motivation or effort (Harrison & Horne, 2000; Wilkinson, 1961). Furthermore, two embedded performance validity indicators within

this study's battery identified no sub-optimal performances. Thus, despite the lack of performance validity measures in the study's battery, the cognitive findings are thought to represent true neurocognitive variation, rather than amotivation or lack of engagement.

Examination of these relationships through creation of clinically meaningful OSA groups (based on AHI severity) showed group differences that were much less consistent with replicative expectations. Lack of subjective sleep report differences across AHI severity groups suggested the constructs to be significantly independent of each other. Unexpectedly, no cognitive performance differences were found across OSA severity groups, for memory or semantic/phonemic word-fluency. The only OSA severity group differences related to mood were limited to trend significance, with the severe group endorsing more depressive symptoms and less positive affect than the other groups. When clinical and non-clinical groups were created via subjective sleep report measures, no significant standard cognitive performance differences were noted, though use of the ESS at two supported clinical cut-offs identified significantly more depressive symptom report.

With regard to the null findings for cognitive differences across OSA severity groups, there are a number of potential explanations, one being that the decrements in neurocognitive functioning are predominantly in those with severe OSA (e.g., as seen in Engleman, Kingshott, Martin, & Douglas, 2000). This study's sample had fairly even distribution between severity groups, which would be suitable for evaluating a severity-dependent pattern of deficit expression. However, if neuropsychological sequelae tend to emerge primarily only within severe OSA populations, our study's sample was too skewed (i.e., 75%) toward "non-clinical" distribution. Thus, the relationship between

neuropsychopathology and sleep pathology in OSA may not be linear, but resemble a rapid accumulation of impairments after a severe-AHI range is present. Compounding this issue, the a priori sample size was determined through amalgamation of dichotomous effect size estimates (i.e., OSA versus HC) from recent meta-analyses, which may have been subject to publication bias – i.e., including studies that found significant differences due to a maximization approach of using a more severe clinical group and comparing them to healthy controls.

Another possible explanation arises from the findings of Beebe and colleagues (2003), who identified resiliency in verbal functions and vulnerability in working-attention like tasks within OSA studies. It is possible that the memory and fluency tasks selected for this study were not as well suited to pick up neurocognitive sequelae as initially hypothesized. Resiliency in verbal functions potentially minimized initiation/divergence variability within the fluency tasks and recall variability within the verbal-memory task. In the context of the significant polysomnogram indicator relationships with cognitive performance (not the case with the subjective sleep variables), the findings support the argument that subjective measures of sleep quality measure a construct that correlates less with neurophysiological sequelae than objective measures of sleep quality (e.g., Buysee et al., 2008's null relationship findings between subjective and objective sleep indicators).

The even distribution of our sample into the four diangnostic OSA severity categories (versus a dichotomous No versus Severe group split) may also explain the null findings across OSA severity group for depressive symptoms; again, due to the potential non-linear relationship. This explanation is reinforced given the trend significance

identified for the Severe group being identified as the potential sole source of variability. As previously cited, while depressive symptoms are associated with AHI, the magnitude of the effect size is quite small for lower AHI levels (i.e., ~0.3) and only with the more severe groups do reliably large effect sizes emerge (i.e., *d* = ~2-3.0; Engleman, Kingshott, Martin, & Douglas, 2000). The lack of findings is not completely unprecedented (e.g., Andrews & Oei, 2004), and lends some additional weight to the hypothesis that the relationship between chronic sleep fragmentation and depression is mediated through secondary conditions acquired through long-term untreated sleep-disordered breathing conditions (e.g., white matter hyperintensities; Aloia, Arnedt, Davis, Riggs, & Byrd, 2004). The findings that the subjective sleep measure related to daytime sleepiness (i.e., the ESS) identified clinical groups reporting significantly more depression is consistent with the hypothesis of previous research that excessive daytime sleepiness contributes to quality of life decrements, thus increasing the odds of depressed mood (Sforza, de Saint Hilaire, Pelissolo, Rochat, & Ibanez, 2002). However, it should be noted that unlike research proposing those causal chain, this study is not longitudinal, and thus cannot provide for causal inferences.

On a final explanative note, beyond the potential for a non-clinical skewing within the OSA severity, the sample's mood, cognitive, and health-comorbidity rates were all skewed toward non-clinical severity. This "high functioning" group may be linked to the non-severe OSA skewing, or be related to a sampling bias toward stronger cognitive reserve (e.g., skewness toward high economic status and average education).

Cognitive-Affective Processing Findings

Given the meticulous effort to match the cognitive-affective processing (CAP) measures on both instruction paradigms and stimuli content, the strong basis for expected acceptable cognitive-affective processing psychometrics was well-founded. The affective-memory measure (CAVLT) had strong internal correlations between subscores, and moderate-to-strong correlations with the standard memory measure (CVLT). The affective-word fluency measure (EWFT), which could be considered a variant of a semantic-category fluency task, correlated more strongly with the animal-category task than the phonemic fluency task. Correlations between the CAVLT and fluency measures were less broad and in the weak-range, demonstrating acceptable divergent validity. These findings suggest that the cognitive-affective processing measures are tapping constructs closely related to, but significantly different from, those processes validated in the CVLT and FAS/Animal fluency tasks.

In contrast with the relatively limited previously discussed findings, cognitive-affective processing performance demonstrated notable statistically significant correlations (see Figure 4) and group differences suggesting the overlapping construct was more sensitive to IV's. There was a wide variety of success amongst the novel and exploratory hypotheses. With regard to sleep, analyses found that objective sleep disturbance indicators significantly correlated with affective-memory, both in terms of number of words recalled and the number of negative words. However, affective-word fluency was more narrowly related, only correlating with sleep efficiency. Subjective sleep disturbance was significantly less related to cognitive-affective processing measures, being negatively related to only one of the four affective-memory valence factors (Long Delay Recall VF). Despite that finding, when a measure of excessive

sleepiness (ESS) was used to create clinical and non-clinical groups, the subjectively sleepy group underperformed on total word production across the total learning trials, short delay recall, and long delay recall.

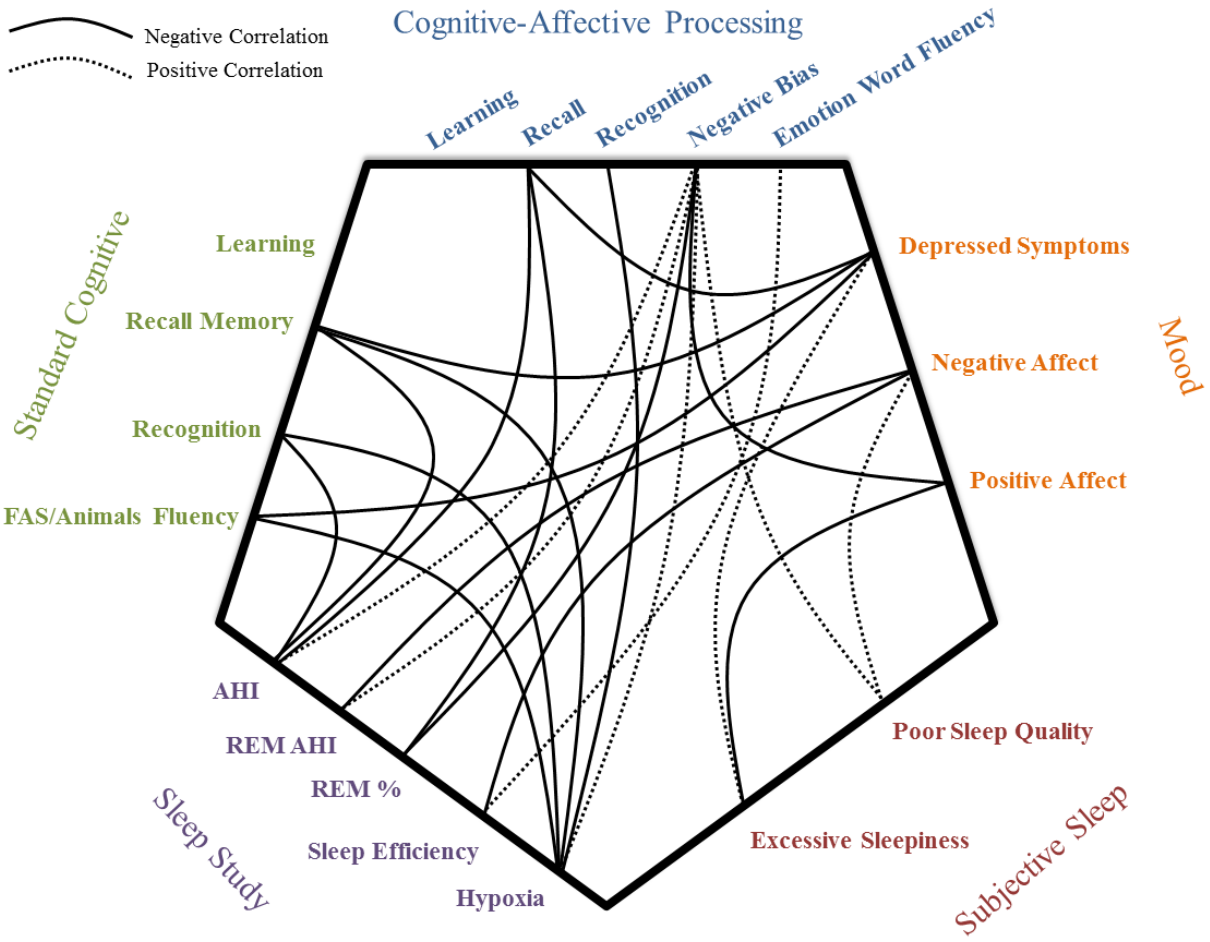

Figure 4. Graphical Representation of Significant Correlation Findings between Five Construct Domains. Note: for purposes of clarity, correlations are not show between variables within domains, as well as correlations between Standard Cognitive and Cognitive-Affective Processing domains.

When AHI severity groups were compared, the non-OSA group outperformed all clinical groups on the affective-memory task's learning trials; however, after a short delay, there were no differences for total word output. Instead, the valence of the recalled

words differed, with a general pattern of less negative valence within the non-OSA group (and to a lesser degree, the mild OSA group). After long-delay, the non-OSA group recalled more words than the clinical groups, and after controlling for that output difference, had less negative delayed recall. Interestingly, there were no group differences for recognition memory in terms of number of words and word valence. Importantly, there were no concreteness-bias differences found for submeasures of affective-memory that demonstrated a negative valence bias. This suggests that the valence finding is not only independent of amount of information recalled, but also independent of any bias related to processing differences due to concreteness versus abstractness of the stimuli, an important factor considering emotional words are semantically abstract.

One pattern of note is the negative correlation between REM-related polysomnogram pathology (i.e., high REM AHI and low REM%) and valence factors (i.e., more negatively biased processing). Alternatively, AHI (i.e., sleep fragmentation in part caused by apnea/hypnea events) and hypoxic blood saturation related more to the actual amount of words produced on recall trials. This pattern suggests the possibility of parallel impacts to memory processes, mediated by different physiological processes disturbed by OSA pathology. Specifically, disrupted sleep architecture (e.g., suppressed REM) may be more related to affective biases in memory, whereas breathing-related pathology (e.g., hypoxia) may be more related to learning and recall ability in general. The OSA clinical group differences are consistent with this impression, though not exclusive to it (i.e., the study did not conduct more refined REM or hypoxia based mean-comparisons to explore this possible interpretation).

Taken overall, the more limited learning and recognition findings, in the context of significant recall production and affective valence bias in the short/long delay free recall trials, suggest a subcortical-frontal retrieval dysfunction mediating CAVLT performance. That this retrieval dysfunction could also be affectively-biased, is of particular note. The absence of CVLT findings further confirms that the cognitive-affective processing measure is tapping a different construct (or subdomain) than learning and memory for neutral verbal information. The ESS differences for CAVLT production, given the lack of any standard cognitive measure findings but significant relationship to negative mood, lends credence to this cognitive-affective processing measure evaluating neurocognitive processes impacted by both physiological and psychological pathology, though specific relationships are beyond comment at this point.

With regard to mood, depressive symptoms demonstrated a small correlation with reduced overall word recall after long delay, but were primarily associated with affective-memory in terms of negative words produced and negative bias during recall and recognition tasks. Negative mood indicators were not associated with affective-word fluency. Given the significant correlational findings for the standard long delay recall and verbal fluency measures, this suggests non-overlapping variability being tapped by the CAVLT and CVLT with regard to potential impacts of depression on performance.

After the promising findings regarding the cognitive-affective processing measures relating to both sleep and mood measures, it was surprising to not confirm the proposed mediation model as posited. Unexpectedly, AHI was not found to significantly predict degree of depression, thus no pathway could be established via CAVLT valence bias. Upon expansion of the model to include promising polysomnogram indicators

predicting mood measures, one relationship was found (i.e., sleep efficiency predicting lower negative affect), but in this case the CAVLT valence factors did not have significant path effects between either predictor or dependent variable. Using either subjective sleep report as a predictor of any of the three mood indicators resulted in a similar problem, i.e., the presence of a significant relationship between IV and DV but no pathway via any of the CAVLT valence factors. While regression analyses themselves cannot confirm a causal model, the failure of the mediation model suggests there is a lack of conceptual fit with our a priori framework.

We hypothesized that sleep disturbance and mood may both be related to cognitive-affective processes, but perhaps produce independent impact on cognitive-affective processing within our sample. Regressions were successful in demonstrating that REM AHI and hypoxia, along with depressive symptoms, were uniquely predictive of negative affective bias at delayed recall. Additional exploratory hypotheses were not supported, including analysis of whether depression as a covariate impacted OSA group differences in cognitive-affective processing scores, as well as including a dichotomous depression variable to investigate potential main/interaction effects on CAP scores. This further suggested that the increased negative bias in affective processing associated with disturbed sleep physiology was independent of negative mood (i.e., the possibility that any relationship between polysomnogram and negatively-biased CAP was due to co-occurring depression leading to a bias toward negative information). A final multivariate analysis did not find enough promising results to warrant further group comparisons amongst other bivariate polysomnogram and reported-sleep quality variables with regard to cognitive-affective processing scores, though this does not rule out their potential

impact, given power limitations for multivariate analyses of that size. Due to the lack of relationship between objective sleep and depression, an attractive alternative order of variables could not be explored (i.e., depressed mood mediating the relationship between sleep pathology and negative bias on the CAVLT). However, the reader is reminded that multiple alternative longitudinal research studies have identified disturbed sleep occurring prior to depression , suggesting a causal relationship (e.g,. Paunio et al, 2009; Peppard, Szklo-Coxe, Hla, & Young, 2006). The same limiations due to potential non-linear relationships and the non-pathologicaly skewed sample outlined above also apply to potential contributors to the null-findings within the proposed model.

Relating Findings to Theory and Clinical Use

The model described by van der Helm and Walker (2009) that suggests disturbed sleep causes cognitive-affective processing dysfunction, which leads to the onset and maintenance of mood disorders, received mixed support from the findings of this study. Due to the cross-sectional nature of this study's methodology, true causal features of the van der Helm and Walker (2009) model cannot be commented on. However, the extent and pattern of relationships demonstrated in this study is not mutually exclusive with the overall conceptualization of a causal sleep, cognitive-affecitve processing bias, and depression model. Valence-biased information processing within the CAVLT related to sleep physiological indicators and mood measures, as we expected. However, the unexpected failure to find a significant relationship between sleep physiology and depression broke down the prospective pathway model for our sample. In an effort to explore a potential alternative model, subjective sleep quality was substituted in place of

objective sleep physiological indicators. However, while this model demonstrated the appropriate predictor to DV relationship, the CAP valence bias pathways broke down. The mean comparisons between OSA severity groups suggests that detectable neuropsychopathology may be limited to the severe OSA group, which suggests that clinical consideration of the model should not be thrown out at this point – rather, a more complex model may be better suited.

Thus, an alternative approach was explored in order to determine whether the constructs could be related to each other in a different manner. Hierarchical regression demonstrated that REM AHI, hypoxia, and depressive symptoms were unique predictors of the valence bias on delayed recall tasks of the CAVLT. Null findings resulted from adding the depression symptoms inventory (CESD) to the previous ANCOVA analyses for CAVLT valence bias in the form of an additional covariate, as well as a dichotomous IV. This further supported the lack of interaction between AHI and depressed mood in our sample. However, the initial investigation of correlations amongst the constructs did find a small correlation between negative affect and non-AHI indicators (i.e., REM-AHI and sleep efficiency). So, while we failed to confirm a proposed model with our sample (see Figure 3), these findings allow some crude alternative modeling specific to *this* sample (Figure 5). Interpreting these results cautiously, we first must consider the possibility that the lack of relationship between AHI and depressed mood is an aberration within the sample, for reasons outlined previously (i.e., severity distribution). An alternative, though not mutually exclusive, consideration is that the model is actually nested within a more complex framework of related constructs. Figure 5 is an example that fits the data collected within our sample. Of note, there is an indirect relationship

between AHI and Depressed Mood via related constructs, though the direct relationship hypothesized was not found. In this sense, while the study could not offer strong support for the proposed model, it instead might be seen as providing methodologically useful information (i.e., alternative variables to focus on within the mood and sleep physiology constructs) in future investigations of CAP functioning/mediation in the same or different patient populations (expanded upon below). Furthermore, as the data collected for this study was cross-sectional, Figure 5 does not imply unidirectional/causal relationships; use of longitudinal methodologies in future research would add clarity in that aspect.

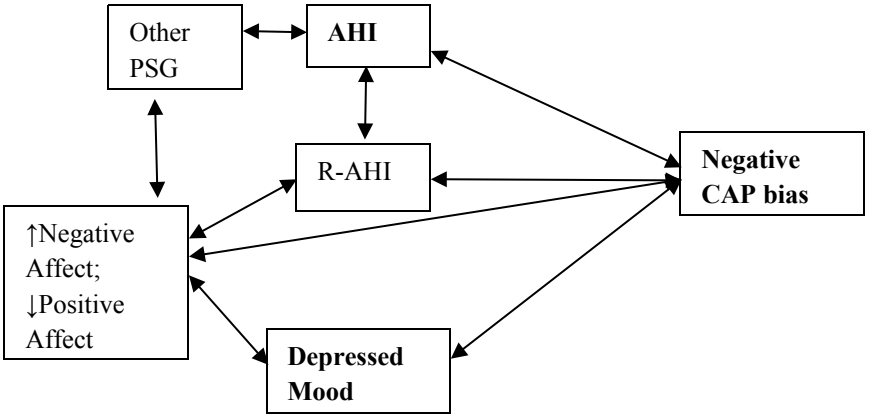

Figure 5. Rough Diagram of Alternative to Proposed Model
Note: original model constructs included are **bold**

From a clinical practice perspective, the findings provide variable confirmation of the neuropsychological impacts of OSA. However, the findings are significantly limited in the applicability to individual patients, both due to effect size and variable intra-construct patterns. While there was correlational evidence connecting disordered sleep and cognitive decrements, OSA severity groups were not detectably different at a group level. This finding suggests that while overall functioning and quality of life issues may

be clinically relevant to the neuropsychological case conceptualization of a patient with untreated OSA, only a small amount of variance within a patient's neurocognitive performance on memory or verbal fluency tasks might be attributable to severity of OSA (though as mentioned previously, within severe OSA groups, these differences may be larger and more reliable). Of note, a number of cognitive-affective processing performance submeasures were significantly different across OSA severity categories (e.g., CAVLT Learning and Long Delay Recall trials). This was in addition to CAP valence bias existing independent of production (i.e., the Valence Factors for the CAVLT submeasures). Thus, the neuropsychological test paradigm was supported as a means of detecting neurocognitive (affective) disturbance secondary to sleep physiology pathology.

However, from a single-patient perspective, the CAVLT production and valence score differences had effect sizes that were still far below a level that might be useful for detecting a recognizable and reliable OSA profile pattern (see Zakzanis, 2001). While explaining depressive presentation due to untreated OSA was not supported by our findings, polysomnogram indicators were significantly related to related the PANAS affect constructs, supporting continued clinical attention to the interaction of sleep quality and emotional experience. In that context, it may be that the CESD was not capturing the potential affective or mood changes related to any negative bias in the processing of emotional information in the world (or on the cognitive-affective processing measures in the lab/clinic). For instance, a construct such as pessimism could feasibly be a result of negative bias in processing, which is a psychological construct intricately related to clinical depression (Abramson, Metalsky, & Alloy, 1989). Alternatively, the study's

premise that an OSA population would be ideal to test the CAP-mediated model may be flawed. Picking a mood or neurological population to run through polysomnograph and neuropsychological evaluation would have been more ideal, though would have significantly higher costs associated with dozens of non-clinically indicated sleep studies.

The pattern of cognitive and cognitive-affective processing performance across severity groups is notable for an apparent cliff or threshold for the OSA severity. Rather than a dose-effect pattern (i.e., progressive deficits across mild, moderate, and severe groups), our data suggests that a tipping-point is reached with regard to neurocognitive functioning for the severe OSA group. Two possible explanations for the abrupt detectability of neurocognitive changes are 1) the pattern reflects a required "minimum" level of sleep-disordered breathing pathology being met, after which neurocognitive functions begin to change and/or, 2) the pattern reflects a breaking point for the brain, which has been compensating for the progressive pathological load by recruiting additional neurocognitive (and perhaps neurophysiological) resources. Neuroimaging research into the apparent normal cognitive performance within mild traumatic brain injury and aging populations provides support for the latter explanation (e.g., Park & Reuter-Lorenz, 2009; Maruishi, Miyatani, Nakao & Muranaka, 2007).

Finally, the findings provide intiail support for a measure (the CAVLT) that has promising clinical utility from a neuropsychological perspective. For instance, with regard to mood disorders and posttraumatic stress disorder, the ability to quantify one potential underlying etiology or exacerbating facotr (negative CAP), might help with differential diagnosis and assessment of prodromal information processing changes. Treatment-response prediction would also be served, if additional research does indeed

identify subgroups of sleep disordered patients who are suffering negative CAP and thus potentially at risk for depression. These individuals might be referred to sleep interventions prior to antidepressant therapies. Finally, within neuriological and rehabilitation settings, evaluation of communication style deficits would be vauable within the sub-acute rehabilitation setting and for family/vocational recommendations during disposition planning.

Relating Findings to Research Utility

If research on the intersect between cognition and affect (i.e., cognitive-affective processing, or, the processing of emotionally-valenced information) is to be integrated more successfully into the clinical domain, the measures produced should be crafted with consideration of research methodology. Specifically, the research must build upon past approaches, fill in missing elements in present literature, and advance novel methodologies. This dissertation provided advancements in each of these areas, though the limitations subsequently discussed leave room for a number of future research directions. One important research consideration was made clear from the variety of polysomnogram indicators involved in identifying significant cognitive/depressive differences. Neuropsychological research with OSA samples should avoid dependency on only one indicator of sleep disturbance severity, due to the multiple parallel pathological and disruptive influences sleep-disordered breathing creates (e.g., hypoxia, sleep architecture disturbance, reduced total sleep time).

Memory measures for words with affective-valence or emotional qualities exist in the research, but are typically created solely for use within the research group's study or

studies (i.e., as a means of operationalizing affective bias in information processing), and not intended for clinical use. In effect, this kind of research demonstrates the impact of various independent variables or manipulations on memory processes for affectively-valenced stimuli, but does not go the extra step of suggesting an optimal methodology to use in measuring affective-memory construct going forward. Only two existing studies assembled affective word memory tests with the goal of wider use in research and clinic (i.e., Affective Auditory Verbal List test, AAVL; Snyder & Harrison, 1997; Emotion Verbal Learning Test, EVLT; Strauss & Allen, 2013). Both measures offer excellent advancement in affective-memory research, but we argue the CAVLT construction is better suited for a number of reasons.

The AAVL was designed with a list-learning paradigm paralleling Rey's Auditory Verbal Learning Test (RAVLT; Rey, 1964). Specifically, the protocol is nearly the same as the CVLT-2 or CAVLT, but uses 15 words that do not relate semantically into categories. Two lists were developed, using high familiarity words of high or low pleasantness ratings. The researchers estimated the RAVL words to represent an equally familiar, but neutral set of words. The EVLT design mirrors that of the CVLT-2 more closely, utilizing emotional categories. The CAVLT offers advantages compared to both of these alternative measures from a methodological standpoint, thereby allowing for future research to better explore the mechanisms of affective-memory. For instance, the AAVL forms are categorically positive or negative, requiring both to be administered to evaluate cognitive-affective processing functioning across the full valence spectrum. The CAVLT incorporates the full valence spectrum into the word-list, allowing for internal comparisons. Additionally, the AAVL is methodologically analogous to a list-learning

paradigm that does not allow for as many memory subprocesses to be evaluated and compared. Specifically, the categorical approach that the CAVLT use, taken from the CVLT-2, allows for evaluation of cued recall and category-comparisons. While the EVLT also uses this category approach, it sacrifices co-evaluation of neutral stimuli in exchange for more specific emotion categories (i.e., happy/sad/anger/anxiety vs. positive/negative in the CAVLT). The CAVLT neutral word categories allow for comparison of emotion versus non-emotion word recall. The splitting of the non-emotion word categories into abstract and concrete categories allows for control of any linguistic processing factors that may be underlying difference in the emotion word memory (i.e,. concreteness of the words). Finally, while the EVLT construction did ensure that word length, frequency, and emotional intensity were equivalent amongst the categories, it does not ensure equivalence between CVLT-2 words and the chosen emotion words. The CAVLT's word selection allows interpretation of performance differences to be more attributed to the cognitive-affective processing differences, rather than methodological differences, a strength in future cognitive-affective processing research conducted with populations where CVLT-2 data has been widely collected.

The EWFT has narrow use in the literature thus far (e.g., Abeare et al., 2009; Freund & Abeare, unpublished dissertation; Abeare et al., unpublished manuscript). The counterpart measures (FAS, Animals) are widely used in research, for both their ease of administration and sensitivity to neurocognitive dysfunction (for review, see Tombaugh, Kozak, & Rees, 1999). As there are no direct alternatives to the EWFT in the research, the argument we make for future use of the EWFT in research is based upon proposed incremental validity beyond standard verbal fluency measures. The only significant

results related to any of these measures in the present study were correlative, higher sleep efficiency was positively related to emotional word production and hypoxia was related to lower animal word fluency. No significant findings resulted from the phonemic fluency measure. The relative lack of findings limits the production of new arguments for inclusion of the EWFT in future research, above and beyond inclusion of cognitive-affective processing measures within batteries in general, and argument outlined in the introduction of this manuscript. However, we can support the notion that the EWFT may be tapping overlapping neurocognitive systems that any semantic/category fluency measure captures. Whether the inclusion of an affective process within the paradigm is differentially impacted (compared to neutral category fluency) is not yet clear.

One promising finding was the valence factor differences found within the CAVLT when deeper analysis of production was analyzed. In order to conduct a similar level of analysis, Abeare and colleagues are currently producing a scoring system that would allow for analysis of various affective-linguistic characteristics of the words produced during an EWFT trial. Based on that finding, as well as research indicating that poor sleep leads to less inhibition of negative information (e.g., Anderson & Platten, 2011), we expect to find an overall negative bias in the affective-valence of the words produced by those with more severe OSA, despite no quantitative production differences. Applications of that scoring system to the content of this study's data (and future research) should allow for capturing more subtle differences in affective-word fluency that might be significantly related to constructs of clinical and research interest.

Limitations and Future Direction of Research

A number of factors should be discussed in the context of limiting the interpretations and conclusions of the present study to appropriate bounds. The sample's demographics were determined through the clinical referral process, and therefore mirrored the OSA patient population's heterogenous nature with regard to age. While age was controlled for during analyses, in the context of a sample size that just met power-estimates requirements, the age-distribution could reflect other age-related factors that might influence neuropsychological factors that were not controlled for (e.g., chronic medical conditions, pain, vulnerability to circadian changes). Additionally, the homogenous ethnicity of our sample (i.e., 58 of 61 participants were white) does not reflect the epidemiological incidence rate of OSA. In fact, Blacks and Hispanics in North America have a higher risk for OSA than whites, though this is thought to reflect socioeconomic status and access to healthcare, the latter being related to higher incidents of obesity and other comorbid medical conditions related to OSA risk (Punjabi, 2008; Ralls & Grigg-Damberger, 2012). The ethnic makeup of our sample suggests a sampling bias within the referrals to the sleep clinic, or, more likely, within those agreeing to participate in the study.

Related to the sample's demographics, was the fact that normative transformations could not be made with the novel measures at this point in their development. Under ideal circumstances, both raw and normative score comparisons would be explored due to the novel nature of many of the hypotheses, thus reducing type II error. As noted above, while valence analysis was possible for the CAVLT, the necessary scoring system was not yet available for the EWFT (though is nearing completed development in this author's

associated lab). This limited the interpretations related to affective-word fluency within the sample to a shallower level (i.e., raw production). Finally, the limited and weak correlations between physiological sleep disturbance and depressive symptomatology in this sample was a barrier to fully exploring the model hypothesized (per van der Helm & Walker, 2009). While the use of sleep disorder patients was advantageous for certain constructs (e.g., naturalistic sleep disturbance, easy access to polysomnogram data), the narrow and suppressed depression severity likely limited our ability to fully investigate variance mediated by CAP valence bias. Finally, while analyses were based on a priori directional hypotheses, and we did use multivariate variance analysis prior to comparisons, the exploratory analyses must be interpreted cautiously . Our findings must therefore be taken as suggestive of potential patterns and rather than absolutes. In contrast, our negative findings for a few of the replicative hypotheses (e.g., polysomnogram and depression) are more notable and the impressions related to them deserve stronger consideration, given the liberal significance approach selected.

The results of this study, as well as continued work within the associated lab, allow for a number of concrete proposals for future research to be presented, falling into two broad categories. First, regarding cognitive-affective processing measures and psychometrics, normative data is currently being collected for the CAVLT and EWFT(along with the other non-discussed CAP measures included in the battery). A CAP battery is currently being administered to student volunteers at the University (by this authors associated lab), and will be a first step toward allowing normative comparisons. Additionally, ongoing development of the EWFT linguistic-affective scoring protocol will allow for the norms to include valence factors and other affective-

process indicators that might be of use in model development/evaluation and clinical practice. Secondly, from a model and theoretical standpoint, additional research should improve upon this study's methodology to better explore a cognitive-affective processing mediated model for the sleep-mood disorder relationship. This might include using known psychiatric groups (e.g., depression, anxiety, PTSD) and acquired brain injury groups (e.g., TBI, right-hemisphere stroke, neurodegenerative disorders), which would provide a much deeper and broader set of affective dysregulation. These populations also are likely to have comorbid sleep disturbance, which would facilitate investigation into the discussed model. Alternatively, a more severe sleep disorder sample might result in a similar depth of mood disorder symptomatology to allow exploration of the model.

Further integration of physiological measures, and inclusion of functional imaging/mapping, would allow for exploration of how our cognitive-affective processing measures differ at a neural network level from other standard counterparts. This would provide information that could guide future hypotheses about types of conditions and injuries that might have clinical/functional decrements associated with as-of-yet unquantified biases in their processing of affective stimuli. This author's associated lab recently acquired simultaneous EEG - near infrared spectroscopy, which will be incorporated in future studies, to facilitate pursuit in these directions. For example, using this functional imaging technology with healthy groups during norm collection could provide neuroanatomical convergent validity data, if CAP-related areas of the brain are recruited during CAVLT versus CVLT performance. Follow-up investigation of compensatory hypotheses as applied to concussion, sleep-deprivation, and normal aging populations would similarly lednt themselves to the concurrent imaging research

methodology. Finally, exploring what ecological and/or psychosocial functioning constructs are associated with the cognitive-affective processing measures would reinforce the importance of exploring the proposed model and provide guidance in further hypothesis generation.

Conclusions

In this study, novel measures of cognitive-affective processing (memory and word fluency) were constructed and administered to patients with obstructive sleep apnea, along with standard neurocognitive measures of memory and word fluency, self-reported sleep quality, and self-reported mood. The polysomnogram (sleep physiology) data of each patient was obtained, and all constructs analyzed, in hopes of validating the new cognitive-affective processing (CAP) measures and evaluating the applicability of a CAP-mediated relationship between sleep and depression. Mixed findings suggested that cognitive-affective processing was related to both sleep physiology and depression, but unexpected null findings between sleep and mood impeded the evaluation of a pathway model. Exploratory analyses suggest there may be a more complex model relating the three constructs of interest, incorporating multiple sleep physiological indicators (e.g., REM sleep pathology, hypoxia, disturbed sleep architecture) and emotional constructs beyond just depression (i.e., positive and negative affect).

Of additional interest, cognitive-affective processing differences between OSA severity groups were broader and more significant than those detected for standard neurocognitive measures, suggesting potential better sensitivity toward dysfunction secondary to sleep-disordered breathing. Dysfunction across constructs was

predominately found in the severe OSA group, suggesting that a threshold-model (rather than dose-dependent model) of OSA pathology might best explain neuropsychological pathological expression. This hypothesis suggests that mild and moderate OSA populations might be eligible targets for neuro-compensation research already being conducted in mild TBI and ageing populations.

Additionally, this study provides initial support for a neuropsychological measure of how humans process emotionally-laden information. The measure has significant potential for use in research, specifically in exploring whether biases in processing certain valenced emotional information contributes to the onset or maintenance of mood and personality disorders. Clinical application will follow advances in the research. Incorporation of the new measures into practice will ideally allow neuropsychologists to improve differentials, treatment-response prediction, and functional coping recommendations. The goals of future research will be to generate normative data and expand the psychometrics of the CAP measures produced by this author and his supervisor. In addition, the biased cognitive-affective processing model of negative mood will be evaluated within psychiatric and neurological samples. Integration of functional imaging in both research directions will further elucidate the mechanisms underpinning normal and dysfunctional cognitive-affective processing.

References

Abeare, C.A., Chauvin, K. A., Kaploun, K. A., Chu, O., Dumitrescu, C., & Pascual-Leone, A. (2009). Validation of the Emotion Word Fluency Test: Preliminary Evidence. *Journal of the International Neuropsychological Society, 15* (S2), 24-5.

Abeare, C.A., Kaploun, K., Freund, S., Dumitrescu, C., & Pascual-Leone, A. (n.d.). The emotion word fluency test (EWFT): Initial evaluation and validation evidence. Manuscript in preparation.

Abramson, L. Y., Metalsky, G. I., & Alloy, L. B. (1989). Hopelessness depression: A theory-based subtype of depression. *Psychological Review, 96*(2), 358.

Akerstedt, T. (1987). Sleep/wake disturbances in working life. *Electroencephalography and Clinical Neurophysiology. Supplement*, *39*, 360.

Alexander, M. P., Stuss, D. T., & Fansabedian, N. (2003). California Verbal Learning Test: performance by patients with focal frontal and non-frontal lesions. *Brain, 126*(6), 1493-1503.

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

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (5th ed.)*. Washington, DC: Author.

Amzica, F., & Steriade, M. (1998). Electrophysiological correlates of sleep delta waves. *Electroencephalography and Clinical Neurophysiology*, *107*(2), 69-83.

Ancoli-Israel, S., Kripke, D. F., Klauber, M. R., Mason, W. J., Fell, R., & Kaplan, O. (1991). Sleep-disordered breathing in community-dwelling elderly. *Sleep*, *14*(6), 486.

Anderson, A. K., & Phelps, E. A. (2001). Lesions of the human amygdala impair enhanced perception of emotionally salient events. *Nature*, *411*(6835), 305-309.

Anderson, C., & Platten, C. R. (2011). Sleep deprivation lowers inhibition and enhances impulsivity to negative stimuli. *Behavioural Brain Research,217*(2), 463-466.

Anderson, A. K., Yamaguchi, Y., Grabski, W., & Lacka, D. (2006). Emotional memories are not all created equal: evidence for selective memory enhancement. *Learning & Memory*, *13*(6), 711-718.

Andrews, J. G., & Oei, T. P. (2004). The roles of depression and anxiety in the understanding and treatment of Obstructive Sleep Apnea Syndrome. *Clinical Psychology Review*, *24*(8), 1031-1049.

Anstey, K. J., Luszcz, M. A., Giles, L. C., & Andrews, G. R. (2001). Demographic, health, cognitive, and sensory variables as predictors of mortality in very old adults. *Psychology and Aging*, *16*(1), 3.

Armitage, R. (2007). Sleep and circadian rhythms in mood disorders. *Acta Psychiatrica Scandinavica*, *115*(s433), 104-115.

Atienza, M., & Cantero, J. L. (2008). Modulatory effects of emotion and sleep on recollection and familiarity. *Journal of Sleep Research*, *17*(3), 285-294.

Baldwin, C. M., Griffith, K. A., Nieto, F. J., O'Connor, G. T., Walsleben, J. A., & Redline, S. (2001). The association of sleep-disordered breathing and sleep symptoms with quality of life in the Sleep Heart Health Study. *Sleep*, *24*(1), 96.

Bardwell, W. A., Moore, P., Ancoli-Israel, S., & Dimsdale, J. E. (2003). Fatigue in obstructive sleep apnea: driven by depressive symptoms instead of apnea severity?. *American Journal of Psychiatry*, *160*(2), 350-355.

Bardwell, W. A., Moore, P., Ancoli-Israel, S., & Dimsdale, J. E. (2000). Does obstructive sleep apnea confound sleep architecture findings in subjects with depressive symptoms?. *Biological Psychiatry*, *48*(10), 1001-1009.

Bassiri, A. G., & Guilleminault, C. (2000). Clinical features and evaluation of obstructive sleep apnea-hypopnea syndrome. *Principles and Practice of Sleep Medicine*, *3*, 869-78.

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

Beebe, D. W., & Gozal, D. (2002). Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *Journal of Sleep Research*, *11*(1), 1-16.

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

Belenky, G., Wesensten, N. J., Thorne, D. R., Thomas, M. L., Sing, H. C., Redmond, D. P., ... & Balkin, T. J. (2003). Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. *Journal of Sleep Research*, *12*(1), 1-12.

Blair, J. R., & Spreen, O. (1989). Predicting premorbid IQ: a revision of the National Adult Reading Test. *The Clinical Neuropsychologist*, *3*(2), 129-136.

Bliwise, D. L. (2004). Sleep disorders in Alzheimer's disease and other dementias. *Clinical Cornerstone*, *6*(1), S16-S28.

Bonnet, M. H. (1985). Effect of sleep disruption on sleep, performance, and mood. *Sleep, 8* (1985), 11–19.

Bonnet, M. H. (1986). Performance and sleepiness following moderate sleep disruption and slow wave sleep deprivation. *Physiology & Behavior*, *37*(6), 915-918.

Bonnet, M. H. (1989). Infrequent periodic sleep disruption: effects on sleep, performance and mood. *Physiology & Behavior*, *45*(5), 1049-1055.

Borbely, A. A., & Achermann, P. (1999). Sleep homeostasis and models of sleep regulation. *Journal of Biological Rhythms*, *14*(6), 559-570.

Bourgeois-Bougrine, S., Carbon, P., Gounelle, C., Mollard, R., & Coblentz, A. (2003). Perceived fatigue for short-and long-haul flights: a survey of 739 airline pilots. *Aviation, Space, and Environmental Medicine*, *74*(10), 1072-1077.

Bradley, M.M., & Lang, P.J. (1999). Affective norms for English words (ANEW): Stimuli, instruction manual and affective ratings. Technical report C-1, Gainesville, FL. The Center for Research in Psychophysiology, University of Florida.

Breslau, N., Roth, T., Rosenthal, L., & Andreski, P. (1997). Daytime sleepiness: an epidemiological study of young adults. *American Journal of Public Health*, *87*(10), 1649-1653.

Bresnitz, E. A., Goldberg, R., & Kosinski, R. M. (1994). Epidemiology of obstructive sleep apnea. *Epidemiologic Reviews*, *16*(2), 210.

Buchanan, T. W., & Lovallo, W. R. (2001). Enhanced memory for emotional material following stress-level cortisol treatment in humans. *Psychoneuroendocrinology*, *26*(3), 307-317.

Buysse, D. J., Hall, M. L., Strollo, P. J., Kamarck, T. W., Owens, J., Lee, L., ... & Matthews, K. A. (2008). Relationships between the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and clinical/polysomnographic measures in a community sample. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine*, *4*(6), 563.

Buysse, D. J., Reynolds, C. F., Monk, T. H., & Hoch, C. C. (1991). Quantification of subjective sleep quality in healthy elderly men and women using the Pittsburgh Sleep Quality Index (PSQI). *Sleep: Journal of Sleep Research & Sleep Medicine*.

Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193-213.

Cahill, L. (2000). Neurobiological mechanisms of emotionally influenced, long-term memory. *Progress in Brain Research*, *126*, 29-37.

Cahill, L., & Alkire, M. T. (2003). Epinephrine enhancement of human memory consolidation: Interaction with arousal at encoding. *Neurobiology of Learning and Memory*, *79*(2), 194-198.

Cahill, L., Gorski, L., & Le, K. (2003). Enhanced human memory consolidation with post-learning stress: Interaction with the degree of arousal at encoding. *Learning & Memory*, *10*(4), 270-274.

Cahill, L., Haier, R. J., Fallon, J., Alkire, M. T., Tang, C., Keator, D., ... & McGaugh, J. L. (1996). Amygdala activity at encoding correlated with long-term, free recall of emotional information. *Proceedings of the National Academy of Sciences*, *93*(15), 8016-8021.

Cahill, L., Prins, B., Weber, M., & McGaugh, J. L. (1994). β-Adrenergic activation and memory for emotional events. *Nature*, *371*(6499), 702-704.

Cahn, D. A., Salmon, D. P., Monsch, A. U., Butters, N., Wiederholt, W. C., Corey-Bloom, J., & Barrett-Connor, E. (1996). Screening for dementia of the Alzheimer type in the community: the utility of the Clock Drawing Test. *Archives of Clinical Neuropsychology*, *11*(6), 529-539.

Carskadon, M. A., & Dement, W. C. (1981). Cumulative effects of sleep restriction on daytime sleepiness. *Psychophysiology*, *18*(2), 107-113.

Carskadon, M. A., & Dement, W. C. (1987). Daytime sleepiness: quantification of a behavioral state. *Neuroscience & Biobehavioral Reviews*, *11*(3), 307-317.

Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Diseases*, *40*(5), 373-383.

Charlson, M., Szatrowski, T. P., Peterson, J., & Gold, J. (1994). Validation of a combined comorbidity index. *Journal of Clinical Epidemiology*, *47*(11), 1245-1251.

Chee, M. W., & Chuah, L. Y. (2008). Functional neuroimaging insights into how sleep and sleep deprivation affect memory and cognition. *Current Opinion in Neurology*, *21*(4), 417-423.

Chee, M. W., & Chuah, Y. L. (2007). Functional neuroimaging and behavioral correlates of capacity decline in visual short-term memory after sleep deprivation. *Proceedings of the National Academy of Sciences*, *104*(22), 9487-9492.

Chen, C., Hardy, M., Zhang, J., LaHoste, G. J., & Bazan, N. G. (2006). Altered NMDA receptor trafficking contributes to sleep deprivation-induced hippocampal synaptic and cognitive impairments. *Biochemical and Biophysical Research Communications*, *340*(2), 435-440.

Cockram, A., Judd, F. K., Mijch, A., & Norman, T. (1999). The evaluation of depression in inpatients with HIV disease. *Australian and New Zealand Journal of Psychiatry*, *33*(3), 344-352.

Cohen, J. (1988). Statistical power for the social sciences. *Hillsdale, NJ: Laurence Erlbaum and Associates*.

Davidson, R. J., Pizzagalli, D., Nitschke, J. B., & Putnam, K. (2002). Depression: perspectives from affective neuroscience. *Annual Review of Psychology*, *53*(1), 545-574.

Davis, C. J., Harding, J. W., & Wright, J. W. (2003). REM sleep deprivation-induced deficits in the latency-to-peak induction and maintenance of long-term potentiation within the CA1 region of the hippocampus. *Brain Research*, *973*(2), 293-297.

Dawson, D., & Reid, K. (1997). Fatigue, alcohol and performance impairment. *Nature*, *388*(6639), 235.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (1987). California verbal learning test, research edition. *New York: The Psychological Corporation*.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (2000). CVLT-II. *The Psychological Corporation, New York*.

Dinges, D. F. (1986). Differential effects of prior wakefulness and circadian phase on nap sleep. *Electroencephalography and Clinical Neurophysiology*, *64*(3), 224-227.

Dinges, D. F. (1990). Are you awake? Cognitive performance and reverie during the hypnopompic state. *Sleep and Cognition. Washington, DC: American Psychological Association*, 159-75.

Dinges, D. F. (1992). *Probing the limits of functional capability: The effects of sleep loss on short-duration tasks* (pp. 176-188). Boston: Birkhauser.

Dinges, D. F., Pack, F., Williams, K., Gillen, K. A., Powell, J. W., Ott, G. E., ... & Pack, A. I. (1997). Cumulative sleepiness, mood disturbance and psychomotor vigilance performance decrements during aweek of sleep restricted to 4-5 hours per night. *Sleep: Journal of Sleep Research & Sleep Medicine, 20*(4), 267-277.

Dinges, D. F., Rogers, N. L., & Baynard, M. D. (2005). Chronic sleep deprivation. *Principles and Practice of Sleep Medicine*, *4*, 67-76.

Dolan, M. C., & Fullam, R. (2010). Emotional memory and psychopathic traits in conduct disordered adolescents. *Personality and Individual Differences*, *48*(3), 327-331.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004). Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. *Neuron*, *42*(5), 855-864.

Doran, S. M., Van Dongen, H. P. A., & Dinges, D. F. (2001). Sustained attention performance during sleep deprivation: evidence of state instability. *Archives Italiennes de Biologie*, *139*(3), 253-267.

Dorrian, J., Dinges, D. F., Rider, R. L., Price, N. J., & Rogers, N. L. (2003). Simulated driving performance during chronic partial sleep deprivation. *Sleep*, *26*, A182.

Dorrian, J., Rogers, N. L., & Dinges, D. F. (2005). Psychomotor vigilance performance: Neurocognitive assay sensitive to sleep loss. *Sleep deprivation: Clinical Issues, Pharmacology and Sleep Loss Effects. New York: Marcel Dekker, Inc*, 39-70.

Downey, R., & Bonnet, M. H. (1987). Performance during frequent sleep disruption. *Sleep: Journal of Sleep Research & Sleep Medicine; Sleep: Journal of Sleep Research & Sleep Medicine*.

Drake, C. L., Roehrs, T. A., Burduvali, E., Bonahoom, A., Rosekind, M., & Roth, T. (2001). Effects of rapid versus slow accumulation of eight hours of sleep loss. *Psychophysiology*, *38*(6), 979-987.

Durmer, J. S., & Dinges, D. F. (2005, March). Neurocognitive consequences of sleep deprivation. In *Seminars in Neurology* (Vol. 25, No. 1, pp. 117-129). [New York]: Thieme-Stratton Inc.,[c1981-2005.]

Engleman, H. M., Kingshott, R. N., Martin, S. E., & Douglas, N. J. (2000). Cognitive function in the sleep apnea/hypopnea syndrome (SAHS). *Sleep*, *23*(4), S102-S108.

Fairclough, S. H., & Graham, R. (1999). Impairment of driving performance caused by sleep deprivation or alcohol: a comparative study. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, *41*(1), 118-128.

Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*(2), 175-191.

Flykt, A., & Caldara, R. (2006). Tracking fear in snake and spider fearful participants during visual search: A multi-response domain study. *Cognition and Emotion*, *20*(8), 1075-1091.

Frank, J. E., & Tomaz, C. (2000). Enhancement of declarative memory associated with emotional content in a Brazilian sample. *Brazilian Journal of Medical and Biological Research*, *33*(12), 1483-1489.

Freund & Abeare. (2012). Unpublished Master's Thesis. University of Windsor.

Fulda, S., & Schulz, H. (2001). Cognitive dysfunction in sleep disorders. *Sleep Medicine Reviews*, *5*(6), 423-445.

Gardizi, E., & Abeare, C.A. (in preparation). Emotion Stroop Test.

George, C. F., & Smiley, A. (1999). Sleep apnea & automobile crashes. *Sleep*, *22*(6), 790.

Golden, C. J. (1978). *Stroop Color and Word Test: Cat. No. 30150M; a Manual for Clinical and Experimental Uses*. Stoelting.

Gottesmann, C., & Gottesman, I. (2007). The neurobiological characteristics of rapid eye movement (REM) sleep are candidate endophenotypes of depression,

schizophrenia, mental retardation and dementia. *Progress in Neurobiology*, *81*(4), 237-250.

Graves, L. A., Heller, E. A., Pack, A. I., & Abel, T. (2003). Sleep deprivation selectively impairs memory consolidation for contextual fear conditioning. *Learning & Memory*, *10*(3), 168-176.

Greiffenstein, M. F., Baker, W. J., & Gola, T. (1994). Validation of malingered amnesia measures with a large clinical sample. *Psychological Assessment, 6*(3), 218.

Gruart-Masso, A., Nadal-Alemany, R., Coll-Andreu, M., Portell-Cortès, I., & Martí-Nicolovius, M. (1995). Effects of pretraining paradoxical sleep deprivation upon two-way active avoidance. *Behavioural Brain Research*, *72*(1), 181-183.

Guilleminault, C. (1990). Benzodiazepines, breathing, and sleep. *The AmericanJournal of Medicine*, *88*(3), S25-S28.

Guilleminault, C., & Robinson, A. (1997). Sleep-disordered breathing and hypertension: past lessons, future directions. *Sleep*, *20*(9), 806.

Hann, D., Winter, K., & Jacobsen, P. (1999). Measurement of depressive symptoms in cancer patients: evaluation of the Center for Epidemiological Studies Depression Scale (CES-D). *Journal of Psychosomatic Research*.

Harris, M., Glozier, N., Ratnavadivel, R., & Grunstein, R. R. (2009). Obstructive sleep apnea and depression. *Sleep Medicine reviews*, *13*(6), 437-444.

Harris, M., Glozier, N., Ratnavadivel, R., & Grunstein, R. R. (2009). Obstructive sleep apnea and depression. *Sleep Medicine Reviews*, *13*(6), 437-444.

Harrison, Y., & Horne, J. A. (2000). The impact of sleep deprivation on decision making: a review. *Journal of Experimental Psychology: Applied*, *6*(3), 236.

Harth, E. (1995). The sketchpad model, a theory of consciousness, perception and imagery. *Consciousness & Cognition, 4*, 346 –368.

Harvey, A. G. (2001). Insomnia: symptom or diagnosis?. *Clinical Psychology Review*, *21*(7), 1037-1059.

Herscovitch, J., & Broughton, R. (1981). Sensitivity of the stanford sleepiness scale to the effects of cumulative partial sleep deprivation and recovery oversleeping. *Sleep*, *4*(1), 83.

Herzog, E. D. (2007). Neurons and networks in daily rhythms. *Nature Reviews Neuroscience*, *8*(10), 790-802.

Heuer, F., & Reisberg, D. (1990). Vivid memories of emotional events: The accuracy of remembered minutiae. *Memory & Cognition*, *18*(5), 496-506.

Horne, J. (1988). *Why we sleep: The functions of sleep in humans and other mammals*. Oxford University Press.

Horne, J. A. (1985). Sleep function, with particular reference to sleep deprivation. *Annals of Clinical Research*.

Horne, J. A., & Baulk, S. D. (2003). Awareness of sleepiness when driving. *Psychophysiology*, *41*(1), 161-165.

Horne, J., & Reyner, L. (1999). Vehicle accidents related to sleep: a review. *Occupational and Environmental Medicine*, *56*(5), 289-294.

Hu, P., Stylos-Allan, M., & Walker, M. P. (2006). Sleep facilitates consolidation of emotional declarative memory. *Psychological Science*, *17*(10), 891-898.

Hublin, C., Kaprio, J., Partinen, M., & Koskenvuo, M. (2001). Insufficient sleep--a population-based study in adults. *Sleep*, *24*(4), 392.

Iber, C. (2007). *The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications*. American Academy of Sleep Medicine.

Ji, J.Z., Wang, X.M., & Li, B.M. (2003). Deficit in long-term contextual fear memory induced by blockade of beta-adrenoceptors in hippocampal CA1 region. *European Journal Neuroscience, 17*(9), 1947-1952.

Johns, M. W. (1991). A new method for measuring daytime sleepiness: the Epworth sleepiness scale. s*leep*, *14*(6), 540-545.

Kamba, M., Inoue, Y., Higami, S., Suto, Y., Ogawa, T., & Chen, W. (2001). Cerebral metabolic impairment in patients with obstructive sleep apnoea: an independent association of obstructive sleep apnoea with white matter change. *Journal of Neurology, Neurosurgery & Psychiatry*, *71*(3), 334-339.

Kane, M. J., & Engle, R. W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-differences perspective. *Psychonomic Bulletin & Review*, *9*(4), 637-671.

Kapur, V., Blough, D.K., Sandblom, R.E., Hert, R., De Maine, J.B., Sullivan, S.D., & Psaty, B.M. (1999). The medical cost of undiagnosed sleep apnea. *Sleep, 22*, 749–755.

Kensinger, E. A., & Corkin, S. (2004). Two routes to emotional memory: Distinct neural processes for valence and arousal. *Proceedings of the National Academy of Sciences of the United States of America*, *101*(9), 3310-3315.

Kilpatrick, L., & Cahill, L. (2003). Amygdala modulation of parahippocampal and frontal regions during emotionally influenced memory storage. *Neuroimage*, *20*(4), 2091.

Kleinsmith, L. J., & Kaplan, S. (1964). Interaction of arousal and recall interval in nonsense syllable paired-associate learning. *Journal of Experimental Psychology; Journal of Experimental Psychology*, *67*(2), 124.

Kleitman, N. (1963). Deprivation of sleep. *Sleep and wakefulness*, 215-229.

Knight, R. G., Williams, S., McGee, R., & Olaman, S. (1997). Psychometric properties of the Centre for Epidemiologic Studies Depression Scale (CES-D) in a sample of women in middle life. *Behaviour Research and Therapy*, *35*(4), 373-380.

Koslowsky, M., & Babkoff, H. (1992). Meta-analysis of the relationship between total sleep deprivation and performance. *Chronobiology International*, *9*(2), 132-136.

Kribbs, N. B., & Dinges, D. (1994). Vigilance decrement and sleepiness.

Kripke, D. F., Ancoli-Israel, S., Klauber, M. R., Wingard, D. L., Mason, W. J., & Mullaney, D. J. (1997). Prevalence of sleep-disordered breathing in ages 40–64 years: a population-based survey. *Sleep*, *20*(1), 65.

Kripke, D. F., Ancoli-Israel, S., Klauber, M. R., Wingard, D. L., Mason, W. J., & Mullaney, D. J. (1997). Prevalence of sleep-disordered breathing in ages 40–64 years: a population-based survey. *Sleep*, *20*(1), 65.

LaBar, K. S., & Cabeza, R. (2006). Cognitive neuroscience of emotional memory. *Nature Reviews Neuroscience*, *7*(1), 54-64.

LaBar, K. S., & Phelps, E. A. (1998). Arousal-mediated memory consolidation: Role of the medial temporal lobe in humans. *Psychological Science*, *9*(6), 490-493.

Landrigan, C. P., Rothschild, J. M., Cronin, J. W., Kaushal, R., Burdick, E., Katz, J. T., ... & Czeisler, C. A. (2004). Effect of reducing interns' work hours on serious

medical errors in intensive care units. *New England Journal of Medicine*, *351*(18), 1838-1848.

Lau, E. Y. Y., Eskes, G. A., Morrison, D. L., Rajda, M., & Spurr, K. F. (2010). Executive function in patients with obstructive sleep apnea treated with continuous positive airway pressure. *Journal of the International Neuropsychological Society*, *16*(6), 1077.

Leger, D. (1994). The cost of sleep-related accidents: a report for the National Commission on Sleep Disorders Research. *Sleep*, *17*(1), 84.

Lewis, P. A., Critchley, H. D., Smith, A. P., & Dolan, R. J. (2005). Brain mechanisms for mood congruent memory facilitation. *Neuroimage*, *25*(4), 1214-1223.

Lewis, R. F. (1995). Digit vigilance test. *Psychological Assessment Resources*.

Lim, J., & Dinges, D. F. (2010). A meta-analysis of the impact of short-term sleep deprivation on cognitive variables. *Psychological Bulletin*, *136*(3), 375.

LoBue, V., & DeLoache, J. S. (2008). Detecting the snake in the grass attention to fear-relevant stimuli by adults and young children. *Psychological Science*, *19*(3), 284-289.

Lockley, Barger, Ayas, Rothschild, & Czeisler, (2007). Effects of Health Care Provider Work Hours and Sleep Deprivation on Safety and Performance, Joint Commission Journal on Quality and Patient Safety

Lubin, A. (1967). *Performance Under Sleep Loss and Fatigue* (No. 67-26).

Lyznicki, J. M., Doege, T. C., Davis, R. M., & Williams, M. A. (1998). Sleepiness, driving, and motor vehicle crashes. *JAMA: The Journal of the American Medical Association*, *279*(23), 1908-1913.

Marrosu, F., Portas, C., Mascia, M. S., Casu, M. A., Fà, M., Giagheddu, M., ... & Gessa, G. L. (1995). Microdialysis measurement of cortical and hippocampal acetylcholine release during sleep-wake cycle in freely moving cats. *Brain Research*, *671*(2), 329-332.

Marshall, L., & Born, J. (2007). The contribution of sleep to hippocampus-dependent memory consolidation. *Trends in Cognitive Science, 11*(10), 442-450.

Martin, S. E., Engleman, H. M., Deary, I. J., & Douglas, N. J. (1996). The effect of sleep fragmentation on daytime function. *American Journal of Respiratory and Critical Care Medicine*, *153*(4), 1328-1332.

Martin, S. E., Wraith, P. K., Deary, I. J., & Douglas, N. J. (1997). The effect of nonvisible sleep fragmentation on daytime function. *American Journal of Respiratory and Critical Care Medicine* , *155*(5), 1596-1601.

Maruishi M., Miyatani M., Nakao T., and Muranaka H. (2007). Compensatory cortical activation during performance of an attention task by patients with diffuse axonal injury: a functional magnetic resonance imaging study. *Journal of Neurology, Neurosurgery, and Psychiatry, 78,* 168–173

Matthews, C. G., & Klove, H. (1964). Instruction manual for the adult neuropsychology test battery. *Madison, WI: University of Wisconsin Medical School*.

McCartt, A. T., Ribner, S. A., Pack, A. I., & Hammer, M. C. (1996). The scope and nature of the drowsy driving problem in New York State. *Accident Analysis & Prevention*, *28*(4), 511-517.

McCartt, A. T., Rohrbaugh, J. W., Hammer, M. C., & Fuller, S. Z. (2000). Factors associated with falling asleep at the wheel among long-distance truck drivers. *Accident Analysis and Prevention*.

McGaugh, J. L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. *Annual Review of Neuroscience*, *27*, 1-28.

McGrath, M. J., & Cohen, D. B. (1978). REM sleep facilitation of adaptive waking behavior: A review of the literature. *Psychological Bulletin*, *85*(1), 24.

Mitler, M. M., Carskadon, M. A., Czeisler, C. A., Dement, W. C., Dinges, D. F., & Graeber, R. C. (1988). Catastrophes, sleep, and public policy: consensus report. *Sleep*, *11*(1), 100.

Moore, P., Bardwell, W. A., Ancoli-Israel, S., & Dimsdale, J. E. (2001). Association between polysomnographic sleep measures and health-related quality of life in obstructive sleep apnea. *Journal of Sleep Research*, *10*(4), 303-308.

Naëgelé, B., Thouvard, V., Pépin, J. L., & Lévy, P. (1995). Deficits of cognitive executive functions in patients with sleep apnea syndrome. *Sleep: Journal of Sleep Research & Sleep Medicine*.

Naismith, S. L., Winter, V. R., Hickie, I. B., & Cistulli, P. A. (2005). Effect of oral appliance therapy on neurobehavioral functioning in obstructive sleep apnea: a randomized controlled trial. *Journal of Clinical Sleep Medicine*, *1*(4), 374-380.

Nishida, M., Pearsall, J., Buckner, R. L., & Walker, M. P. (2009). REM sleep, prefrontal theta, and the consolidation of human emotional memory. *Cerebral Cortex*, *19*(5), 1158-1166.

Nofzinger, E. A., Price, J. C., Meltzer, C. C., Buysse, D. J., Villemagne, V. L., Miewald, J. M., ... & Kupfer, D. J. (2000). Towards a neurobiology of dysfunctional arousal in depression: the relationship between beta EEG power and regional cerebral glucose metabolism during NREM sleep. *Psychiatry Research: Neuroimaging*.

Norris, C. J., & Cacioppo, J. T. (2007). I know how you feel: Social and emotional information processing in the brain. *Social Neuroscience: Integrating Biological and Psychological Explanations of Social Behavior*, 84-105.

Ohayon, M. M. (2003). The effects of breathing-related sleep disorders on mood disturbances in the general population. *The Journal of Clinical Psychiatry*, *64*(10), 1195-1200.

Okamura, H. (2007, January). Suprachiasmatic nucleus clock time in the mammalian circadian system. In *Cold Spring Harbor Symposia on Quantitative Biology* (Vol. 72, pp. 551-556). Cold Spring Harbor Laboratory Press.

Olson, L. G., King, M. T., Hensley, M. J., & Saunders, N. A. (1995). A community study of snoring and sleep-disordered breathing. Prevalence. *American Journal of Respiratory and Critical Care Medicine*, *152*(2), 711-716.

Pace-Schott, E. F., & Hobson, J. A. (2002). The neurobiology of sleep: genetics, cellular physiology and subcortical networks. *Nature Reviews Neuroscience*, *3*(8), 591-605.

Paré, D., Collins, D. R., & Pelletier, J. G. (2002). Amygdala oscillations and the consolidation of emotional memories. *Trends in Cognitive Sciences*, *6*(7), 306-314.

Park, D. C., & Reuter-Lorenz, P. (2009). The adaptive brain: aging and neurocognitive scaffolding. *Annual Review of Psychology, 60*, 173.

Park, K. M., Nam, W. H., Lim, E. J., Song, S. H., Lee, H. W., & Kim, J. S. (2007). Correlation Analysis between Self-reported Measures in Patients with OSA. *Korean Journal of Otorhinolaryngology-Head and Neck Surgery*, 50(10), 888-895.

Paunio, T., Korhonen, T., Hublin, C., Partinen, M., Kivimäki, M., Koskenvuo, M., & Kaprio, J. (2009). Longitudinal study on poor sleep and life dissatisfaction in a nationwide cohort of twins. *American Journal of Epidemiology, 169*(2), 206-213.

Peppard, P. E., Szklo-Coxe, M., Hla, K. M., & Young, T. (2006). Longitudinal association of sleep-related breathing disorder and depression. *Archives of Internal Medicine*, *166*(16), 1709.

Phelps, E. A. (2004). Human emotion and memory: interactions of the amygdala and hippocampal complex. *Current opinion in Neurobiology*, *14*(2), 198-202.

Pilcher, J. J., & Huffcutt, A. J. (1996). Effects of sleep deprivation on performance: a meta-analysis. *Sleep: Journal of Sleep Research & Sleep Medicine*.

Porkka-Heiskanen, T., Strecker, R. E., Thakkar, M., Bjørkum, A. A., Greene, R. W., & McCarley, R. W. (1997). Adenosine: a mediator of the sleep-inducing effects of prolonged wakefulness. *Science*, *276*(5316), 1265-1268.

Posner, M.I. (1994). Attention: the mechanism of consciousness. *Proceedings of the National Academy of Sciences*, USA, 91, 7398 –7403.

Powell, N. B., Riley, R. W., Schechtman, K. B., Blumen, M. B., Dinges, D. F., & Guilleminault, C. (1999). A Comparative Model: Reaction Time Performance in

Sleep-Disordered Breathing Versus Alcohol-Impaired Controls. *The Laryngoscope*, *109*(10), 1648-1654.

Power, A. E., & McGaugh, J. L. (2002). Cholinergic activation of the basolateral amygdala regulates unlearned freezing behavior in rats. *Behavioural Brain Research*, *134*(1), 307-315.

Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods, 40*, 879-891.

Price, W. J., & Holley, D. C. (1990). Shiftwork and safety in aviation. *Occupational Medicine (Philadelphia, Pa.)*, *5*(2), 343.

Punjabi, N. M. (2008). The epidemiology of adult obstructive sleep apnea. *Proceedings of the American Thoracic Society, 5*(2), 136-143.

Radloff, L. S. (1977). The CES-D scale A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*(3), 385-401.

Raguet, M. L., Campbell, D. A., Berry, D. T., Schmitt, F. A., & Smith, G. T. (1996). Stability of intelligence and intellectual predictors in older persons. *Psychological Assessment*, *8*(2), 154.

Ralls, F. M., & Grigg-Damberger, M. (2012). Roles of gender, age, race/ethnicity, and residential socioeconomics in obstructive sleep apnea syndromes. *Current Opinion in Pulmonary Medicine, 18*(6), 568-573.

Rechtschaffen, A., & Kales, A. (1968). A manual of standardized terminology, techniques, and scoring systems for sleep stages of human subjects. US Department of Health, Education, and Welfare, Public Health Service, National

Inst. of Health, National Inst. of Neurological Diseases and Blindness, Neurological Information Network.

Reid, M. C., Fiellin, D. A., & O'Connor, P. G. (1999). Hazardous and harmful alcohol consumption in primary care. *Archives of Internal Medicine, 159*(15), 1681-1689.

Reimer, M. A., & Flemons, W. W. (2003). Quality of life in sleep disorders. *Sleep medicine reviews*, *7*(4), 335-349.

Reiten, R. M. (1955). The relation of trail making test to organic brain damage. *Journal of Consulting Psychology*, *10*, 76-88.

Rey, A. (1964). L'Examin clinique en psychologie. Paris: Universitaire de France.

Richardson, G. S., Miner, J. D., & Czeisler, C. A. (1989-1990). Impaired driving performance in shiftworkers: the role of the circadian system in a multifactorial model. *Alcohol, Drugs & Driving*, 5&6, 265–273.

Roberts, R. E., Vernon, S. W., & Rhoades, H. M. (1989). Effects of language and ethnic status on reliability and validity of the Center for Epidemiologic Studies-Depression Scale with psychiatric patients. *Journal of Nervous and Mental Disease*.

Rosen, W. G. (1980). Verbal fluency in aging and dementia. *Journal of Clinical and Experimental Neuropsychology*, *2*(2), 135-146.

Rosenthal, M. S. (1998). Physiology and neurochemistry of sleep. *American Journal of Pharmaceutical Education*, *62*, 204-207.

Rosenthal, L. D., & Dolan, D. C. (2008). The Epworth sleepiness scale in the identification of obstructive sleep apnea. *The Journal of Nervous and Mental Disease, 196*(5), 429-431.

Rosenwasser, A. M., & Turek, F. W. (2005). Physiology of the mammalian circadian system. *Principles and Practice of Sleep Medicine*, *4*, 351-362.

Rupp, T., Arnedt, J.T., Acebo, C., Carskadon, M.A. (2004). Performance on a dual driving simulation and subtraction task following sleep restriction. *Perceptual and Motor Skills*, *99*(3), 739-753.

Saletin, J. M., & Walker, M. P. (2012). Nocturnal mnemonics: sleep and hippocampal memory processing. *Frontiers in Neurology*, *3*.

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

Sanford, L. D., Silvestri, A. J., Ross, R. J., & Morrison, A. R. (2001). Influence of fear conditioning on elicited ponto-geniculo-occipital waves and rapid eye movement sleep. *Archives Italiennes de Biologie*, *139*(3), 169-183.

Sanford, L. D., Tang, X., Ross, R. J., & Morrison, A. R. (2003). Influence of shock training and explicit fear-conditioned cues on sleep architecture in mice: strain comparison. *Behavior Genetics*, *33*(1), 43-58.

Saper, C. B., Chou, T. C., & Scammell, T. E. (2001). The sleep switch: hypothalamic control of sleep and wakefulness. *Trends in Neurosciences*, *24*(12), 726-731.

Schretlen, D. J., Testa, S., Winicki, J. M., Pearlson, G. D., & Gordon, B. (2008). Frequency and bases of abnormal performance by healthy adults on neuropsychological testing. *Journal of the International Neuropsychological Society*, *14*(03), 436-445.

Schroeder, J. P., & Packard, M. G. (2002). Posttraining intra-basolateral amygdala scopolamine impairs food-and amphetamine-induced conditioned place preferences. *Behavioral Neuroscience*, *116*(5), 922.

Sforza, E., de Saint Hilaire, Z., Pelissolo, A., Rochat, T., & Ibanez, V. (2002). Personality, anxiety and mood traits in patients with sleep-related breathing disorders: effect of reduced daytime alertness. *Sleep Medicine*, *3*(2), 139-145.

Sharot, T., & Phelps, E. A. (2004). How arousal modulates memory: Disentangling the effects of attention and retention. *Cognitive, Affective, & Behavioral Neuroscience*, *4*(3), 294-306.

Smith, A. (1982). Symbol Digit Modality Test Manual. *Los Angeles, Western Psychological Services*.

Smith, C. (1985). Sleep states and learning: a review of the animal literature. *Neuroscience & Biobehavioral Reviews*, *9*(2), 157-168.

Snyder, K. A., & Harrison, D. W. (1997). The affective auditory verbal learning test. *Archives of Clinical Neuropsychology, 12*(5), 477-482.

Spreen, O., & Benton, A. L. (1977). *Neurosensory Center Comprehensive Examination for Aphasia (NCCEA), 1977 Revision: Manual of Instructions*. Neuropsychology Laboratory, University of Victoria.

Steenhuis, R. E., & Østbye, T. (1995). Neuropsychological test performance of specific diagnostic groups in the Canadian Study of Health and Aging (CSHA). *Journal of Clinical and Experimental Neuropsychology*, *17*(5), 773-785.

Strange, B. A., Hurlemann, R., & Dolan, R. J. (2003). An emotion-induced retrograde amnesia in humans is amygdala-and β-adrenergic-dependent. *Proceedings of the National Academy of Sciences*, *100*(23), 13626-13631.

Strauss, G. P., & Allen, D. N. (2013). Emotional verbal learning test: development and psychometric properties. Archives of Clinical Neuropsychology: *The Official Journal of the National Academy of Neuropsychologists, 28*(5), 435–451.

Strauss, E., Sherman, E. M., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms, and commentary*. Oxford University Press, USA.

Stutts, J. C., Wilkins, J. W., Osberg, S. J., & Vaughn, B. V. (2003). Driver risk factors for sleep-related crashes. *Accident Analysis and Prevention, 35,* 321-331.

Suchy, Y. (2011). *Clinical Neuropsychology of Emotion*. The Guilford Press.

Sugarman, M. A., & Axelrod, B. N. (2015). Embedded measures of performance validity using verbal fluency tests in a clinical sample. *Applied Neuropsychology: Adult, 22*(2), 141-146.

Tabachnick, B. G., & Fidell, L. S. (2001). Using multivariate statistics.

Taylor, W. D., MacFall, J. R., Steffens, D. C., Payne, M. E., Provenzale, J. M., & Krishnan, K. (2003). Localization of age-associated white matter hyperintensities in late-life depression. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *27*(3), 539-544.

Thomas, A. J., O'Brien, J. T., Barber, R., McMeekin, W., & Perry, R. (2003). A neuropathological study of periventricular white matter hyperintensities in major depression. *Journal of Affective Disorders*, *76*(1), 49-54.

Thomas, K. S., Bardwell, W. A., Ancoli-Israel, S., & Dimsdale, J. E. (2006). The toll of ethnic discrimination on sleep architecture and fatigue. *Health Psychology; Health Psychology*, *25*(5), 635.

Tombaugh, T. N., Kozak, J., & Rees, L. (1999). Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. *Archives of Clinical Neuropsychology*, *14*(2), 167-177.

Turner, T. H., Drummond, S., Salamat, J. S., & Brown, G. G. (2007). Effects of 42 hr of total sleep deprivation on component processes of verbal working memory. *Neuropsychology*, *21*(6), 787.

Van Der Werf, Y. D., Altena, E., Schoonheim, M. M., Sanz-Arigita, E. J., Vis, J. C., De Rijke, W., & Van Someren, E. J. (2009). Sleep benefits subsequent hippocampal functioning. *Nature Neuroscience*, *12*(2), 122-123.

Van Dongen, H. P. A., Baynard, M. D., Maislin, G., & Dinges, D. F. (2004). Systematic interindividual differences in neurobehavioral impairment from sleep loss: evidence of trait-like differential vulnerability. *Sleep*, *27*(3), 423-433.

Van Dongen, H. P., Maislin, G., Mullington, J. M., & Dinges, D. F. (2003). The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep*, *26*(2), 117-129.

Wagner, U., Kashyap, N., Diekelmann, S., & Born, J. (2007). The impact of post-learning sleep vs. wakefulness on recognition memory for faces with different facial expressions. *Neurobiology of Learning and Memory*, *87*(4), 679-687.

Walker, M. P. (2009). The role of sleep in cognition and emotion. *Annals of the New York Academy of Sciences*, *1156*(1), 168-197.

Walker, M. P., & Stickgold, R. (2006). Sleep, memory, and plasticity. *Annual Reviews of Psychology, 57*, 139-166.

Walker, M. P., & van Der Helm, E. (2009). Overnight therapy? The role of sleep in emotional brain processing. *Psychological Bulletin; Psychological Bulletin*, *135*(5), 731.

Waller, D. A., Hardy, B. W., Pole, R., & Giles, D., Guillion, & Rush. (1989). Sleep EEG in bulimic, depressed, and normal subjects. *Biological Psychiatry*.

Waters, F., & Bucks, R. S. (2011). Neuropsychological effects of sleep loss: Implication for neuropsychologists. *Journal of the International Neuropsychological Society*, *17*(04), 571-586.

Watson, D., & Clark, L. A. (1999). The PANAS-X: Manual for the positive and negative affect schedule-expanded form.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology*, *54*(6), 1063.

Weaver, T. E., & Grunstein, R. R. (2008). Adherence to Continuous Positive Airway Pressure Therapy The Challenge to Effective Treatment. *Proceedings of the American Thoracic Society*, *5*(2), 173-178.

Wechsler, D. (1981). Wechsler adult intelligence scale (rev. ed.). *New York: Psychological Corporation*.

Wehr, T. A., Moul, D. E., Barbato, G., Giesen, H. A., Seidel, J. A., Barker, C., & Bender, C. (1993). Conservation of photoperiod-responsive mechanisms in humans. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *265*(4), R846-R857.

Wilkinson, R. T. (1961). Performance under sleep-deprivation. *Acta Psychologica*, *19*, 803.

Williams, H. L., Lubin, A., & Goodnow, J. J. (1959). Impaired performance with acute sleep loss. *Psychological Monographs: General and Applied*, *73*(14), 1.

Williamson, A. M., & Feyer, A. M. (2000). Moderate sleep deprivation produces impairments in cognitive and motor performance equivalent to legally prescribed levels of alcohol intoxication. *Occupational and Environmental Medicine*, *57*(10), 649-655.

Wolfe, P. L., Millis, S. R., Hanks, R., Fichtenberg, N., Larrabee, G. J., & Sweet, J. J. (2010). Effort indicators within the California verbal learning test-II (CVLT-II). *The Clinical Neuropsychologist, 24*(1), 153-168.

Yoo, S. S., Gujar, N., Hu, P., Jolesz, F. A., & Walker, M. P. (2007). The human emotional brain without sleep—a prefrontal amygdala disconnect. *Current Biology*, *17*(20), R877-R878.

Yoo, S. S., Gujar, N., Hu, P., Jolesz, F. A., & Walker, M. P. (2007). The human emotional brain without sleep—a prefrontal amygdala disconnect. *Current Biology*, *17*(20), R877-R878.

Young, T., Palta, M., Dempsey, J., Skatrud, J., Weber, S., & Badr, S. (1993). The occurrence of sleep-disordered breathing among middle-aged adults. *New England Journal of Medicine*, *328*(17), 1230-1235.

Zich, J. M., Attkisson, C. C., & Greenfield, T. K. (1990). Screening for depression in primary care clinics: the CES-D and the BDI. *The International Journal of Psychiatry in Medicine*, *20*(3), 259-277.

Zohar, D., Tzischinsky, O., Epstein, R., & Lavie, P. (2005). The effects of sleep loss on medical residents' emotional reactions to work events: a cognitive-energy model. *Sleep: Journal of Sleep and Sleep Disorders Research, 28*(1), 47-54.

Appendix A: Additional Sleep Physiology Information

Sleep

Sleep Stages and Characteristics

Sleep in mammalian species has been generally categorized into two separate types - rapid eye movement (REM) sleep, and non-rapid eye movement (NREM) sleep, which has predominently been further subdivided in primates into four, progressively deeper, stages (Rechtschaffen & Kales, 1968). Research in human sleep patterns has identified a 90 minute alternating, ultraradian cycle between NREM and REM sleep. The length of this cycle generally does not change throughout a normal sleep session, however, the ratio of NREM to REM sleep shifts from predominantly stage 3 and 4 NREM sleep early in the sleep session to stage 2 NREM and REM sleep in the latter half of the sleep session. Thus far, the purpose or principal behind this sleep-type organization is not well understood (Walker, 2009).

More recently, NREM sleep stages have undergone a terminology transition; the American Academy of Sleep Medicine (2007) concluded that there no significant physiological or clinical differentiation existed for NREM stage 3 and stage 4 sleep, thus they were combined into a final NREM sleep stage termed N3. The original NREM stage 1 and stage 2 sleep terms were altered to N1 and N2, respectively. In this review, the new terminology will be used, unless otherwise noted.

Electroencephalographic & Associated Physiological Characteristics

Progression through sleep stages usually is tracked using electroencephalographic (EEG) activity and patterns, with progression through NREM sleep being associated with a slowing of brain wave frequency. The most recent scoring manual of the AASM (2007) provides classification guidelines in part based upon EEG phenomena, as well as certain physiological activity. During alert wakefulness, desynchronized beta waves (12-30 Hz) with a high mixture of frequencies dominate EEG readings. In stage N1, the brain transitions from alpha waves (8-12 Hz; associated with relaxed wakefulness with closed eyes) to theta waves (4-7 Hz). This stage is characterized as a state of drowsiness/somnolence and is associated with hypnic jerks (also known as positive myoclonus), and some loss in conscious environmental awareness and muscle tone. If aroused during this stage, most individuals will report having been fully awake. Stage N2 (see Figure 2*inset sleep graph of spindles & k-complexes) is characterized by EEG waves in the 11-16 Hz range (12-14 Hz is most common). Sleep spindles, brief bursts of activity, occur during this stage, and are thought to represent the brain inhibiting processing and response to external stimuli in order to maintain a tranquil state (Dang-Vu, McKinney, Buxton, Solet, & Ellenbogen, 2010). K-complexes are also present, which are thought to represent a brief evaluation of how dangerous external stimuli are before an inhibition of cortical arousal (Cash, Halgren, Dehghani, Rossetti, Thesen, Wang, et al., 2009). Roughly 50 percent of a normal sleep session is spent in N2 sleep (NIH, 2007). Reports of dreaming during N1 and N2 sleep is rare (AASM, 2007).

The AASM (2007) characterizes stage N3 (formerly stages 3 and 4) as the deepest stage of sleep, and is often referred to as slow-wave sleep (SWS) due to the occurrence of low frequency brain waves (0-4 Hz), with a minimum of 20% activity being delta waves (.5-2 Hz). Delta waves begin emerging at the onset of N3, eventually dominating the EEG. During delta wave sleep, global inhibition of neurons occurs via the release of gamma-aminobutyric acid (GABA), which will be discussed further in the neurobiology

section (Hobson & Pace-Schott, 2002). The global slowing represents a mass cortical synchronization (Steriade & Amzica, 1998), which is thought to represent an organizational processing related to daytime cognition and will be discussed later. N3 sleep is often when parasomnias (e.g., night terrors, somniloquy, sleepwalking, nocturnal enuresis) occur. Though dreaming was previously thought not to occur during any stage of NREM sleep, recent research has suggested that more disconnected, and less vivid and memorable dreams can occur during this stage (McNamara, McLaren, & Durso, 2007).

A shift in frequency occurs during REM sleep, with a reemergence of theta waves (4-7 Hz) along with the occurrence of high frequency gamma waves (30-80 Hz) that demonstrate synchronic activity (Llinas & Ribary, 1993). Another defining phenomena of REM sleep is the presence of bursts of rapid eye movement in rhythm with phasic endogenous waveforms. The waveforms primarily occur in the pons, lateral geniculate nuclei of the thalamus, and the occipital cortex, and thus are sometimes referred to as PGO waves (Callaway, Lydic, Baghdoyan, & Hobson, 1987). A typical sleep session will have REM sleep make up 20-25% (90-120 minutes) of sleep time, over the course of 4-5 progressively longer REM periods. A period of light sleep or brief arousal often occurs following a period of REM. Vivid and easily recalled dreams occur during this stage of sleep. During periods of REM sleep an increase in the variability of breathing rate, heart rate, and temperature occurs, along with increased blood flow and engorgement in the genitals (AASM, 2007). Descending muscle atonia also occurs, which has been hypothesized to be a protective process designed to prevent acting out dream sequences (Mahowald & Schenck, 2009). Thus, failure of this process is thought to be the cause of REM behavior disorder (Schenck & Mahowald, 2002).

Neurochemical Characteristics

Wakefulness is associated with ascending, efferent projections from the reticular activating system, located in the brainstem. These ascending projections arrive in the hypothalamus, thalamus, and basal forebrain, which eventually continue to the cortex. The neurotransmitters associated with the reticular formation include the catecholemines, histamine, acetycholine, asparate, and glutamate. Behavioral consequences like increased arousal after use of amphetamines and somnolence after use of anti-histamines primarily impact this system.

As an individual progresses through the different stages of sleep, dramatic changes occur to the neurochemical makeup of the brain. Saper, Chou, and Scammell (2001) offered a review that concluded the sleep-wake cycle is regulated by a reciprocally inhibitory sleep/wake switch made up of the ventrolateral preoptic nucleus (activated during sleep; GABA-ergic and galanergic) and the posterior lateral hypothalamus (activated during arousal and wakefulness maintenance; consists of orexin and hypocretin neurons). During NREM sleep GABAergic neurons in the cortex, thalamus, hypothalamus, and brain are at their highest activation. An increase of intracerebroventricular adenosine levels has also been associated with increased NREM sleep time (Rosenthal, 1998). Different studies of NREM sleep have found a decrease in the activity of subcortical cholinergic systems found in the forebrain and brainstem (Hobson, McCarley, & Wyzinski, 1975; Lydi & Baghdoyan, 1988). Additionally, compared to wakeful activation levels, the noradrenergic locus coeruleus neurons and serotonergic Raphe neurons have decreased firing rates (Aston-Jones & Bloom, 1981; Shima, Nakahama, & Yamamoto, 1986).

The acetycholinergic neurons in the pontine tegmentum (specifically, the medullary reticular and lateral pontine areas) have been termed "REM on cells," and innervate hypothalamus, hippocampus, and thalamus. Rising levels of physostigmine (a catabolic enzyme inhibitor) during NREM precipitate the initiation of REM sleep. Additionally, research has demonstrated that introducing carbochal (a muscarinic agonist) to REM on cells causes REM sleep to occur (Rosenthal, 1998). During REM sleep, both of the previously mentioned aminergic centers are significantly inhibited and the cholinergic systems become as (or more) activated as wakeful levels. This results in a neurochemical environment dominated by acetylcholine with little, if any, amingergic modulation (Kametani & Kawamura, 1990; Marrosu, Portas, Mascia, Casu, Fa, Giagheddu, et al., 1995). The Raphe and locus coeruleus contain serotonergic and noradrenergic cells that have been labeled "REM off cells," which are completely or largely inactive during REM sleep, with higher degrees of activation during NREM and wakeful periods (Rosenthal, 1998). The finding that serotonin and norepinepherine levels impact REM sleep is supported by research demonstrating that anti-depressants that increase these two neurotransmitters decrease the percentage of REM sleep individuals experience, and that this decrease is proportional to the effectiveness of the drug (Benca, Obermeyer, Thisted, & Gillin, 1991; Vogel, Thurmund, Gibbons, Sloan, Boyd, & Walker, 1975).

Functional Anatomical Characteristics

NREM and REM sleep have been found to have distinctly different functional anatomy patterns, across a variety of neuroimaging techniques. Generally speaking, reduced activity in the prefrontal and temporal lobes, basal ganglia, thalamus, and brainstem occurs during NREM (specifically, stage N3). In contrast, REM sleep is associated with elevated activity in the mediobasal prefrontal lobes, occipital cortex, thalamic nuclei, and pontine tegmentum. Additionally, affect-related areas like the anterior cigulate cortex, amygdala, and hippocampus are activated. Conversely, the posterior cigulate, parietal cortex, and dorsolateral prefrontal cortex are the least activated during REM sleep (Nofzinger, 2005).

Sleep-Wake Cycle

Three separate yet networked neuroanatomical systems regulate the sleep-wake cycle in humans (Borbely & Achermann, 1999; Pace-Schott & Hobson, 2002). A homeostatic regulation system is responsible for intensity, length, and quantity of sleep. The cyclical vacillation between REM and NREM sleep within each sleep period is controlled by an ultradian system. Finally, a circadian system manages the timing of sleep and wake periods within the overall day-night cycle. Preoptic neural circuitry has been associated with the homeostatic functions, mesencephalic and pontine rostral brainstem areas with the REM/NREM regulation, and anterio-hypothalamic elements with circadian functions. With the REM/NREM relationship discussed in detail previously, the present section will focus on the remaining two drives, how the two drives interact to consolidate sleep, and finally, the current conceptualization of how the switch between sleep and wake occurs.

Homeostatic Regulation

There exists no exact understanding of the physiological processes responsible for the sleep drive that humans (and all mammals) experience, it is currently conceptualized as a homeostatic pressure that accrues during wakefulness and dissipates during sleep periods. This propensity for sleep can be thought of as how much an individual is in need of sleep

to regain homeostatic balance. The power of delta EEG waves (mentioned previously) have been demonstrated as a marker for the degree of homeostatic pressure (Fuller, Gooley, & Saper, 2012). While no cellular substrate for the process has thus been identified, adenosine has been identified as a molecular-level somnogen at the cellular level. During wakeful periods, it is hypothesized to naturally accumulate to levels that impact sleep/wake related areas of the brain. This nucleoside has an activating effect on VLPO neurons bordering the basal forebrain and an inhibitory effect on wake-promoting areas of the basal forebrain (Porkka-Heiskanen, Strecker, Thakkar, Bjorkum, Greene, & McCarley, 1997). Thus, during wakeful accumulation of adenosine, a drive towards sleep accrues.

Consistent with this model, research has demonstrated that blood serum levels of adenosine rise during extended periods of wakefulness, decrease during sleep, that adenosine agonists promote sleepiness when injected intraventricularly, and that adenosine antagonists (e.g., the commonly known substance caffeine) increase wakefulness and decrease sleepiness when introduced near the VLPO (Porkka-Heiskanen, Alanko, Kalinchuk, & Stenberg, 2002). At the same time, the cellular basis for homeostatic pressure to sleep has not been identified, as recent research pointing out that accumulation of adenosine in the basal forebrain is not required for sleep propensity (Blanco-Centurion, Xu, Murillo-Rodriguez, Gerashchenko, Shiromani, Salin-Pascual, Hof, & Shiromani, 2006).

Circadian Regulation

Reactive homeostatic drives are useful for restoring physiological equilibrium. However, there exists another regulatory process, termed the circadian timing system, that provides temporal organization of most biochemical, physiological, and neurobehavioral processes. The advantage of temporal organization, as opposed to homeostatic reaction, is its predictive and anticipatory nature (Moore-Ede, Sulzman, & Fuller, 1982). For example, prior to waking, the circadian timing system (CTS) cues processes that will be advantageous to the wakeful state (e.g., increased sympathetic autonomic activity, rise in body temperature, increased circulating cortisol levels).

The CTS is comprised of three components, the central of which is the suprachismatic nucleus (SCN) of the anterior hypothalamus, which acts as a circadian pacemaker - coordinating circadian oscillator subcomponents via control over melatonin secretion by the pineal gland (Rossenwasser & Turek, 2005). The SCN is responsible for establishing the sleep-wake circadian rhythm. Support for SCN regulation of the 24.2 hour sleep-wake cycle has been demonstrated via continuation of the cycle in the absence of temporal environmental cues, but only when the nucleus is intact (Mistlberger, 2005). The SCN is entrained (i.e. synchronized) via physiological and environmental signals, these include the retinohypothalamic tract (responsive to light-dark cycles), geniculohypothalamic tract (secondary light-dark cycle entrainment, with a moderating effect rather than direct influence), mesencephalic raphe nuclei (seratonergic modulation of photic inputs and mediation of behavioral activity-states), and other neurochemical-specific afferent tracts (histaminergic projections from the hypothalamus, cholinergic projections from basal forebrain and pontine tegmentum, and noradrenergic projections from the brainstem) (Bina, Rusak, & Semba, 1993; Moga & Moore, 1997; Morin & Allen, 2006; Morin & Pace, 2002; Stephan & Zucker, 1972; Wada, Inagaki, Itowi, & Yamatodani, 1991). The subcomponent circadian-oscillators in peripheral tissues are in

turn entrained by physiological signals from the pacemaker component. Peripheral circadian oscillators are understood to also contain endogenous, cellular-level pacemaker "clock cells," independent of the circadian system as a whole (Herzog, 2007). The SCN is thus thought to entrain the various peripheral cellular oscillators rather than sustain their rhythmic activity (Okamura, 2004). Finally, the third component of the CTS are the efferent projections that serve to regulate otherwise non-rhythmic physiological and behavioral systems (e.g., body temperature, autonomic/endocrine systems, feeding, sleep/wake state, locomotor activity). Most SCN efferent projections reach regions of the thalamus, basal forebrain, preoptic area, and hypothalamus (Morin & Allen, 2006). Current understanding of the circadian system posits that it promotes both wakefulness and sleep - at opposite phases (Mistlberger, 2005).

Sleep-Wake "Switch"

Saper, Chou, and Scammell (2001) reviewed recent literature on sleep regulation and identified a substantial amount of evidence that a reciprocal inhibition model of sleep and arousal systems exists. GABAergic and galaninergic neurons of the ventrolateral preoptic nucleus (VLPO) are active and necessary for normal sleep. In contrast, hypocretin/orexin (exchangeable names) neurons within the posterior lateral hypothalamus (PLHT) are necessary for maintaining normal wakefulness. These two systems are thought to exist in a sustained state of balanced reciprocal inhibition (a bistable feedback loop) when not influenced from external pressures. Once either of the systems is excited, it inhibits the other, thereby resulting in further excitation due to decreased inhibitory afferents from its partner.

This neuroanatomical equivalent of a "flip-flop" circuit has the advantage of resulting in two potential firing patterns and an avoidance of an intermediary state. The result is a behaviorally stable wakeful or sleep state, with switches occurring rapidly and therefore transition periods being brief. Additionally, the self-reinforcing characteristic means the wakeful/sleep states are relatively resistant to switching due to normal projection fluctuations occurring over the day and night. Instead, the switch can only be "flipped" by the large, accumulating, physiological pressure from homeostatic and circadian inputs. Dysfunction of either system decreases the balance of the switch, lowering the threshold for one behavioral state to be initiated and raising the needed pressure to "flip" the switch to the other. To summarize the effects of both the individual wakeful/sleep systems, and their reciprocal relationship, let us consider a lesion to the VLPO. This would result in decreased sleep-encouraging projections, more wakefulness, and therefore increased homeostatic pressure for sleep on the flip-flop circuit. This results in the circuit nearing its switch-point more often, and more episodes of falling asleep, however, due to the self-reinforcing characteristic of the switch having been weakened, this sleep-state is interrupted more often. The overall result being shortened periods of wakefulness and sleep, switching more frequently.

Appendix B: Demographics

DATE: _____

TIME:_____

Please provide the following information. You are not obligated to answer questions that you do not feel comfortable answering.

1) Gender: __Female __Male

__Other:_____

2) Age: _____

3) Country of birth: _____

Length of residence in Canada: _____

4) Ethnicity:

__ Caucasian/White __ African-Canadian/Black __ Asian/Southeast Asian

__Hispanic __ First Nation/Indigenous __ Arabic

__ Other:

5) First language: _____

Other languages spoken:

If English is 2nd language, at what age did you begin speaking it?

6) Highest grade completed in high school: _____

If you attended school after high school was it a (check all that apply):

__Technical or Vocational School?

__ College or University?

How many years of education did you complete after high school? _____

7) History of military service?

__ No

__ Yes; please specify length of service, and if you were deployed in combat:

_____

8) What is your current occupation, if you are retired, what was your primary occupation before you retired?

_____

_____

__

9) Approximately what was the total combined income of all members of this family in 2011?

___ 0 - $10,000
__ $10,001 - $15,000
__ $15,001 - $20,000
__ $20,001 - $30,000
__ $30,001 - $40,000
__ $40,001 - $50,000
__ $50,001 - $75,000
__ $75,001 or more

10) List of current medications (if you cannot remember the name, please describe what the medication looks like and what reason it is being taken):

_____
_____
_____
_____
____

11) Have you ever been assessed, diagnosed, and/or treated for a psychological disorder (e.g., Attention-deficit hyperactivity disorder, Depression, Anxiety, Bipolar Disorder, Schizophrenia, etc.)?

__ No

__ Yes; please specify disorder/s, and whether you currently use or in the past used medication to treat the symptoms:

_____
_____
_____
_____

12) Do you smoke tobacco products currently?

__ Yes; specify type and amount per week: _____

__ No

If you smoked in the past, how much, for what period of time, and when did you quit?

_____

13) Do you drink alcoholic beverages currently?

__ Yes; specify type and amount per week: _____

__ No

If you drank in the past, how much, for what period of time, and when did you quit?

_____

14) Do you use any other recreational drugs (e.g. cocaine, marijuana, heroin, etc.) currently?

__ Yes; specify type and amount per week: _____

__ No

If you used the past, how much, for what period of time, and when did you quit?

_____

15) Have you ever suffered a hard hit to the head (sometimes called a concussion)?

__ No

__ Yes; How many instances (estimate if you need)?_____

Did you lose consciousness?

__ No

__ Yes, for how long? _____

16) Have you ever suffered from seizures or any other neurological conditions (e.g., cerebral-vascular accidents, strokes, traumatic brain injuries, etc.)?

__ No

__ Yes; please specify condition and the time period it occurred:

_____

17) Do any of your blood relatives suffer from psychological disorders (e.g., Depression, Bipolar Disorder, Schizophrenia, etc.)?

__ No

__ Yes; please specify relation and disorder:
_____

18) Do any of your blood relatives suffer from neurological disorders (e.g., Alzheimer's disease, Parkinson's disease, other dementias, etc.)?

__ No

__ Yes; please specify relation and disorder:
_____

19) Do you suffer from any sort of chronic pain?

__ No

__ Yes; please specify source of pain and whether it is controlled with medication:
_____
_____

Are you in pain today?

__ No

__ Yes; please draw an **X** on the line below indicating the severity of pain you are in at this moment

|----------|

No Pain Worst Pain Imaginable

20) Are you diagnosed with any sleep-related disorder?

__ No

__ Yes; please specify type of disorder and when you were diagnosed:

_____

21) Approximately what month & year did you undergo a sleep study, also called a polysomnogram study?
(This would have entailed you coming into a sleep lab, being hooked up to many wires, and monitored throughout the night)

Year: ____ Month: ____ Day (if you can recall): ____

22) How many hours of sleep did you get **last** night? _____ Hours

Was your sleep last night restful?

__ Yes

__ No; why?

_____

23) How many times do you take a nap each week? _____ times per week

How many minutes do your naps usually last? _____ minutes

24) Do you have a Continuous Positive Airway Pressure (CPAP) device?

__ Yes

__ No; why not? (e.g., doctor never prescribed one; too expensive; it got lost; it broke, etc.)_____

25) Has your physician ever recommended you use a Continuous Positive Air Pressure (CPAP) device?

__ No

__ Yes;

Please specify how long ago the CPAP was suggested/prescribed

_____

How often do you use your CPAP?

__ every night (7 nights per week)
__ most (5-6 nights per week)
__ every other night (3-4 nights per week)

__ infrequently (1-2 nights per week)
__ rarely to never (0-1 nights per week)

If you are currently using a CPAP, how many nights have you used it in the past week?

____ nights (1-7)

If you do not use your CPAP every night, what stops you? Mark those descriptors that if improved, would result in you using your CPAP significantly more often.

__ too uncomfortable __ too loud
__ too embarrassing __ I forget to put it on before sleeping
__ I do not understand how to use it, I was not given enough instruction
__ I do not understand how to use it, I have forgotten the instructions I was given

26) How tall are you? _____ How much do you weigh? _____

27) List any cardio-vascular or metabolic disorders or diseases (e.g., diabetes, congestive heart disease, arthrosclerosis, history of heart attack, history of stroke)

_____
_____
__

28) List any respiratory disorders, diseases, or problems you have (e.g., asthma, Chronic Obstructive Pulmonary Disorder - COPD, chronic bronchitis, emphysema, etc.)

_____
_____

29) Do you exercise regularly?

__ No
__ Yes
How many days per week? _____ (1-7)
On days you do exercise, how long does your workout last on average? _____
What types of exercise do you use (check all that apply)?

__ Brisk walking __ Jogging/Running

__ Swimming __ Bicycling

__ Other cardio (e.g., jumping jacks, lunges, aerobics, stair-climbing, etc.)

__ Weight-lifting __ Other:_____

30) Please place a check mark next to any of the below medical conditions that you have been diagnosed with:

__ Myocardial infarction
(heart attack)

__ Congestive heart failure

__ Peripheral vascular disease
(also known as peripheral arterial disease, peripheral artery occlusive disease)

__ Cerebrovascular disease

__ Dementia

__ Chronic pulmonary disease

__ Connective tissue disease

__ Peptic ulcer disease

__ Mild liver disease (without portal hypertension, inlcudes chronic hepatitis)

__ Diabetes without end-organ damage (excludes diet-controlled alone)

__ Hemiplegia (one-sided paralysis of limbs/trunk of body)

__ Moderate or severe renal disease

__ Diabetes with end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes)

__ Tumor without metastasis (found within last 5 years)

__ Leukemia (acute or chronic)

__ Lymphoma

__ Moderate or severe liver disease

__ Metastatic solid tumor

__ AIDS (not just HIV positive)

Appendix C: Pittsburgh Sleep-Quality Index (PSQI)

INSTRUCTIONS:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, what time have you usually gone to bed at night?
BED TIME _____

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
NUMBER OF MINUTES _____

3. During the past month, what time have you usually gotten up in the morning?
GETTING UP TIME _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be
different than the number of hours you spent in bed.)
HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

f) Feel too cold

Not during the	Less than	Once or twice	Three or more

past month_____	once a week_____	a week_____	times a week_____

g) Feel too hot

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

h) Had bad dreams

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

i) Have pain

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

j) Other reason(s), please describe_____
How often during the past month have you had trouble sleeping because of this?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

6.
During the past month, how would you rate your sleep quality overall?
Very good _____Fairly good _____Fairly bad ___Very bad _____

7.
During the past month, how often have you taken medicine to help you sleep (prescribed or
"over the counter")?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

8.
During the past month, how often have you had trouble staying awake while driving, eating
meals, or engaging in social activity?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

9.
During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____
Only a very slight problem _____
Somewhat of a problem _____
A very big problem _____

10. Do you have a bed partner or room mate?

No bed partner or room mate _____

Partner/room mate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

If you have a room mate or bed partner, ask him/her how often in the past month you have had . . .

a) Loud snoring

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Long pauses between breaths while asleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Legs twitching or jerking while you sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Episodes of disorientation or confusion during sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Other restlessness while you sleep; please describe_____

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Appendix D: Epworth Sleepiness Scale (ESS)

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation.

0 = would **never** doze
1 = **slight** chance of dozing
2 = **moderate** chance of dozing
3 = **high** chance of dozing

Situation	**Chance of Dozing**
Sitting and reading	
Watching TV	
Sitting, inactive, in a public place (e.g., a theater or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking with someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in traffic	
Total	

Appendix E: Center for Epidemiological Studies Depression Scale (CES-D)

Below is a list of the ways you might have felt or behaved. Please tell me how often you have **felt this way during the past week.**

	Rarely or none of the time **(less than 1 day)**	Some or a little of the time **(1-2 days)**	Occasionally or a moderate amount of time **(3-4 days)**	Most or all of the time **(5-7 days)**
1. I was bothered by things that usually don't bother me.				
2. I did not feel like eating; my appetite was poor.				
3. I felt that I could not shake off the blues even with help from my family or friends.				
4. I felt I was just as good as other people.				
5. I had trouble keeping my mind on what I was doing.				
6. I felt depressed.				
7. I felt that everything I did was an effort.				
8. I felt hopeful about the future.				
9. I thought my life had been a failure.				
10. I felt fearful.				
11. My sleep was restless.				
12. I was happy.				
13. I talked less than usual.				
14. I felt lonely.				
15. People were unfriendly.				
16. I enjoyed life.				
17. I had crying spells.				
18. I felt sad.				
19. I felt that people dislike me.				
20. I could not get "going."				

Appendix F: Positive and Negative Affect Schedule - Expanded (PANAS-X)

This scale consists of a number of words and phrases that describe different feelings and emotions. Read each item and then mark the appropriate answer in the space next to that word. Indicate to what extent you have felt this way during the past few weeks. Use the following scale to record your answers:

1	2	3	4	5
very slightly or not at all	a little	moderately	quite a bit	extremely

1. _____ cheerful
2. _____ disgusted
3. _____ attentive
4. _____ bashful
5. _____ sluggish
6. _____ daring
7. _____ surprised
8. _____ strong
9. _____ scornful
10. _____ relaxed
11. _____ irritable
12. _____ delighted
13. _____ inspired
14. _____ fearless
15. _____ disgusted with self
16. _____ sad
17. _____ calm
18. _____ afraid
19. _____ tired
20. _____ amazed
21. _____ shaky
22. _____ happy
23. _____ timid
24. _____ alone
25. _____ alert
26. _____ upset
27. _____ angry
28. _____ bold
29. _____ blue
30. _____ shy
31. _____ active
32. _____ guilty
33. _____ joyful
34. _____ nervous
35. _____ lonely
36. _____ sleepy
37. _____ excited
38. _____ hostile
39. _____ proud
40. _____ jittery
41. _____ lively
42. _____ ashamed
43. _____ at ease
44. _____ scared
45. _____ drowsy
46. _____ angry at self
47. _____ enthusiastic
48. _____ downhearted
49. _____ sheepish
50. _____ distressed
51. _____ blameworthy
52. _____ determined
53. _____ frightened
54. _____ astonished
55. _____ interested
56. _____ loathing
57. _____ confident
58. _____ energetic
59. _____ concentrating
60. _____ dissatisfied with self

Appendix G: North American Adult Reading Test (NAART)

Please read the following words aloud:

DEBT	**RARELY**	**ASSIGNATE**
DEBRIS	**GIST**	**TOPIARY**
AISLE	**CORPS**	**CAVEAT**
REIGN	**HORS D'OUERVE**	**SUPERFLOUS**
DEPOT	**SIEVE**	**LEVIATHAN**
SIMILE	**HIATUS**	**PRELATE**
LINGERIE	**GAUCHE**	**QUADRUPED**
RECIPE	**ZEALOT**	**SIDEREAL**
GOUGE	**PARADIGM**	**ABSTEMIOUS**
HEIR	**FACADE**	**BEATIFY**
SUBTLE	**CELLIST**	**GAOLED**
CATACOMB	**INDICT**	**DEMESNE**
BOUQUET	**DETENTE**	**SYNCOPE**
GAUGE	**IMPUGN**	**ENNUI**
COLONEL	**CAPON**	**DRACHIM**
SUBPOENA	**RADIX**	**CIDEVANT**
PLACEBO	**AEON**	**EPERGNE**
PROCREATE	**EPITOME**	**VIVACE**
PSALM	**EQUIVICAL**	**TALIPES**
BANAL	**REIFY**	**SYNECDOCHE**
	INDICES	

Appendix H: California Verbal Learning Test - Second Edition (CVLT-2)

The details of this measure have been redacted from the appendix to comply with copyright law. Committee members were provided an example copy for review purposes.

Appendix I: FAS & Animal Fluency

In a moment, I will give you a letter. List as many words that you can think of that begin with that letter, you will have 1 minute. Do not give me proper nouns (e.g., Boston, Betty), or simply change the ending of a word repeatedly (e.g., eat, eats, eating, eaten).

Now tell me as many animals as you can in 1 minute.

F	**A**	**S**	**Animals**
15			
30			
45			

Appendix J: Cognitive-Affective Verbal Learning Test (CAVLT)

Instructions: I am going to read a list of words to you. Listen carefully, because after I am done, I would like you to repeat back as many words as you can remember. Do not worry about the order of the words, just try to repeat back as many as you can remember. Are you ready? *Trial 1*
I will now read that same list of words again. Repeat back as many of the words as you can remember, in any order. Do not leave out words simply because you repeated them in the last trial.
Are you ready? *Trials 2-5*

	1st Trial	**2nd Trial**	**3rd Trial**	**4th Trial**	**5th Trial**
column					
triumphant					
context					
theory					
aroused					
sad					
method					
engine					
happy					
utensil					
lonely					
misery					
reserved					
tool					
afraid					
proud					

Now I am going to read a second list of words to you. When I am done, I would like you to repeat back as many words as you can remember from this second list as you can. Do not give words from the first list, just this second list.
Are you ready? *Distracter Trial*

Now I would like you to repeat back the words from the first list, the one I read to you multiple times. Do not repeat back words from the second list, just the first list. *Short Delay Free Recall*

Now tell me words from the first list that were (+/-/nonemotion) words. ***Short Delay Cued Recalls***

	Distracter	**SDFR**	**SDC+**	**SDC-**	**LDNE**
despise					
pleasure					
journal					
confident					
noisy					
terrific					
helpless					
hatred					
industry					
elbow					
depression					
detail					
statue					
umbrella					
kindness					
serious					

After 20 minutes. Remember earlier I read two lists of words to you? The first list I read to you multiple times, tell me all the words you remember from that first list, the one I read to you multiple times. *Long Delay Free Recall*
Now tell me words from the first list that were (+/-/nonemotion) words. *Long Delay Cued Recalls*

LDFR	LDFR	LDC+	LDC-	LDCNE

I am going to read you a long list of word. It will contain all the words from the first list, the one we repeated multiple times, as well as many other words. For each word say "Yes" if the word was on the first list, or "No" if it was not on the first list. *Recognition List*

terrified	locker	helpless	detail
time	**triumphant**	**utensil**	**engine**
sad	**reserved**	hatred	odd
aroused	lucky	month	confident
elbow	**misery**	terrific	**tool**
kindness	romantic	concentrate	pleasure
journal	**column**	**lonely**	
clock	**happy**	serious	
method	delight	depression	
afraid	unhappy	history	
grief	rejected	swamp	
umbrella	**proud**	noisy	
context	statue	**theory**	
success	industry	despise	

Recognition	*Total*				
Correct		**Breakdown**			
		Neg Emotions	*Pos Emotions*	*NonEm Conc*	*NonEm Abs*
False Positive					
False Negative					

Appendix K: Emotion Word Fluency Test (EWFT)

For this next task, I would like you to give me as many different EMOTION words as you can in 1 minute.

Emotions
15”
30”
45”
60”

Emotions: Total Correct Perseverations Non-Emotion Words

Appendix L: Sample Polysomnogram Report

Split Night Polysomnography Report

History: Upon review of the available data, the patient reports symptoms including: snoring and daytime sleepiness. The Epworth Sleepiness score is 19 / 24.

Technical Summary: Attended in-laboratory recording montage included: EEG, EOG, EMG, EKG, nasal thermistor flow, nasal pressure, pharyngeal snoring, respiratory effort (2 channels), anterior tibialis EMG, SaO2 and body position. Continuous Positive Airway Pressure (CPAP) was initiated after the patient demonstrated clinically significant obstructive sleep apnea. This study was performed in accordance with the AASM scoring manual.

Pre-CPAP						**All Night**	
Baseline Duration	184.0 min	**Total RDI**	**93.2**	WASO	51.0 min	Total Recording Time	412.0 min
Sleep Time	114.0 min	NREM RDI	95.8	Stage N1	49.1 %	Total Sleep Time	238.0 min
Sleep Efficiency	62.0%	Stage R RDI	66.0	Stage N2	42.1 %	Sleep Efficiency	63.8%
Sleep Latency	10.5 min	Supine RDI	91.11	Stage N3	0.00 %		
Obstructive Apnea	3	Non-supine RDI	107.4	Stage R	8.8 %		
Mixed Apnea	0	Medicare AHI	88.9	Stage R Latency	132.0 min		
Central Apnea	16	**Min %SaO2**	**69 %**			PLM index	0.0
Hypopnea	158	Baseline %SaO2	92 %			PLM arousal index	0.0

Snoring: Frequent and loud during the diagnostic portion of the study.

PAP was titrated from 5 to 11 cm of water pressure. At a CPAP pressure of 10 cm of water, supine-REM sleep was observed with very rare respiratory events. Lower pressures were associated with respiratory events.

EKG Findings: Single-lead demonstrated isolated premature atrial and ventricular complexes.

EEG Findings: Three channel EEG demonstrated no seizure activity.

Further Interpretive Notes: The patient reported that sleep was better than usual, awoke feeling rested and would be willing to wear CPAP at home.

Diagnosis: Obstructive Sleep Apnea 327.23

Discussion: Treatment for severe obstructive sleep apnea is often warranted even in the absence of clinical symptoms. Recommended options include positive airway pressure, custom-made oral appliances, or upper airway surgery. Regardless of treatment approach for the obstructive sleep apnea, maximization of nasal airway patency, weight loss if appropriate, and avoidance of sedatives and alcohol in proximity to bedtime are strongly encouraged.

• This study shows the effectiveness of CPAP in treating sleep-disordered breathing. Consider a trial of CPAP at 10 cm of water pressure during sleep with clinical follow-up to assess treatment response.

Appendix M: Phone Script

Telephone Recruitment Script

Hello Mr./Ms. _____, my name is _____ and I am a researcher associated with the University of Windsor and the Windsor Regional Hospital. Do you have a moment to talk, or is there a better time I could reach you?

We obtained your number from the Windsor Regional Hospital and Dr.'s Anil Dhar & Winston Rajkumar, of the Windsor Pulmonology & Sleep Clinic. The reason we are contacting you is that you may be eligible to participate in a research project investigating certain characteristics related to obstructive sleep apnea, sleep quality, thinking, and mood. Could I tell you a little more about the project and its potential benefits for the field and yourself?

Other research has found that when sleep is poor, individuals sometimes experience more problems than usual with certain types of thinking, such as sustaining attention and processing information quickly. Additionally, sleep has sometimes been found to be related to mood. You may in fact have had firsthand experience with these phenomena, for example, having a night where you slept very little, and the next day feeling grumpy and/or finding it hard to think straight. As you likely know, sleep apnea disrupts sleep often throughout the night.

Regardless of when you were diagnosed with sleep apnea and how frequently you follow your treatment regimen, we would really appreciate your involvement in the study. Could I tell you about what participating would entail?

If you agree to participate, we would arrange a date and time that work for you to come to the hospital to meet with a researcher. Once there, you would fill out a series of questionnaires asking about your sleep quality, daytime sleepiness, and mood lately. The hospital has data on how well you slept during your sleep evaluation, which we will look at with your permission. Finally, the researcher would lead you through a series of cognitive tasks, designed to measure how well you perform in different domains of thinking, such as memory, attention, and language. Your name will not be attached to ANY of the data we collect. The whole session should not last longer than 2 or 2.5 hours. Could I tell you about what potential benefits participating has?

First off, there is free parking; second, we will provide you a free Tim Horton's gift card for 1 small item as thanks for participating (there is even a Tim's in the hospital, if you would like). But also, by participating, you would be helping researchers learn more about possible cognitive complications associated with a sleep problem that you have experienced. This could guide screening and treatment options for healthcare providers and apnea sufferers in the future. Additionally, there is a personal benefit that we can offer you, if you wish. Individuals who suspect that their thinking abilities have changed (such as recently noticing a lot of trouble with memory) due to age, a disorder or disease, an injury to the head, etc., often go to a clinical psychologist to have testing done and help handle any changes to their thinking. If you participate, you can request us to take a

look at your scores, and we will offer an opinion on whether you might benefit from at least discussing your cognitive health with your primary care physician. We will also give you some clinical psychologist referral information you can discuss with him or her. All of that is only done if you ask us to. To be clear, our assessment would not be like that conducted in a patient-clinician relationship, but merely a screening system that MAY indicate you could benefit from talking with your physician about your cognitive health.

Do you have any questions or concerns about participating that I could answer for you?

Could I arrange a time and date for an appointment right now?

We appreciate your involvement, and look forward to meeting you. If you would like, we can call the day before to remind you of the appointment, would you like that?

Thank you.

Appendix N: Brochure

Contact

To learn more about the project, or sign up to participate please call (***) *** - **** and/or email windsor.sleep.study@gmail.com

Potential Benefits

By participating, you would be helping researchers learn more about possible cognitive complications associated with a sleep problem that you have experienced.

As a sign of gratitude, we also will offer you a gift card for 1 small Tim Horton's item (there's even a TH in the hospital!), along with validating your parking costs.

Finally, If you participate, you can request us to take a look at your scores, and we will offer an opinion on whether you might benefit from at least discussing your cognitive health with your primary care physician. We will also give you some clinical psychologist referral information you can discuss with him or her.

All of that is only done if you request it. You would not be entering a patient-clinician relationship, but merely receiving results of a cognitive screen.

Sleep, Cognition, & Mood Research Project

WINDSOR REGIONAL HOSPITAL
OUTSTANDING CARE - NO EXCEPTIONS

University of Windsor

Impact of Sleep Quality

Research has found some interesting correlations between sleep quality and everyday functioning

Individuals who suffer from poor sleep quality have more problems than usual with thinking

The quality of someone's sleep has been found to be related to mood. Sometimes the impact is serious enough to result in depression.

You may have firsthand experience with these problems. For example, having a night of poor sleep and the next day feeling cranky, irritable, or unhappy. Or, feeling like your mind is sluggish and not as sharp as normal.

Sleep Apnea

Sleep apnea and other sleep disorders disrupt sleep quality, and have been associated with some of the symptoms described to the left.

For the benefits of participating, and contact information to learn more, see the back and inset!

Research Opportunity

If you agreed to participate, we would arrange a time and date that work for you to come to the Windsor Regional Hospital to meet with a researcher

Next, you would fill out a series of questionnaires asking about your sleep quality, sleepiness, and mood lately.

If you have undergone a sleep study before, we will ask permission to look at the lab values of that study.

Finally, the researcher would lead you through a series of tasks designed to measure how well people think in different ways, like memory, problem solving, and attention.

Your name will not be attached to ANY of the data we collect.

The whole session should take around 2 hours.

Appendix O: Referral Information

Referral Information

You have expressed interest in further information related to cognitive health, the following information should assist you with the suggested process.

Suggested Referral Process:

The best first step is to contact your primary care physician, or another physician who you see regularly.

Inform him or her that you recently participated in a study related to cognition, and are interested in discussing the possible benefits of undergoing neuropsychological evaluation to evaluate your current cognitive health.

Discuss with your doctor whether he or she also feels a referral might be useful for you and your healthcare team.

Your doctor will likely have his or her own preferred referral sources for cognitive health screening and/or neuropsychological evaluation services. However, below are some popular programs through the **Windsor Regional Hospital** that may be appropriate to contact as a referral source, depending on your eligibilities:

The Geriatric Assessment - Consultation Program (GAP)
Service Director: Rose Grant-Rennie,
Phone: (519) 257-5112
Fax: (519) 257-5242

The Community Psychogeriatric Outreach Program
Service Director: Bill Marcotte
Phone: (519) 257-5105
Fax: (519) 257-5197

The Acquired Brain Injury Program (ABI)
Service Director: John Norton
Phone: *Program Secretary* - (519) 257-5458
Manager: Chris Edwards - (519) 254-5577 Extension, 75230
Fax: (519) 257-5242

Alternatively, there are private neuropsychologist service providers who can be contacted by your doctor or yourself:

Hobbs & Associates
Phone: (519) 948-1212

Referral Information

You have expressed interest in further information related to psychological health, the following information should assist you with the suggested process.

Suggested Referral Process:

The best first step is to contact your primary care physician, or another physician who you see regularly.

However, if an emergency arises related to your mood (e.g., suicidal thoughts), please immediately call 911 or 999 or go immediately to your nearest Emergency Department.

Inform him or her that you recently participated in a study related to cognition, and are interested in discussing the possible benefits of receiving psychological services.

Discuss with your doctor whether he or she also feels a referral might be useful for you and your healthcare team.

Your doctor will likely have his or her own preferred referral sources for psychological services. However, below are some popular programs through the **Windsor Regional Hospital** that may be appropriate to contact as a referral source, depending on your eligibilities:

The Specialized Inpatient Mental Health Care Program
Service Director: Judy Smith
Phone: (519) 254-5577 Extension 75186
Fax: (519) 257-5197

Geriatric Mental Health Outreach Team
Service Director: Bill Marcotte
Phone: (519) 257-5105
Fax: (519) 257-5197

Alternatively, there are private psychology service providers who can be contacted by your doctor or yourself:

Sandwich Community Health Centre
Phone: (519) 258-6002

VITA AUCTORIS

NAME: Ciaran Michael Considine

PLACE OF BIRTH: Maidstone, England

YEAR OF BIRTH: 1987

EDUCATION:

University of Michigan, B.A., High Honors, Ann Arbor, MI, 2008
University of Windsor, M.A., Windsor, ON, 2011
University of Windsor, Ph.D., Windsor, ON, 2015