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Associations between sleep and memory in aging

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Associations between sleep and memory in aging

by

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Associations between sleep and memory in aging

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The goal of this dissertation was to understand how changes in sleep influence memory performance in healthy older adults. Previous research suggests that older individuals experience parallel declines in sleep and episodic memory. These age-related changes appear to be linked such that sleep disruptions contribute to deficits in memory performance. We examined the components of episodic memory that changed following sleep loss and correlated with aspects of sleep physiology. Healthy older adults completed two overnight sessions: an in-lab sleep recording session and a 24-hour sleep deprivation session. The morning after each sleep manipulation, participants completed both episodic memory and sustained attention tasks. We applied computational models, specifically drift-diffusion models, to the episodic memory tasks to examine whether sleep loss affected memory indirectly through lapses in sustained attention (vigilance hypothesis) or specifically through declines in the strategic processes associated with memory (neuropsychological hypothesis). Our results showed that memory functions that depend on processes associated with the prefrontal cortex were impaired following sleep deprivation. In addition, sleep loss caused a small but robust impairment in sustained attention. Since multiple cognitive processes were impaired by sleep loss in older adults, these findings do not provide unequivocal support for either the neuropsychological hypothesis or the vigilance hypothesis. In addition, we explored which aspects of sleep

physiology (recorded during the sleep session) optimized components of memory performance. Our results illustrated that more slow wave power during sleep was correlated with higher next-day source memory strength. Additionally, individuals who spent more time in slow wave sleep had better memory retention. These results support further efforts to investigate sleep as a general indicator of cognitive function across the lifespan and highlight the importance of reinforcing healthy sleep behaviors as a method to preserve cognitive functioning in older adults.

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Chapter 1: Introduction

One of the prominent features of cognitive aging is the decline in memory for episodes and events, known as episodic memory (Rajah, Maillet, & Grady, 2015). Although age-related deficits in episodic memory are common in older adults, the magnitude varies significantly across the population. One potential source of variability that may contribute to individual differences in memory is sleep. Similar to memory, sleep quality and quantity declines during aging (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004), but at varying degrees. Although many survey studies illustrate that older adults who report poorer sleep quality experience more cognitive decline (Jelicic et al., 2002; Nebes, Buysse, Halligan, Houck, & Monk, 2009), the aspects of sleep that affect each cognitive domain is still under debate (for review see: Scullin & Bliwise, 2015). The goal of this dissertation was to pinpoint which cognitive components rely on sleep (Chapter 2) and which aspects of sleep physiology optimize memory function (Chapter 3) in older adults. We investigated the mechanisms of sleep that are associated with better memory, with the ultimate goal of understanding whether improving sleep has the potential to improve cognition in aging. Below we review research separately examining how episodic memory and sleep decline across the lifespan to provide background for Chapters 2 and 3 that explore the link between these common age-related changes.

EPISODIC MEMORY IN AGING

Episodic memory declines across the lifespan (for review see: Rajah et al., 2015). Specifically, when encoding and retrieval involve inhibiting related information and remembering associations, age-related impairments are significant (Schacter, Koutstaal,

& Norman, 1997). A meta-analysis examining different types of episodic memory in older adults found that memory involving associations is consistently more impaired than memory for individual items (Old & Naveh-Benjamin, 2008). One study by Chalfonte and Johnson had younger and older adults remember features of an object (i.e. color) and their context (i.e. location within an array). While both age groups performed similarly on retrieving features, older adults were significantly worse at remembering context (Chalfonte & Johnson, 1996). Countless studies have replicated and extended these findings by showing that older adults experience deficits in retrieving associations regardless of the stimulus type (Mitchell & Johnson, 2009). For example, when older adults studied face-name pairs, they were able to recognize the face and name separately but showed impairments in retrieving the pair. These results formed the associative deficit hypothesis (Naveh-Benjamin, 2000), which states that older adults show specific deficits in creating and retrieving combined information.

Brain regions implicated in the binding and control processes involved in episodic memory are the medial temporal lobe (MTL) and the prefrontal cortex (PFC; Buckner, 2003; Wilckens, Erickson, & Wheeler, 2012). Strong evidence for the role of the MTL in associative memory comes from patient work. Patients with MTL damage showed greater deficits in associative, compared to item, memory (Giovanello, Verfaellie, & Keane, 2003). To rule out the possibility that associative deficits were due to a higher memory load, they also tested recognition memory for two items, but did not require patients to associate the items. They illustrated that recognition performance for two items was equivalent to one item in the MTL patients, which further supports the conclusion that the MTL is specifically involved in associative memory.

The PFC is implicated in cognitive control processes important for episodic memory. Control processes are involved in goal-directed retrieval to appropriately select information while inhibiting competing information (Wilckens et al., 2012). Patients with frontal lobe damage show impairment in using controlled processes to retrieve the relevant information and ignore false information (Schacter, Curran, Galluccio, & Milberg, 1996). Furthermore in healthy adults, memory retrieval tasks that heavily involve controlled processes show greater PFC activity (Velanova, Lustig, Jacoby, & Buckner, 2006). Retrieving associative information also relies on control processes implicated in the PFC. Greater activity in regions of the PFC were exhibited when memory tasks relied more on retrieving strong associations compared to simple recognition (Rugg, Fletcher, Chua, & Dolan, 1999) and even weak associations (Bunge, Burrows, & Wagner, 2004). Together, this work demonstrates that episodic memory depends on the binding function of the MTL and the strategic control of the PFC.

Neuroimaging studies have illustrated that age-related atrophy in the structure (Resnick, Pham, & Kraut, 2003) and changes in the function of the MTL and PFC contribute to episodic memory declines in older adults (Buckner, 2004; Gunning-Dixon & Raz, 2003). During a feature binding task, older adults exhibited less hippocampal activity than younger adults (Mitchell, Johnson, & Raye, 2000). Moreover, when episodic memory performance was matched across age groups, older adults still showed reduced activity in the hippocampus compared to young adults (Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2005). Since lower levels of brain activity are thought to reflect deficits in brain function, these studies suggest that hippocampal function during episodic memory is impaired in older adults. Evidence of decreased white matter integrity in PFC regions has been linked to impairments in executive control processes important for

memory retrieval (Buckner, 2004; Gunning-Dixon & Raz, 2000). Although there are clear declines in PFC structure (Resnick et al., 2003), no consistent age-related change in PFC activity has emerged (Rajah et al., 2015). Several studies have found that older adults show greater PFC activity compared to younger adults during episodic memory tasks (Buckner, 2004). The interpretation of these results is still under debate, but it is clear that prefrontal function is involved in episodic memory retrieval and the integrity of the region is affected by aging. In summary, age-related changes in the MTL and PFC contribute to age-related declines in episodic memory. Older adults who exhibit less atrophy in MTL and PFC regions show less age-related cognitive decline (Gunning-Dixon & Raz, 2003; Persson, 2005). This suggests if we understand the factors that contribute to changes in MTL and PFC function, then we can work to ameliorate age-related cognitive declines. The factor explored in this dissertation that is associated with MTL and PFC changes is sleep.

SLEEP IN AGING

Foley and colleagues surveyed 9,000 older adults and found that over half reported experiencing at least one of the following sleep problems: difficulty falling asleep, waking up in the middle of the night, waking up too early, waking but not feeling rested, or having to nap during the day (Foley, Monjan, & Brown, 1995). Similarly, objective measures of sleep indicate that, compared to young adults, older individuals experience less sleep that is more shallow and disrupted (Pace-Schott & Spencer, 2013). When measuring basic sleep characteristics, older adults consistently earn less total sleep time, less time asleep compared to their total time in bed (sleep efficiency), and have more awakenings following the onset of sleep (wake after sleep onset). Consequently,

this disrupted sleep period also reflects changes in sleep physiology. A meta-analysis illustrated that in aging, the amount of light sleep, including stage 1 and stage 2 sleep, increases while deep sleep, including slow wave sleep and rapid eye movement sleep (REM), decreases (Ohayon et al., 2004).

Changes in sleep, especially slow wave power, are linked to changes in PFC and MTL (specifically the hippocampus) structure and function. Frontal lobe metabolism significantly decreases following sleep deprivation (Wu et al., 2006). Additionally, less slow wave power in older adults has been associated with lower PFC grey matter volume (Mander, Rao, Lu, Saletin, Lindquist, et al., 2013b) and thickness (Dube et al., 2015). The hippocampus is also influenced by changes in sleep. In a pilot study, participants with chronic insomnia showed reduced hippocampal volume (Riemann et al., 2007). Furthermore, hippocampal activity was reduced when slow wave sleep was disrupted in older adults (Van Der Werf et al., 2009). These results illustrate that complementary to age-related declines in memory, age-related declines in sleep, especially slow wave power, are linked to changes in the PFC and MTL (specifically the hippocampus).

SLEEP AND MEMORY IN AGING

This dissertation explored how the age-related changes in sleep contribute to the age-related declines in episodic memory. In Chapter 2 we explored which cognitive components of episodic memory rely on sleep using a sleep deprivation paradigm in older adults. In Chapter 3 we examined how different cognitive components of episodic memory are related to aspects of sleep physiology, especially slow wave power. Together these findings help us understand how sleep contributes to cognitive function in older adults.

Chapter 2: How Sleep Loss Affects Memory Function in Older Adults

INTRODUCTION

The majority of adults over 60 have experienced significant changes in their sleep as they age, such as decreases in their sleep time, sleep efficiency, and slow wave sleep (Ohayon et al., 2004). In parallel to their changes in sleep, older individuals demonstrate significant declines in cognitive functioning, including episodic memory performance (Rajah et al., 2015). Previous research sought to link changes in sleep and memory, suggesting that age-related declines in sleep may contribute to the declines observed in memory (Nebes et al., 2009). The specific mechanism by which sleep influences memory functioning in aging is still under investigation.

Two Prominent Hypotheses Regarding the Effects of Sleep Loss on Memory Performance

There are two opposing hypotheses concerning how cognition is affected by sleep loss, the vigilance hypothesis (Lim & Dinges, 2008) and the neuropsychological hypothesis (Harrison, Horne, & Rothwell, 2000; Jones & Harrison, 2001). The vigilance hypothesis suggests that sleep loss primarily affects sustained attention. This hypothesis states that because sustained attention declines following sleep loss, "higher order" cognitive tasks that require sustained attention, such as memory, will be impaired predominantly through the effects on attention (Lim & Dinges, 2010). By contrast, the neuropsychological hypothesis states that sleep loss specifically impairs performance on tasks that depend on executive function. This hypothesis suggests that performance on complex memory and decision-making tasks degrade, whereas simple reaction time tasks would be unaffected by sleep loss (Couyoumdjian et al., 2010).

Considerable research and debate has focused on which of these two hypotheses best accounts for how sleep loss affects memory and other cognitive functions. One reason it has been difficult to distinguish between these two hypotheses is that most cognitive functions are multi-component. Disentangling which component(s) have been affected by sleep loss is not a trivial task. One approach that has been applied to disentangle the contribution of multiple cognitive processes to a single task, coined the "task impurity problem", is computational modeling (Jackson et al., 2012). For example, a study investigating executive function found that global task performance was compromised under sleep deprivation (Tucker, Whitney, Belenky, Hinson, & Van Dongen, 2010) and computational modeling revealed that performance declines were entirely explained by variability in sustained attention, supporting the vigilance hypothesis. Recent studies in young adults have arrived at similar conclusions after modeling working memory task performance (Drummond, Anderson, Straus, Vogel, & Perez, 2012; Wee, Asplund, & Chee, 2012). This suggests that decision-related processes are unaffected by sleep deprivation in young adults. Computational modeling appears to be an effective tool in identifying specific cognitive components that are influenced by sleep disruptions, even when they are embedded in multi-component cognitive processes. To date, there has been no application of this approach to understand the relationship between sleep and memory in aging.

The Effects of Sleep Loss on Older Adults

Previous research examining the difference between young and older adults following sleep loss has focused on sustained attention, as measured by the Psychomotor Vigilance Task (PVT; Dinges et al., 1997). The PVT has been employed in hundreds of

studies to measure attentional deficits because it is reliable, valid, and highly sensitive to sleep loss (for review see: Lim & Dinges, 2008). Quite striking and contrary to conventional wisdom, older adults perform better on sustained attention tasks after sleep loss relative to young adults (Pace-Schott & Spencer, 2013). This phenomenon is consistent across different sleep loss manipulations, including 26 hours of sleep deprivation (Duffy, Willson, Wang, & Czeisler, 2009), 40 hours of sleep deprivation (Adam, Retey, Khatami, & Landolt, 2006), 3 nights of sleep restricted to 4 hours (Stenuit & Kerkhofs, 2005), and altered circadian phase using a forced desynchrony paradigm (days were shortened to 20 hours; Silva, Wang, Ronda, Wyatt, & Duffy, 2010). Since attentional processes do not rely on sleep to the same extent across the lifespan, other cognitive processes, such as memory, may also be differentially affected by sleep loss. Several studies have shown disrupted sleep negatively influences memory performance in older adults (Blackwell et al., 2014; Carvalho-Bos, Riemersma-van der Lek, Waterhouse, Reilly, & Van Someren, 2007; Jelicic et al., 2002; Lim et al., 2012; Nebes et al., 2009). Although declines in cognitive performance following sleep loss may be explained by attentional deficits in young adults (Jackson et al., 2012), this may not be the case in older adults. The extent to which sleep loss specifically affects new episodic learning in older adults remains an area of intense interest.

Drift-Diffusion Modeling

One computational model that has been widely used to investigate the cognitive components of memory retrieval is the drift-diffusion model (Ratcliff, 1978). The diffusion model has been successfully applied to investigate age-related differences in source memory (Spaniol & Grady, 2012; Spaniol, Madden, & Voss, 2006) and the effects

of sleep deprivation on a numerical discrimination task in young adults (Ratcliff & Van Dongen, 2009). The premise of the diffusion model is that in a 2-choice decision task, participants gradually accumulate information over time to reach one of two decisions called boundaries (see Figure 1). This is a type of sequential sampling model that assumes the path to the boundary is noisy and involves discrete components that can be dissociated by investigating the relationship between the speed and accuracy of each response. The advantage of diffusion modeling is in the ability to dissociate the cognitive components of the decision process and account for the time involved in non-decision related components. Additionally each component of the decision process has a clear psychological interpretation explained in detail below.

The decision-related components include starting point, boundary separation, and drift rate. The initial component of the decision process is the starting point. Starting point describes the extent to which a participant is biased toward one of the two decision boundaries. A shift in the starting point, or bias, shifts the decision closer to one boundary relative to the other. If an individual is bias toward a decision, less evidence is needed to reach that particular boundary. This behavior is illustrated by faster reaction times when individuals choose the biased response. When a reward is associated with one of the boundaries, participants shift their starting point toward that boundary (A. Voss, Rothermund, & Voss, 2004). Another component of the decision process is the distance between the boundaries known as boundary separation. Boundary separation describes the amount of evidence required to reach either decision boundary. Importantly, this component is an index of the speed/accuracy tradeoff since wider boundary separation suggests that an individual needs to accumulate more evidence to make a decision (reflected in slower and more accurate responses). Boundary separation can be

interpreted as response caution. If an individual is instructed to avoid errors, they will show a cautious response style by taking more time to gather evidence to reach the decision (A. Voss et al., 2004). A final and crucial component for the present project is drift rate. Drift rate describes the quality of the accumulated evidence. In the depicted model (see Figure 1), drift rate is the slope. A steep slope represents high drift rate because the better the quality of evidence, the faster a boundary is reached. In memory tasks, high drift rate indicates a high memory strength or accuracy. Higher drift rates occur when a word was studied more recently compared to a word that was studied less recently (Spaniol et al., 2006). Drift rate is similar to d prime in signal detection theory in that it provides an index of the strength of the evidence that drives the decision process. The within-trial variability in drift rate (depicted as the noise surrounding the slope in Figure 1) is the scaling parameter, which is often fixed. Between-trial variability parameters for starting point, boundary separation, and drift rate are included in the model to account for fluctuations in the parameters across several trials (Ratcliff & Tuerlinckx, 2002).

Changes in drift rate, starting point, and boundary separation all affect patterns of accuracy, but are paired with very different patterns of reaction times. Therefore models that do not utilize reaction times, such as signal detection theory (for review see: Wixted, 2007), cannot differentiate between these components. Consequently, if we do not estimate the boundary separation parameter, higher accuracy from slower, more cautious responses may be misattributed to better memory strength. Therefore the diffusion model offers a better measure of the cognitive component specific to memory functioning.

Outside of the decision process, the diffusion model includes a non-decision parameter to account for the component of the reaction time involved in stimulus

detection and response execution. This component captures encoding time and motor speed. Previous research suggests that the non-decision component is larger when the motor demands of a response are higher (A. Voss et al., 2004). In addition, the model includes a parameter for the variability in the non-decision component to account for trial-to-trial fluctuations in motor speed and stimulus detection. The total reaction time is the sum of the non-decision component and the decision components from the diffusion process.

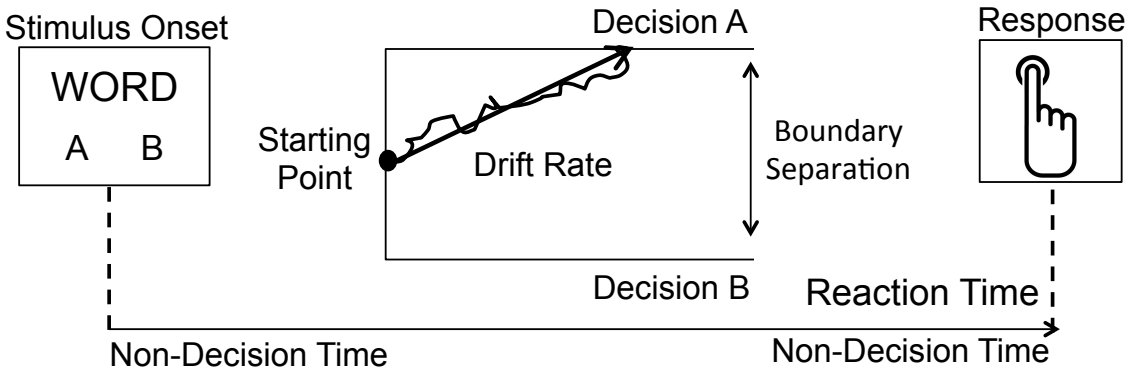

Figure 1. Drift-Diffusion Model

Drift-diffusion model involves the diffusion processes surrounded by non-decision time. The distinct cognitive components are illustrated in the diagram including starting point, drift rate, boundary separation, and non-decision time.

Illustrating How Different Patterns of Behavior Influence the Diffusion Model Parameters

Below we describe the relationship between reaction times and accuracy when there is an increase in each diffusion model parameter (all else being equal; see Figure 2). Since the variability parameters affect trial-to-trial fluctuations and not overall patterns of

behavior, they are not included. If there is an overall increase in the length of reaction times that is not related to accuracy, then the non-decision component will be larger. In contrast, if the increase in reaction times corresponds to slightly higher accuracy, the boundary separation parameter will be larger. If increased accuracy is alternatively accompanied by faster reaction times, then the drift rate parameter will be larger. Lastly, if responses to the upper boundary are more frequent and faster relative to the lower boundary, then the starting point will be larger (since bias toward the upper boundary is closer to one and a bias toward the lower boundary is closer to zero; Spaniol, Voss, & Grady, 2008).

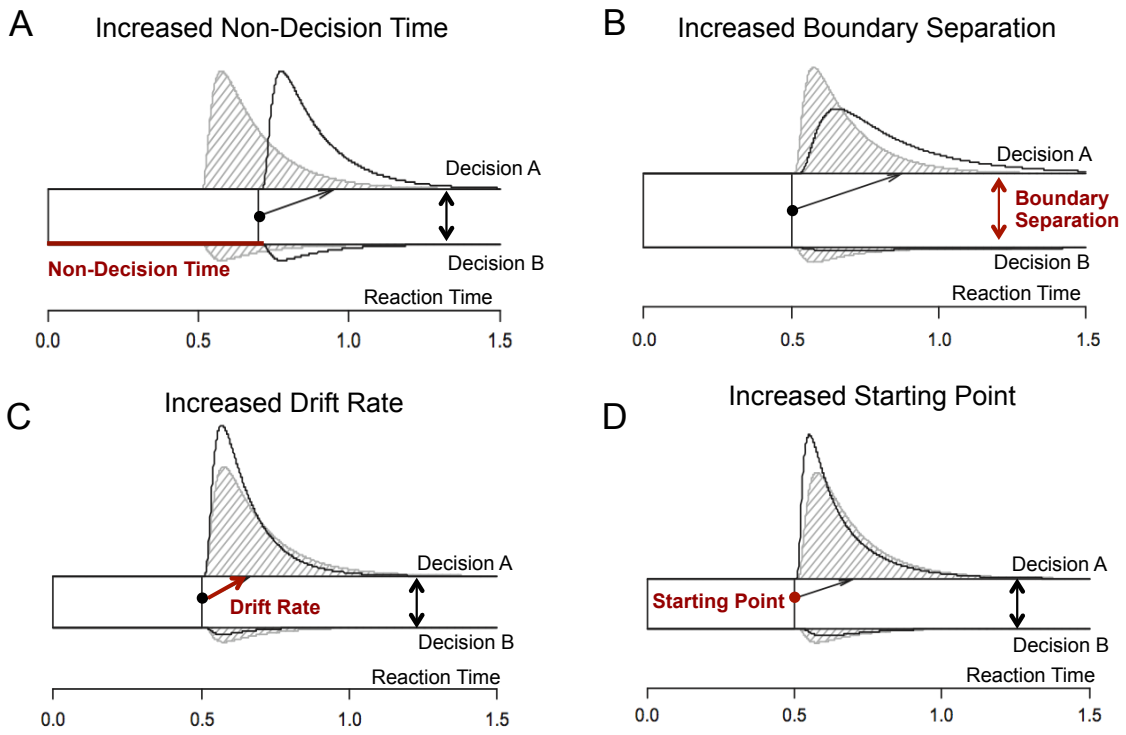

Figure 2. Changing the Diffusion Model Parameters

This figure was modified from (A. Voss, Nagler, & Lerche, 2013). Each panel illustrates the reaction time distributions when the correct response is "Decision A" (top distribution) and the incorrect response is "Decision B" (bottom and upside down distribution). Voss and colleagues created standard parameters, simulated reaction times, and plotted them as the shaded distribution. Each panel includes the same shaded distribution but the overlapping distribution (bold line) illustrates what happens to the reaction times when one of the parameters is increased. The increased parameter is in red (and titled). Panel A demonstrates that the non-decision time parameter increases when the reaction time distribution is overall shifted to the left (overall increased RT). Panel B shows that the boundary separation parameter increases when the reaction time distribution is wider, representing slower RTs. Panel C illustrates that when the drift rate parameter increases, the reaction time distribution is thinner and RTs are faster. Lastly, Panel D demonstrates that when the starting point parameter increases (showing a bias toward Decision A), the reactions are also faster.

Purpose of Present Study

The purpose of present study was to investigate how sleep loss affects memory in older adults. Specifically we examined whether 24 hours of sleep deprivation in older adults affects memory indirectly through lapses in sustained attention (vigilance hypothesis) or specifically through declines in the strategic processes associated with memory (neuropsychological hypothesis). We applied the diffusion model (Ratcliff, 1978) to a well established episodic memory task completed following sleep and sleep deprivation to tease apart which components of performance were affected by sleep loss. Additionally participants completed the Psychomotor Vigilance Task (PVT) to measure sustained attention. We examined whether sleep loss uniquely affected memory function (reflected in the drift rate), sustained attention (reflected in the PVT), or both.

MATERIALS AND METHODS

Participants

Thirty-six healthy older adults (25 females; age: mean = 69.48, SD = 2.63, range = 65 – 75 years old) were recruited from communities in the greater Austin area. Prior to entrance into the study, interested individuals completed a self-reported health screening (see Appendix) and a neuropsychological assessment battery. The health screening excluded individuals who reported current psychological or neurological illnesses, current use of medications affecting the nervous system, were diagnosed with hypertension, had a body mass index (BMI) greater than 30, a diagnosis of major depression in the past five years, sleep disorders, or poor sleep quality from the Pittsburg Sleep Quality Index (global score greater 8). The neuropsychological assessment battery included measures of memory and executive function. The memory measures were the

California Verbal Learning Test (CVLT-II; Delis, et al., 2000) and the Wechsler Memory Scale (WMS IV) Logical Memory Subtests. The second version of the California Verbal Learning Test (CVLT-II) measured several trials of both recall and recognition over immediate and delayed time courses. If time permitted the battery included the Wechsler Memory Scale (WMS IV) Logical Memory I & II subtests (Wechsler, 2009) as a complementary measure of learning and recall (short and long term). The executive function measures included Wechsler Adult Intelligence Scale IV (WAIS IV) Digit Span subtest (Wechsler, 2008), Trail Making Tests (Reitan, 1992), and Controlled Oral Word Association Test (COWAT; Benton et al., 1983). The z-scores from each of the tasks were averaged to create a cognitive domain composite score. All participants included scored within 1 SD of normal performance on the composite scores for the cognitive domains of memory and executive function (see Table 1).

Measure	Mean	SD	Range
Age	69.48	2.63	65 - 75
Education (years)	18.31	1.51	16 - 20
BMI	24.51	3.49	17.8 - 30.5
PSQI Global Score	3.94	1.82	1 - 8
Neuropsychological Battery: Memory			
CVLT-II Long delay free recall (z-score)	0.85	0.81	-0.5 – 3
WMS IV Logical Memory II (z-score)	1.06	0.86	-1.0 – 2.67
Memory Component Score	0.91	0.72	-0.5 – 2.25
Neuropsychological Battery: Executive Function			
WAIS-IV Digit Span (z-score)	1.05	0.90	-0.67 – 2.67
Trails Making Test Part B (z-score)	0.52	0.46	-0.79 – 1.51
COWAT (z-score)	0.40	1.00	-1.32 – 2.89
Executive Function Component Score	0.65	0.47	-0.23 – 1.68

Table 1. Study Demographics

The demographics and neuropsychological assessment battery information for all participants included in the study.

Procedure

Overview

Each participant took part in a sleep deprivation session and an in-lab sleep session, in a counterbalanced order (see Figure 3). The sessions began at least two days after the neuropsychological assessment (M = 20.72, SD = 37.92, range 2 – 187 days) and were separated by a minimum of one week (M = 19.8 days, SD = 20.2, range = 7 – 111 days). Prior to each session, participants completed sleep diaries to report their sleep behavior across the 3 nights before each session. Participants were required to sleep at least 6 hours each night for the 3 days before each session, not consume alcohol for 48 hours, or nap the day of the session. Table 2 illustrates that the basic sleep characteristics from the sleep diaries did not differ before the sleep and deprivation sessions. On the day of both overnight sessions, participants arrived at the lab approximately 1.5 hours prior to their habitual bedtime. Following the completion of a self-reported wakefulness rating, participants underwent the night portion of the overnight word-pair recall task. The protocol for each sleep manipulation is explained below (see: Overnight Session Protocols). In the morning, (approximately 8 hours following habitual bedtime) participants were given breakfast and the opportunity to clean up and get ready. At least 30 minutes later, participants rated their wakefulness and then completed a series of cognitive tasks, including the morning portion of the overnight word-pair recall task, a source and item memory task, and the Psychomotor Vigilance Task (PVT).

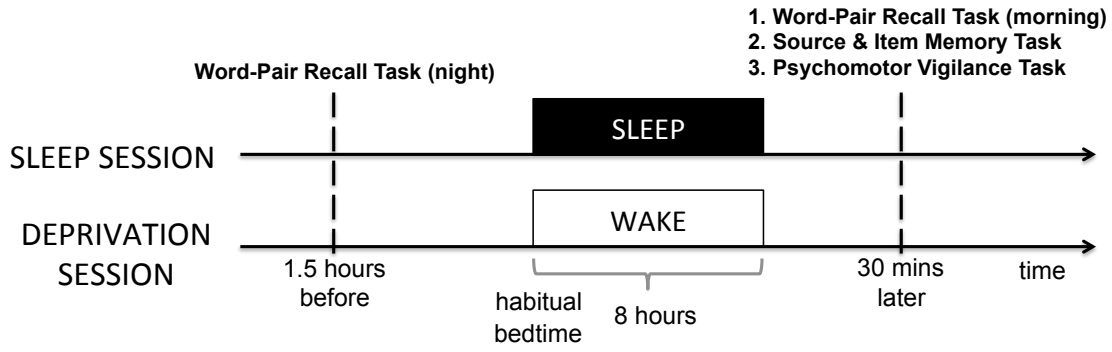

Figure 3. Study Design

The figure depicts the study design. All participants completed both the sleep and deprivation session.

Variable	Before Sleep	Before Deprivation	p-value
Mean Time in Bed (hours)	7.97 ± .69	8.09 ± .85	.27
Mean Sleep Time (hours)	7.42 ± .71	7.51 ± .67	.32
Mean Sleep Efficiency (%)	93.14 ± 5.11	93.19 ± 4.94	.94

Table 2. Sleep Diaries

The mean of the basic sleep characteristics from the sleep diaries 3 nights before the sleep and sleep deprivation sessions. One-way within subject ANOVAs demonstrated that there were no differences between time in bed, sleep time, or sleep efficiency before the sleep and deprivation sessions.

Overnight Session Protocols

Sleep Deprivation Session: Participants completed 24 hours of sleep deprivation. The day of the session, participants were prohibited from napping or drinking more than their usual amount of caffeine. This information was verified through their responses to the sleep diaries. Participants arrived in the laboratory approximately 1.5 hours before their usual bedtime. Trained research assistants continuously monitored participants to confirm they did not fall asleep or consume any caffeine until the completion of the

morning cognitive testing. Across the overnight interval, participants engaged in light physical and mental activities including card games, board games, and taking walks. Participants were provided light snacks such as pretzels, chips, popcorn, and granola bars.

Sleep Session: Sleep electroencephalography (EEG) was collected during the night (detailed description and results presented in Chapter 3). Participants followed their typical bedtime schedule and were given up to 8 hours to sleep without disturbances (Mander, Rao, Lu, Saletin, Lindquist, et al., 2013b). In the morning, participants completed questionnaires regarding their sleep quality and quantity.

Cognitive Testing

Source and Item Memory Task: The morning after both sleep manipulations, participants completed a source and item memory task (see Figure 4). The task was identical on both occasions except each version had a unique set of word stimuli. This task was chosen because it draws heavily on the strategic functions associated with cognitive control processes dependent upon the prefrontal cortex (Dobbins, 2005) and has been shown to be sensitive to the memory decline we see in the aging population (Dennis et al., 2008). The stimuli were taken from a previously normed list in which half the words were living and the other half were nonliving (Spaniol & Grady, 2012). The task consisted of a study phase and a test phase separated by a 10-min interval. Participants first completed a practice trial of the study and test phase that they repeated until they reached 100% accuracy on source and item memory to demonstrate that they understood the instructions. During the study phase, participants completed an animacy (living/non-living) or pleasantness (pleasant/unpleasant) judgment on each word for a total of 90 words. The judgment type served as the "source" association in the test phase and

predictably changed every second trial to reduce task-switching demands (Spaniol & Grady, 2012). The judgment of the words was counterbalanced and two additional words were presented at the beginning and end of each list that were not presented in the test phase to eliminate primacy and recency effects. Participants had 2 seconds to respond to each judgment.

Following a 10-minute delay, participants completed the test phase. The test phase involved a separate item memory test and source memory test (60 words in each test). The order of the tests was randomized. The assignment of the words to the item memory or source memory task was fully counterbalanced. During the item memory test trials participants were cued to indicate whether the presented word was old or new. During the source memory trials participants were cued to indicate whether the presented word from the study phase was associated with an animacy or a pleasantness judgment. Immediately following each memory decision, participants rated their level of confidence in the answer they selected on a scale from 1) guess, 2) 25% sure, 3) 75% sure, 4) sure. Participants had 3.5 seconds to respond to the memory probe and 2 seconds to respond to the confidence probe.

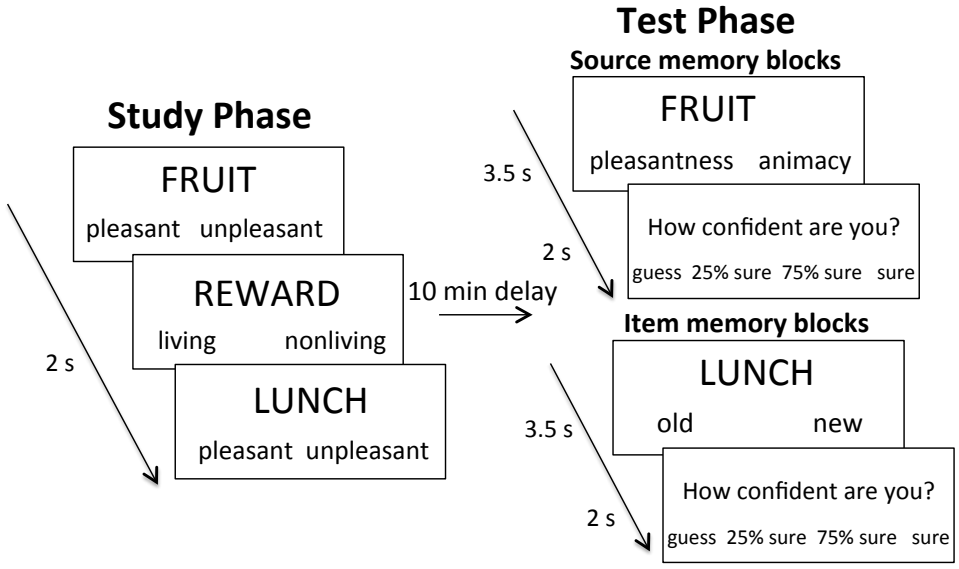

Figure 4. Source and Item Memory Task

A depiction of the source and item memory task administered the morning of each session.

Psychomotor Vigilance Task: During the delay between the study and test phase of the source and item memory task, participants completed a computerized reaction time test that measures sustained attention called the Psychomotor Vigilance Task (PVT). The PVT is a high-signal load reaction time test that has a high degree of sensitivity to sleep loss (Lim & Dinges, 2008). Participants attended to a fixation cross at the center of a computer screen. At random intervals, a millisecond timer appeared at the screen center (2 to 10 second inter-trial intervals). Participants were instructed to press a button the instant they detected the timer. The button press stops the timer and displayed the reaction time for 1 second. The PVT was 10 minutes in length and required constant attention in order to detect the timer.

Overnight word-pair recall: In addition to the morning memory testing described above, participants completed an additional word-pair recall task that was adapted from previous studies examining sleep-dependent memory consolidation (Marshall, Helgadóttir, Mölle, & Born, 2006; Plihal & Born, 1997; Westerberg et al., 2012). The task involved an encoding phase, two short delay cued recall phases, and one long delay cued recall phase. The night of arrival, participants completed the encoding phase and the two short delay cued recall phases. During the encoding phase, participants studied 50 related word pairs for 4-seconds each. The words were randomized, except for the two words that were added at the beginning and end of the task to control for primacy and recency effects. Throughout the first short delay cued recall phase, participants were shown the first word of all the studied word pairs one at a time and instructed to verbally recall the other word. Participants had 3.5 seconds to recall the other word in the pair before a tone sounded and the correct answer was revealed for 4 seconds. In the second short delay cued recall phase, participants were tested on half of the studied word pairs using the same procedure as the first cued recall phase, except the correct answer was not given. In the morning, participants were tested on the other half of the studied word pairs. Correctly recalled words during the second short delay cued recall phase were used to compute evening memory performance, and performance on the morning long delay cued recall task was used to compute morning memory performance.

DATA ANALYSIS

Source and Item Memory

One participant was dropped due to an error during the administration of the memory task at the deprivation session, which caused the participant to see different words for the study and test. Therefore the source and item memory task analyses included 35 participants total.

Accuracy: Source accuracy was computed by taking the percent of correctly identified source memory trials across both pleasantness and animacy conditions. Recognition memory was calculated by computing the proportion of hits (studied words correctly identified as old) and subtracting the proportion of false alarms (new words incorrectly identified as old) from the item memory trials.

Metamemory Accuracy: The Hamann Index (Schraw, 1995) was computed to examine the degree to which the confidence judgments following each memory trial corresponded to memory accuracy. Since the Hamann Index requires binary measures of confidence, the 4-point confidence rating scale was divided into "low confidence" (answer choices 1 and 2) and "high confidence" (answer choices 3 and 4). The calculation involved subtracting the number of trials where the confidence rating matched accuracy from the number of trials where the confidence did not match accuracy, and then dividing this difference by the total number of trials. The trials where the confidence ratings matched the accuracy occurred when the participants gave a high confidence rating and were correct, as well as when participants gave a low confidence rating and were incorrect. The trials where the confidence ratings did not match the accuracy occurred when the participants gave a high confidence rating and were incorrect, as well as when the participants gave a low confidence rating and were correct. Simply stated,

the Hamann Index is the difference between the mismatches and matches divided by the total number of responses.

Drift-diffusion model fitting: Using the fast-dm-30 software (A. Voss, Voss, & Lerche, 2015), we fit diffusion models (for review see: White, Ratcliff, Vasey, & McKoon, 2010) to the source and item memory task data from the sleep session and sleep deprivation session. Parameters were estimated using the Kolmogorov-Smirnov (KS) method (Kolmogoroff, 1941) using each participant's accuracy (proportion of responses to each decision) and reaction time (RT) measures separately for the source memory and item memory tasks. The KS method was chosen as the optimization criteria over other methods because it uses the raw reaction times and takes advantage of the entire distribution, instead of binning the reaction times into quantiles (A. Voss & Voss, 2008). The goal of the optimization criteria is to find diffusion model parameters that predict reaction times that closely corresponded to the observed reaction times. The parameters that were fixed to zero in the fitting process included the difference in non-decision time for the upper and lower threshold, inter-trial variability in starting point, and inter-trial variability in drift rate. The difference in non-decision time for the upper and lower threshold (boundaries) was fixed because the difficulty of executing a motor response should not vary across the decisions of "pleasantness" and "animacy" for the source task or "old" and "new" for the item task. Similarly, stimulus detection was not predicted to vary between decision boundaries since all words were presented at the same position and size on the computer screen. The inter-trial variability parameters for both starting point and drift rate were fixed because there were not enough trials to accurately estimate these parameters (A. Voss et al., 2013; 2015). Previous work suggests when there are a small number of trials, fixing the variability in drift rate and starting point parameters

make the estimations of the other parameters more robust even if there is variability present (A. Voss et al., 2015). Therefore, in cases of small trial numbers, these variability parameters should be fixed. Additionally the within-trial variability in drift rate was fixed to one because it acts as a scaling factor.

The parameters left free to vary were drift rate, starting point, boundary separation, non-decision time, and inter-trial variability in non-decision time (Ratcliff & Tuerlinckx, 2002). Unlike the decision-related variability parameters, the inter-trial variability in non-decision time parameter should be estimated even when there is a small number of trials because it has a large impact on the reaction time distribution (A. Voss et al., 2015). Drift rate was set to vary as a function of condition so that each participant had a separate drift rate for old, new, pleasantness, and animacy responses. The drift rates associated with the upper boundary (pleasantness and old) yielded a positive number and the drift rate associated with the lower boundary (animacy and new) yielded a negative number. Therefore six parameters were estimated for each diffusion model ($drift_{old/pleasantness}$, $drift_{animacy/new}$, starting point, boundary separation, non-decision, variability in non-decision time). The main outcome measure of drift rate for the source memory task was the absolute value of the "pleasantness" minus the "animacy" drift rate. This was calculated as a measure of between judgment discriminability. Similarly, the drift rate for the item memory task was the absolute value of the "old" minus the "new" drift rate.

Psychomotor Vigilance Task

The reaction times from the PVT were used to calculate summary statistics (mean and standard deviation of reaction times) after removing response lapses (i.e. RTs > 500

ms), and false starts (i.e. RTs < 100 ms). We also computed the mean of the fastest and slowest 10 percent of the trials, the number of response lapses (responses greater than 500 ms), and the number of false starts (i.e. RTs < 100 ms).

Overnight Word-Pair Recall

The percent of correctly recalled words were calculated during the second short-delay free recall night and during the long-delay free recall morning task. Memory change scores were morning performance (proportion of correctly recalled words during the long-delay free recall phase) minus evening performance (proportion of correctly recalled words during the second short-delay free recall phase; Mander, Rao, Lu, Saletin, Lindquist, et al., 2013b). Higher memory change scores indicated fewer incidences of forgetting across the night interval.

RESULTS

Protocol Deviations

One participant reported taking a 30-minute nap the day of the sleep deprivation protocol and one participant reported earning less than 6 hours of sleep the night before his/her sleep session. Following computations of critical results, we removed these 2 individuals and found it did not significantly change the results. Therefore they were included in all analyses below.

Assessing Diffusion Model Fit

To assess the fit of the diffusion model parameters, reaction times data were simulated based on the estimated parameters to create a predicted dataset separately for the source and item memory task. We did not rely on the statistical test of the KS criteria to assess model fit because the outcome greatly depends on the number of trials. Since we have a small number of trials, there putatively is not enough power to detect a model misfit (A. Voss et al., 2015). The rationale for completing the simulation was to visually inspect whether the data simulated matched the observed data. If the diffusion model parameters explain the behavior well (high goodness of fit) then simulated (predicted) data will be similar to the observed data. The simulation procedures were identical for the source and item memory task even though the response boundaries differed (source: upper = pleasantness, lower = animacy; item: upper = old, lower = new). For each memory task, we simulated the reaction times for 10,000 trials during each session (sleep, deprivation). The simulation involved a diffusion/random walk process where the values for the starting point, non-decision component, and boundary separation were drawn from a uniform distribution and the drift rate was drawn from the normal distribution. The simulated data were summarized into RT quantiles (.1, .3, .5, .7, .9) and the proportion of responses to the upper and lower boundary. Therefore each participant had four sets of RT quantiles (sleep session: upper, lower; deprivation session: upper, lower) and a response proportion for the upper and lower boundary. In order to compare the simulated to the observed data, the same RT quantiles and proportion of responses were calculated using the observed data. Figure 5 illustrates the relationship between the predicted data from the simulation and the observed data at the RT quantiles. The line illustrates a perfect match between the observed and predicted output. The closer the

points are to the line, the better the match between the predicted and observed values. Based on Figure 5, we determined that the diffusion model parameters appropriately fit the data for the source and item memory tasks across both overnight sessions.

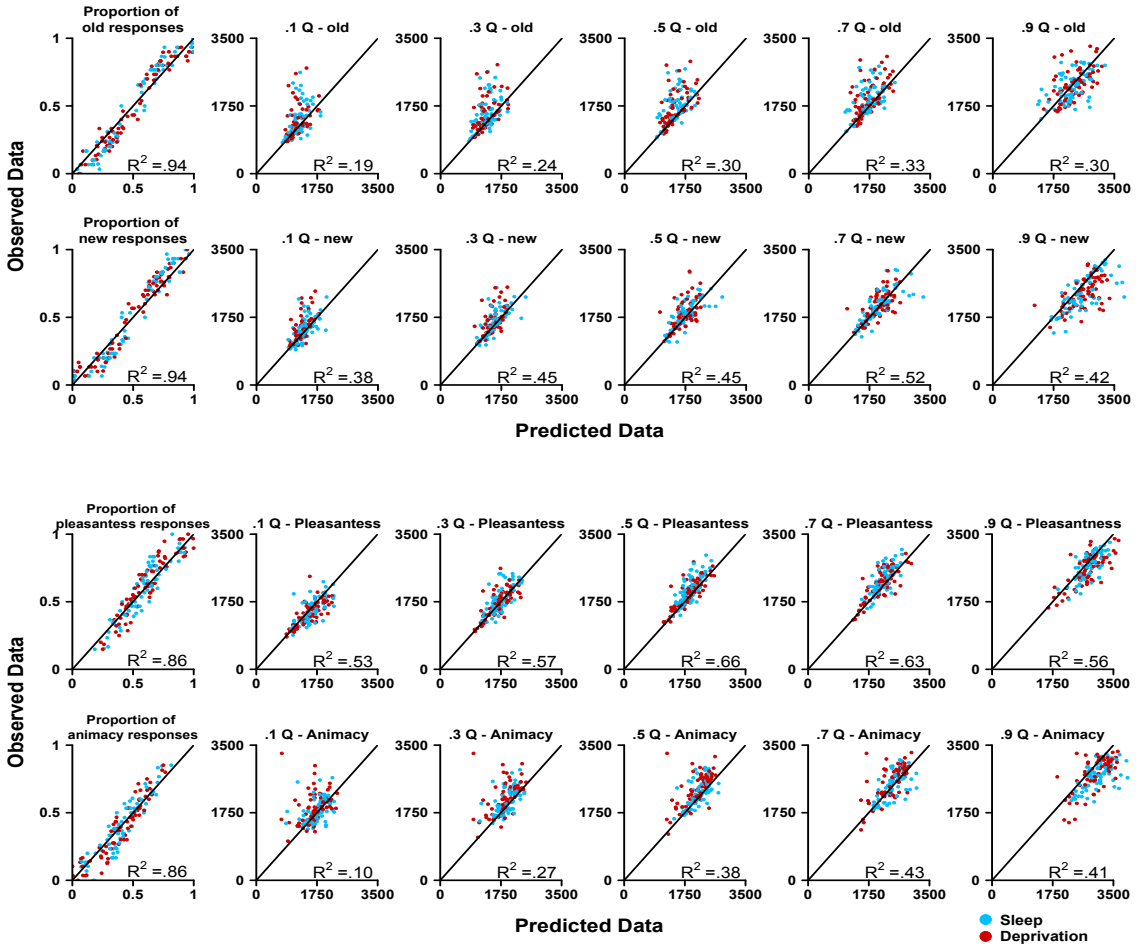

Figure 5. Diffusion Model Simulation to Assess Fit

These graphs illustrate the goodness of fit of the drift-diffusion model parameters by plotting the observed data by the predicted/simulated data. The two tops rows display the fit from the item memory task and the two bottom rows display the fit from the source memory task. In each plot there are two data points for each participant. Performance during the sleep session is in blue and the deprivation session is in red. The closer the points are to the line the better the parameter estimates match the observed data and the larger the R^2.

Performance Changes Across Sleep and Sleep Deprivation Sessions

Source Memory

One way within subjects ANOVAs were conducted separately using source accuracy, metamemory accuracy, and diffusion model parameters as the outcome variable and session (sleep, sleep deprivation) as the predictor. Source accuracy did not differ across the sleep (M = .66, SD = .07) and the sleep deprivation (M = .64, SD = .09) sessions, F(1,34) = .46, p = .50. In contrast, metamemory accuracy, as measured by the Hamann Index, was significantly lower following sleep deprivation (M = .23, SD = .19) compared to the sleep session (M = .31, SD = .19), F(1,34) = 5.37, p = .03, η_p^2 = .14. When age and sex were added to the model they were not significant predictors (F(1,32) = .95, p = .34; F(1,32) = 2.46, p = .13, respectfully). This suggests that participants were more accurate in judging their item-by-item memory when they slept. To further examine the difference in Hamann Index across sessions, percent correct was calculated for low and high confidence responses during the sleep and sleep deprivation sessions (see Figure 7). There were no differences in percent correct across sessions when examining the low and high confidence responses separately, ps > .05.

Complementary to the source accuracy results, there was no difference in source drift rate across the sessions, F(1,34) = 1.91, p = .18. The only diffusion model parameter that significantly differed across the sessions was boundary separation, F(1,34) = 4.11, p = .05. This suggests that participants had a more conservative response style during the sleep deprivation session (M = 2.01, SD = .34) compared to the sleep session (M = 1.89, SD = .38). The starting point, non-decision component, and variability in the non-decision component did not differ between the sleep and deprivation sessions (ps > .1). These findings suggest source memory performance did not differ across sessions on

measures of accuracy, drift rate, starting point, or non-decision components. In contrast, participants were more accurate at evaluating their source memory and exhibited a more cautious response style after they did not sleep compared to when they did sleep.

Item Memory

One way within subjects ANOVAs were conducted separately using recognition, metamemory accuracy, and diffusion model parameters as the outcome variable and session (sleep, sleep deprivation) as the predictor. Recognition (hits – false alarms) was significantly lower following sleep deprivation (M = .51, SD = .15) compared to the sleep session (M = .60, SD = .15), F(1,34) = 7.00, p = .01, η_p^2 = .17. When age and sex were added to the model, they were not significant predictors (F(1,32) = .03, p = .86; F(1,32) = .70, p = .41, respectfully). Examining the components of recognition (hits and false alarms) separately revealed that false alarm rate significantly differed across the two sessions (F(1,34) = 5.91, p = .02, η_p^2 = .14) while hit rate was unchanged (F(1,34) = .37, p = .54). Similar to the source memory task results, we discovered that metamemory accuracy (Hamann Index) was significantly lower following sleep deprivation (M = .38, SD = .28) compared to the sleep session (M = .48, SD = .25), F(1,34) = 6.23, p = .02, η_p^2 = .15. When age and sex were added to the model they were not significant predictors (F(1,32) = .0004, p = .98; F(1,32) = .99, p = .33, respectfully). There were no differences in percent correct between low and high confidence responses across sessions (see Figure 7), ps > .05.

Item memory drift rate was higher in the sleep session (M = 1.61, SD = .75) compared to the sleep deprivation session (M = 1.27, SD = .60), F(1,34) = 3.95, p = .055, η_p^2 = .11. To further investigate what was driving the difference in drift rate, we

separately examined the drift rate from the old and new conditions. Interestingly, drift rate only differed for the new condition across the sleep (M = -1.10, SD = .55) and the sleep deprivation sessions (M = -.82, SD = .38), F(1,34) = 7.18, p = .01, η_p^2 = .17. The drift rate for the old condition did not differ across sessions, F(1,34) = .13, p = .73.

There was no difference in the non-decision component across the sleep and sleep deprivation sessions, F(1,34) = 2.63, p = .11. During the sleep session (M = .39, SD = .28) participants had a significantly higher variability in the non-decision component compared to the sleep deprivation session (M = .29, SD = .19), F(1,34) = 4.05, p = .052, η_p^2 = .11. There was no difference in starting point (F(1,34) = .27, p = .61) or boundary separation (F(1,34) = .99, p = .32) suggesting that neither response bias or response caution differed across the sessions.

These findings suggest that item memory strength as measured by accuracy and drift rate was better in the sleep session relative to the sleep deprivation session. In the sleep session, lower false alarm rate and higher drift rate for the new condition suggested that participants were better at identifying which words were not presented in the study phase (new words) when they slept compared to when they were deprived of sleep. In addition, participants were more accurate at evaluating their memory when they slept compared to when they were sleep deprived. Response caution (boundary separation), response bias (starting point), and non-decision components did not change across sessions while variability in the non-decision component was higher during the sleep session.

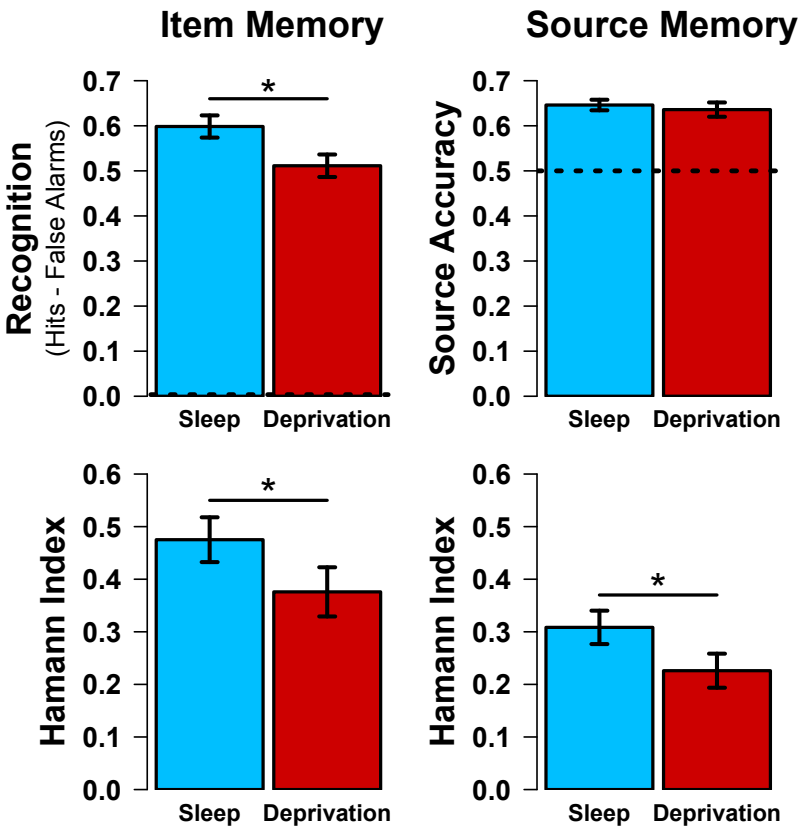

Figure 6. Source and Item Memory Results

*The left graphs display performance on item memory and the right graphs display performance on source memory across the sleep (blue) and sleep deprivation (red) sessions. The dotted line represents chance performance. *p < .05*

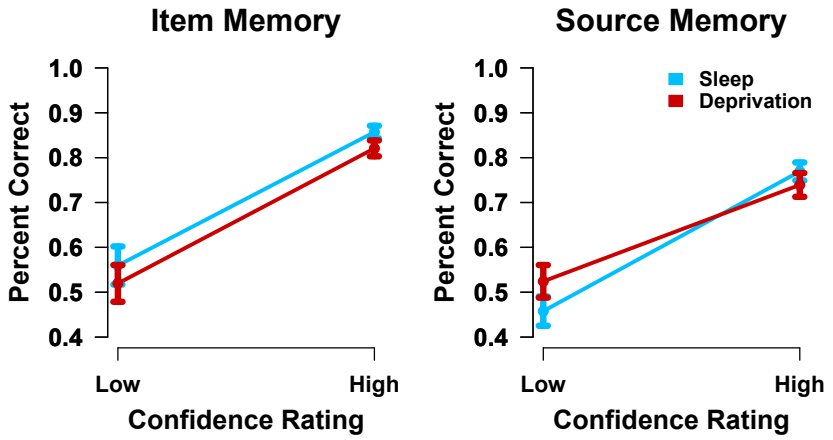

Figure 7. Source and Item Memory Percent Correct by Confidence Ratings

These plots illustrate percent correct separately for low confidence (1-guess, 2 - 25% sure) and high confidence (3 - 75% sure, 4 – sure) trials across the sleep (blue) and deprivation (red) sessions for the item and source memory task. Percent correct did not differ at either the low or high confidence ratings between the sleep and deprivation sessions for either task, ps > .05.

Psychomotor Vigilance Task

One way within subjects ANOVAs were conducted separating for each summary measure of the PVT as the outcome variable and session (sleep, sleep deprivation) as the predictor. Participants' mean reaction times (RTs) were significantly slower, and overall more variable (as measured by the standard deviation of reaction times) during the sleep deprivation session (mean RT: M = 270.87ms, SD = 26.59ms; variability in RT: M = 45.05ms, SD = 10.01ms) compared to the sleep session (mean RT: M = 251.77ms, SD = 19.76ms; variability in RT: M = 37.36ms, SD = 10.66ms), mean RT: $F(1,35) = 39.56$, $p = .0000003$, $\eta_p^2 = .53$; variability in RT: $F(1,35 = 24.94$, $p = .00001$, $\eta_p^2 = .42$. Age and sex were not significant predictors when added as a covariate to the model ($F(1,33) = .56$, $p = .46$; $F(1,33) = .33$, $p = .57$, respectfully). The mean of the top 10% and the bottom 10% of

trials were slower in the sleep deprivation session (top 10%: M = 216.43ms, SD = 16.18ms; bottom 10%: M = 368.82ms, SD = 44.10ms) compared to the sleep session (top 10%: M = 208.30ms, SD = 14.46ms; bottom 10%: M = 334.87ms, SD = 41.29ms; top 10%: F(1,35)=20.20, p = .00007, η_p^2 = .37; bottom 10%: F(1,35) = 35.17, p = .0000009, η_p^2 = .50). The number of instances where participants had trials with RTs > 500ms was also significantly higher during the deprivation session (M = 2.17, SD = 3.08) compared to the sleep session (M = .72, SD = 1.06), suggesting that when participants were deprived of sleep they had more response lapses, F(1,35) = 10.39, p = .003, η_p^2 = .23. The only measure that did not differ across the sessions was false starts (F(1,35) = .37, p = .55), which has been interpreted as an index of motivation (Adam et al., 2006). The lack of difference suggests that motivation did not differ across the sessions. These findings illustrate that sustained attention, as measured by the PVT, was significantly impaired during the sleep deprivation session compared to the sleep session.

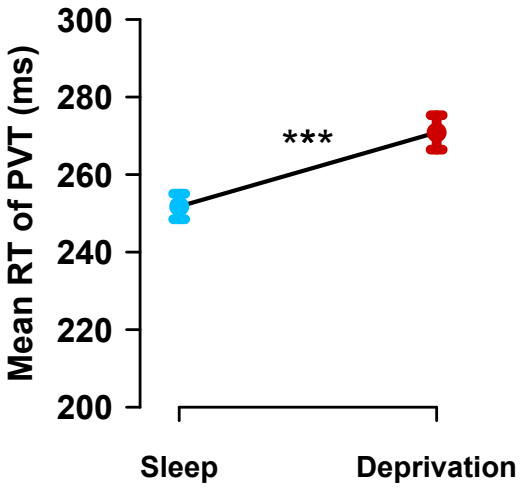

Figure 8. Psychomotor Vigilance Task Results

*The mean reaction time (RT) from the Psychomotor Vigilance Task (PVT) was significantly slower following sleep deprivation. ***p < .001.*

Overnight Word-Pair Recall

Memory change scores (morning - evening performance) were significantly better during the sleep session (M = -.20, SD = .12) relative to the deprivation session (M = -.26, SD = .14), F(1,35) = 4.66, p = .04, η_p^2 = .12 (see Figure 9). Age and sex were not significant predictors when added as a covariate to the model (F(1,33) = .48, p = .49; F(1,33) = .21, p = .65). Importantly, prior to the sleep manipulations performance on the night short-delay cued recall phase did not differ across the sleep (M = .72, SD = .16) and the sleep deprivation sessions (M = .76, SD = .17), F(1,35) = 2.47, p = .12. These results suggest that memory was better preserved across a night interval of sleep compared to a night interval of wake.

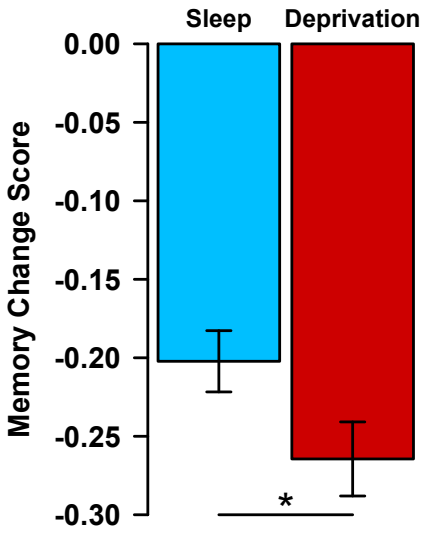

Figure 9. Overnight Word-Pair Recall Results

*Memory change (morning – evening performance) on the overnight word-pair recall task significantly declined in the sleep deprivation session, *p < .05.*

Wakefulness Ratings

The wakefulness ratings that were taken before the night memory task did not differ across the sleep and the sleep deprivation sessions, $F(1,35) = .71$, $p = .41$. In contrast, before the morning cognitive testing session, participants reported feeling more alert in the sleep session ($M = 3.44$, $SD = 1.23$) compared to the sleep deprivation session ($M = 5.31$, $SD = 1.67$), $F(1,35) = 37.53$, $p = .0000005$, $\eta_p^2 = .53$. As expected, participants reported lower levels of alertness the morning of the sleep deprivation session compared to the sleep session.

Testing Vigilance and Neuropsychological Hypothesis

To account for multiple within subject measures, we conducted mixed linear models (afex and lme4 packages in R: Singmann, Bolker, & Westfall, 2015; Bates et al., 2015) to demonstrate which cognitive processes (memory function and/or sustained attention) changed across the sleep deprivation and sleep sessions. The p-values were calculated based on the Kenward-Roger estimation (Kenward & Roger, 1997). Since age and sex were not significant predictors in any model above, they were not included. The standardized beta coefficients (β) reflect the outcome of the sleep deprivation session minus the sleep session. Negative coefficients represent lower values during the sleep deprivation sessions.

The first model using recognition memory as the outcome variable found that recognition significantly declined following sleep deprivation after adjusting for mean reaction times (RT) from the PVT, $\beta = -.24$ CI[-.48, -.01], $p = .05$. Mean RT was not a significant predictor in the model, $\beta = -.12$ CI[-.35, .14], $p = .40$. A second model tested whether sleep deprivation affects sustained attention by examining whether mean RT

from the PVT changed across sessions when adjusting for recognition. Mean RT from the PVT was slower following sleep deprivation, even when adjusting for recognition, β = .35 CI[.23, .48], p = .000003. Interestingly, recognition significantly contributed to this relationship, β = -.17 CI[-.34, -.005], p = .05. These models suggest that both recognition (hits – false alarms from the item memory task) and sustained attention (mean RT from the PVT) reflect independent changes as a result of sleep loss.

Another set of models using item memory drift rate as the outcome variable demonstrated that drift rate marginally declined following sleep deprivation after adjusting for mean RT from the PVT, β = -.23 CI[-.48, .01], p = .07. The mean RT predictor did not significantly change across sessions, β = -.03 CI[-.28, .22], p = .84. A second model tested whether sleep deprivation affects sustained attention by examining whether mean RT from the PVT changed across sessions when adjusting for item drift rate. Mean RT from the PVT was slower following sleep deprivation even when adjusting for item drift rate, β = .36 CI[.24, .48], p =.000001. Interestingly, item drift rate significantly contributed to this relationship, β = -.15 CI[-.30, .003], p = .058.

DISCUSSION

Summary of Results

We compared new learning, overnight recall, and sustained attention performance following a night of sleep and 24 hours of sleep deprivation in healthy older adults. Our results demonstrated that recognition memory, metamemory accuracy, and sustained attention declined following sleep deprivation relative to normal sleep. Contrary to expectations, source memory performance did not differ between sessions. Applying

diffusion models to participants' behavior during the item and source memory task generated multiple components that have previously been associated with different aspects of cognition. The drift rate parameter from the item memory task, which has been associated with memory strength, was sensitive to the sleep manipulation. This suggests that memory strength was lower following sleep deprivation. The application of the diffusion model to the source memory trials revealed that participants had a more cautious response style (larger boundary separation parameter) during the sleep deprivation condition resulting from slower response times and slightly higher accuracy. During both the source and item memory tasks, participants were less accurate at judging their memory (Hamann Index) following sleep deprivation. Reaction times from the Psychomotor Vigilance Task (PVT) were consistently slower in the sleep deprivation condition suggesting that sustained attention was reduced after sleep loss. Retention of previously learned items was affected by sleep deprivation. We set out to test whether sleep loss affects memory indirectly through lapses in sustained attention (vigilance hypothesis) or specifically through declines in strategic memory processes (neuropsychological hypothesis). Using mixed linear models we discovered that recognition memory and sustained attention were uniquely impaired by sleep loss. These results suggest that multiple cognitive processes are affected by sleep loss and the current picture is more complex than either the neuropsychological hypothesis or the vigilance hypothesis has articulated.

Evidence for Hypotheses of Sleep Loss and Memory Performance

Our findings illustrated that sleep loss in older adults contributed to lower recognition memory performance even after adjusting for changes in sustained attention.

Sleep loss also contributed to lower sustained attention when adjusting for recognition memory. The results are partially consistent with the neuropsychological hypothesis, which states that sleep loss affects strategic memory processes that are associated with frontal function and not sustained attention. Strategic control processes are involved in goal-directed memory retrieval to appropriately select information while inhibiting competing information (Dobbins & Wagner, 2005; Wilckens et al., 2012). Patients with frontal lobe damage show high false alarm rates because of impairment in using controlled processes to retrieve the relevant information and ignore false information (Schacter et al., 1996).

Our memory monitoring results from the source and item memory task further support the neuropsychological hypothesis since metamemory accuracy was significantly lower following sleep deprivation. Metamemory (Hamann Index) represents an individual's ability to monitor his or her performance on an item-by-item level. Previous studies illustrate that memory monitoring processes involve the prefrontal cortex (Schnyer, Nicholls, & Verfaellie, 2005). Patients with damage to the right medial prefrontal cortex were significantly worse at judging their accuracy compared to control participants (Schnyer et al., 2004). Additionally, prefrontal function has been particularly sensitive to sleep loss (for review see: Muzur, Pace-Schott, & Hobson, 2002). When an individual is sleep-deprived there is a significant decrease in frontal lobe metabolism (Wu et al., 2006). Some hypothesize this sensitivity to sleep deprivation in prefrontal regions arises from a lack of slow wave sleep since slow wave sleep restores frontal function (see Chapter 3 for more information about slow wave sleep; Wilckens et al., 2012). Therefore these results partially support the neuropsychological hypothesis, which postulates that sleep loss specifically impairs performance on tasks that depend on executive function.

This hypothesis suggests that performance on complex memory and decision-making tasks degrade, whereas simple reaction time tasks are unaffected by sleep loss. Our findings suggest that strategic control processes that have been associated with PFC function decline following sleep loss as well as sustained attention.

In addition to effects on processes associated with PFC, we found that sustained attention performance was affected by sleep deprivation. Although the older participants were only about 20ms slower on the PVT in the deprivation condition, the results were extremely consistent and robust. While young adults experience significant deficits in sustained attention following sleep loss (Lim & Dinges, 2008), numerous studies match our results demonstrating that older adults show a smaller decrement in performance (Pace-Schott & Spencer, 2013). Consequently, studies comparing sustained attention performance across age groups find that older adults perform better relative to younger adults following sleep loss (Pace-Schott & Spencer, 2013). In conjunction with better sustained attention performance, these studies find that older adults are subjectively and objectively less sleepy during sleep deprivation (Adam et al., 2006; Duffy et al., 2009). The most commonly proposed explanation for these paradoxical finding is that older individuals do not need as much sleep (Duffy et al., 2009). Since their sleep is shorter, more fragmented, and includes less slow wave sleep it is possible that sleep homeostasis, the neurobiological component of sleep regulation that balances sleep and wake, is weakened in aging. Sleep homeostasis is thought to promote sleep after extensive wakefulness by building up sleep pressure the longer an individual is awake (Dijk & Lockley, 2002). If older adults have a weaker regulation of sleep homeostasis they may not experience as much sleep pressure across an extended period of wake. Without the high sleep pressure that young adults experience, it is possible that older individuals can

better sustain their attention and therefore not show as much of a performance decrement due to lack of sleep (Forsman & Van Dongen, 2013).

Countless studies report that vigilant attention is a consistent deficit following sleep deprivation (J. Lim & Dinges, 2010). Since the PVT involves frontal function (Drummond et al., 2005) it is unclear whether the sustained attention impairment following sleep deprivation was due to deterioration in frontal function. Future work should apply our framework of examining dissociated components of memory and attention using neuroimaging in order to pinpoint whether these tasks elicit similar or unique brain activity particularly in prefrontal regions. Using a sleep deprivation paradigm allowed us to discover that strategic processes involved in memory retrieval rely on sleep as well as sustained attention in older adults.

Sleep Loss and Source Memory

Contradictory to our hypothesis that source memory performance would be uniquely affected by sleep loss, we did not see a significant difference in accuracy performance between the sleep and sleep deprivation sessions. The results from the diffusion model demonstrated that older adults were more cautious during the sleep deprivation condition by taking more time to respond which resulted in slightly increased accuracy that matched their performance during the sleep session. Although this shift in response style partially describes why performance did not differ across sessions, there is likely another explanation. Importantly, in parallel to the false alarm rate results from the item memory task, confidence ratings from the source and item memory tasks declined following sleep loss. These results suggest that sleep deprivation leads to declines in frontal function in older adults. Since the majority of research investigating the effects of

sleep deprivation on cognition in older adults has focused primarily on sustained attention tasks, very little is known about how other cognitive functions are affected (Scullin & Bliwise, 2015). It is possible that the present source memory task was too difficult and therefore lacked sensitivity. Accuracy in the sleep condition was relatively low so the difference between the two sessions may have been masked by a floor effect. Future work should use an associative/source memory task where older adults' accuracy is higher under normal sleep conditions to better under how associative memory changes following sleep loss.

Sleep Loss and Memory Consolidation

Considerable research has focused on the role of sleep in consolidating previously learned information (for review see: Alger, Chambers, Cunningham, & Payne, 2014). Our findings from the memory task where participants learned new word-pair associations on the night preceding either sleep or a night of no-sleep illustrated that memory was better preserved when the night interval included sleep compared to wake. These results are in line with previous studies demonstrating that sleep leads to less forgetting (Stickgold & Walker, 2007). Our results strengthen previous findings showing that sleep better preserves word-pair associations compared to wake (Marshall, 2004; Marshall et al., 2006; Plihal & Born, 1997; Westerberg et al., 2012) because we modified the design and administration of the word-pair recall task. The word-pair recall task previously included testing the same words in the evening and the morning. During the last evening test, participants were shown the correct answer, resulting in an additional encoding event, which may have inflated memory scores. Therefore memory change scores from the evening to the morning may have reflected the additional encoding

opportunity instead of solely sleep or wake processes. Instead of presenting the same words during the evening and morning test, we split the studied words so that half were tested during the night and the other in the morning. By splitting the learned items and testing half in the evening and half in the morning, we removed the additional encoding event during the last evening recall trial which allowed us to measure only the difference in performance due to sleep compared to wake. Another key difference between our study and past work is the time of testing. In previous experiments, participants in the sleep condition study at night and are tested in the morning whereas participants in the wake condition study in the morning and are tested at night. Since older adults exhibit better memory retrieval in the morning compared to the night (May, Hasher, & Stoltzfus, 1993), participants in the sleep condition may exhibit a boost in performance due to the morning testing time. Therefore in the present paradigm, the time of study and test was matched across the sleep and wake conditions. Importantly, this required the wake condition to include sleep deprivation. During the sleep deprivation session participants engaged in a variety of activities including reading, taking walks, and playing games that may have affected memory consolidation but did not differ from the previous paradigms. Although our design introduced other confounds (i.e. unmatched sleepiness) we think our results uniquely demonstrate that periods of offline processing that include sleep results in better preservation of memory compared to offline periods of wake. Results from the present design did not differ from previous studies demonstrating that sleep compared to wake is better for memory preservation. Future work should explore experimental designs where time of day and sleepiness are matched across wake and sleep conditions to better understand the role of sleep in episodic memory consolidation.

Conclusion

Our results suggest that sleep loss affected memory retrieval, memory monitoring, memory consolidation, and sustained attention. Since each participant completed both the sleep and the sleep deprivation sessions, we were able to account for baseline differences in cognitive performance among older individuals. This gave us a unique opportunity to examine which distinct cognitive processes rely on sleep. We expanded on previous work demonstrating that sleep is important for acquiring new information (Yoo, Hu, Gujar, Jolesz, & Walker, 2007) separate from vigilant attention. Since older adults experience significantly poorer sleep quantity and quality (Ohayon et al., 2004) compared to when they were younger these results informed us about which cognitive processes may suffer due to age-related changes in sleep. In conclusion, these findings provide novel insight into how sleep maintains effective cognitive functioning and may facilitate the development of interventions to improve cognition in aging.

Chapter 3: How Sleep Physiology is Associated with Memory Function in Older Adults

INTRODUCTION

Sleep prior to learning contributes to the formation of memories (Feld & Diekelmann, 2015). Following sleep deprivation, young adults demonstrated a significant impairment in learning on an episodic memory task (Yoo et al., 2007). In fully rested individuals, introducing a nap prior to testing increased the ability to encode new information (Mander, Santhanam, Saletin, & Walker, 2011). These findings illustrate that one function of sleep is to prepare an individual to learn. Since sleep behaviors may differentially contribute to cognition (Plihal & Born, 1997), separately examining aspects of sleep physiology is an important next step in understanding how sleep supports episodic learning.

Many hypothesize that slow wave power (0.5 – 4 Hz) during sleep restores learning capacity (Feld & Diekelmann, 2015). Slow wave sleep is synchronous brain activity dominant in the 0.5 – 4 Hz range that is thought to largely arise from the prefrontal cortex (Murphy et al., 2009). Electroencephalography (EEG) data clearly demonstrates that slow wave power is predominant in frontal electrode sites (Münch et al., 2004). Cortical maturation is associated with increased slow wave power during sleep (Buchmann et al., 2011) and consequently less slow wave power has been related to reduced grey matter volume in the medial prefrontal region (Mander, Rao, Lu, Saletin, Lindquist, et al., 2013b). According to the synaptic homeostasis hypothesis, slow wave power renormalizes synapses to restore learning capacity during the subsequent wake period (Tononi & Cirelli, 2003). Evidence for this hypothesis in young adults showed that increasing slow wave power through stimulation led to better performance on an

episodic memory task the following day (Antonenko, Diekelmann, Olsen, Born, & Mölle, 2013)

Since aging is associated with parallel declines in episodic memory and slow wave sleep (Wilckens et al., 2012), the amount of slow wave power may account for individual differences in memory. When the amount of slow wave power was experimental reduced, older participants showed impaired performance on an episodic memory task (Van Der Werf et al., 2009). Although these results suggest a link between slow wave power and new episodic learning, some studies have failed to replicate or extend this association (for review see: Scullin & Bliwise, 2015). One reason for the inconsistent results may be because memory performance encompasses multiple cognitive components including vigilant attention, response bias, and response caution. Since different episodic memory tasks rely on other cognitive functions to varying degrees, it is unclear whether slow wave power independently enhances the strategic processes that support memory.

The purpose of the present study was to examine which physiological aspects of sleep were related to components of next day memory performance. Additionally, the design of the study allowed us to include a measure of overnight memory consolidation. Our goal was to test how modifications to an existing word-pair recall task (Westerberg et al., 2012) affected the results. These modifications involved removing additional encoding events following night memory testing. To examine next day memory performance we used a computational model, the diffusion model (see detailed background in Chapter 2) to investigate which physiological aspects of sleep optimize distinct cognitive processes involved in source and item memory. While both the source and item memory tasks measure episodic memory, source memory more heavily involves

the retrieval of context information (Spaniol et al., 2006) which draws on the strategic functions associated with the prefrontal cortex and is sensitive to the memory decline we see in the aging population (Mitchell & Johnson, 2009). Since slow wave sleep declines in aging, we examined whether older adults who exhibit more slow wave power have better next day source memory strength.

MATERIALS AND METHODS

Participants

Thirty-three participants (24 females; age: mean = 69.45, SD = 2.66, range = 65 – 75 years old) were included in the final analyses out of thirty-six eligible participants (for detailed eligibility information and exclusion criteria see Chapter 2). Two participants were excluded because of issues during sleep EEG data acquisition and one participant was dropped because of chance accuracy (50%) on the source memory task.

Procedure

Overview

Participants arrived in the sleep lab 1.5 hours before their habitual bedtime based on 3 days of sleep diaries. Following the completion of a self-reported wakefulness rating, participants underwent the night portion of the overnight word-pair recall task. Participants followed their typical bedtime schedule and were given up to 8 hours to sleep without disturbances (Mander, Rao, Lu, Saletin, Lindquist, et al., 2013b). In the morning, participants completed questionnaires regarding their sleep quality and quantity. To minimize sleep inertia, participants were given at least 30 minutes to get ready and eat

prior to cognitive testing (Cunningham et al., 2014). Cognitive testing included the morning portion of the overnight word-pair recall task, a source and item memory task, and the Psychomotor Vigilance Task (PVT).

Sleep Electroencephalography

Sleep EEG was monitored in the laboratory and recorded at standard locations using an elastic cap laid out in a modified 10-20 system (EasyCAP electrode system, Brain Products; F3, F4, C3, C4, P3, PZ, P4, O1, O2, M1, M2). The reference electrode was recorded at Cz as well as electrooculography and chin electromyography. Data were sampled at 200Hz. All analyses were conducted offline.

Cognitive Testing

Details regarding the overnight word-pair recall task, the source and item memory task, and the Psychomotor Vigilance Task can be found in Chapter 2.

DATA ANALYSIS

Behavioral Analysis

Details regarding the analysis of overnight word-pair recall task, the source and item memory task, and the Psychomotor Vigilance Task can be found in Chapter 2.

Sleep EEG Analysis

The raw EEG signals were imported into BrainAnalyzer 2.0 Software (Brain Products, Munich, Germany). The left and right Electrooculography (EOG) channels were created from the bipolar montage of the electrode placed under the eye (right, left) and the corresponding frontal electrode (right, left). The EMG channel was computed from the bipolar montage of the right and left chin electrodes. Data were re-referenced to linked mastoids (M1, M2) and all channels were filtered for frequencies between 0.1 and 40 Hz except the EMG channel, which was left unfiltered. Semiautomatic artifact inspection was completed and data were segmented into 30-second epochs for sleep staging. Sleep staging was accomplished based on the standard criteria (Iber, 2007). Briefly, Stage 1 sleep was identified by activity between 4 – 7 Hz along with slow eye movements. The presence of Stage 2 sleep was scored when sleep spindles and K complexes were also present. Slow wave sleep was recognized when the frequency was between 0.5 and 4 Hz and the peak to peak amplitude was about 75μV. Lastly, Rapid Eye Movement (REM) sleep was identified by sharp and irregular eye movements along with lower EMG activity than the other sleep stages.

Epochs scored as sleep were selected and then divided into 5-s epochs. Epochs containing artifacts were removed to ensure that signal including large fluctuations in amplitude were not included in the subsequent spectral power analyses. A Fast Fourier Transform was applied using a 10% Hanning window to calculate spectral power density (μV) on each individual 5-s epoch. Those epochs were averaged across all sleep stages and the delta frequency band (0.5 – 4 Hz) was examined. This approach has been utilized in past aging studies (Mander, Rao, Lu, & Saletin, 2013a; Mander, Rao, Lu, Saletin, Lindquist, et al., 2013b) because standard sleep scoring is often not sensitive to age-

related changes in brain function that is reflected in the EEG signal, especially with respect to periods of slow wave sleep (delta). Past studies indicate that low levels of slow wave power evident in older adults may not pass the standard criteria for slow wave sleep (Westerberg et al., 2012). Therefore the primary approach to the analysis was focused on slow wave power (delta; 0.5 – 4 Hz) in the two frontal F3 and F4 electrodes across all sleep periods. The analyses were also re-ran to examine delta between 0.5 – 1 Hz but this did not change the pattern of results presented below.

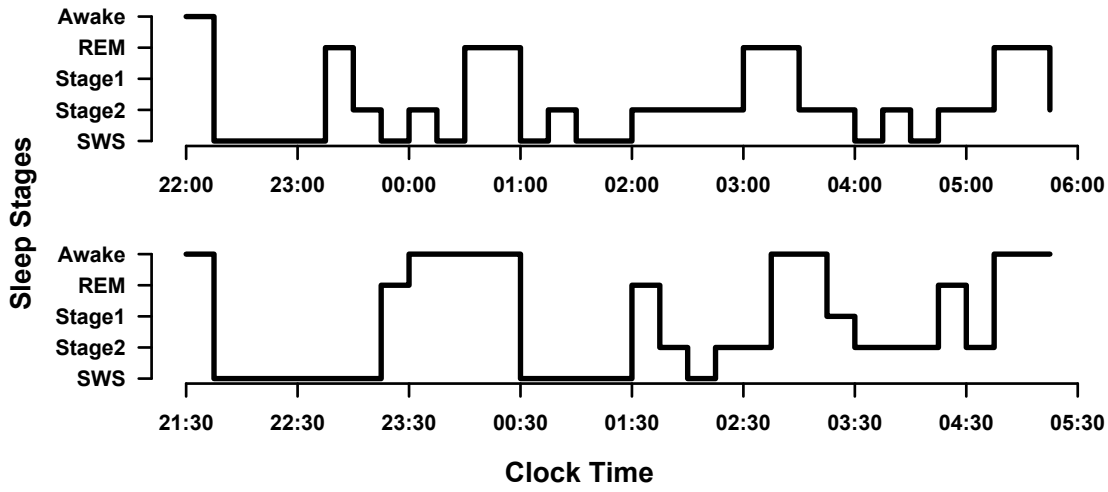

Figure 10. Hypnograms

These figures illustrate sleep across the in-lab session in two participants. The top panel shows sleep from one participant who slept well and the bottom panel shows sleep from one participant who slept poorly in the lab.

Variable	Mean	SD	Range
Total Recording Time (min)	472.6	15.39	424 – 485
Total Sleep Time (min)	379.5	41.51	303.5 – 454
Wake After Sleep Onset (min)	78.86	39.62	14 – 163
Stage 1 (min)	25.29	11.38	5.5 – 58
Stage 1 (%)	6.85	3.46	1.22 – 17.53
Stage 2 (min)	175.9	35.86	119.5 – 259.5
Stage 2 (%)	46.45	8.61	33.00 – 65.86
Slow Wave Sleep (min)	119.5	39.72	42.5 – 192
Slow Wave Sleep (%)	31.44	9.86	13.51 – 50.20
Rapid Eye Movement Sleep (min)	58.7	21.04	21.5 – 103.5
Rapid Eye Movement Sleep (%)	15.25	4.56	6.46 – 25.18
Sleep Efficiency (%)	80.31	8.66	63.54 – 94.45

Table 3. Sleep Characteristics

The sleep characteristics during the in-lab sleep recording session.

RESULTS

Sleep Associations with Cognitive Performance

Source and Item Memory

More slow wave power (0.5 - 4 Hz) across the entire night of sleep was associated with higher drift rates from the source memory task (β = .49 CI[.15, .81], p = .005) but not the item memory task (β = -.15, p = .4; see Figure 11). The association between source drift rate and slow wave power did not change when adjusting for age, β = .45, CI[.12, .78], p = .009. Although females (M = 45.46, SD = 13.05) earned more slow wave power compared to males (M = 30.84, SD = 9.42; F(1,31) = 10.86, p = .002), examining each sex demonstrated that the direction and strength of association were similar (males: β = .37, p = .25; females: β = .48, p = .03). Additionally, source and item memory performance did not differ across males and females, p < .05. Accuracy from the

source memory task had a similar but weaker relationship with slow wave power, β = .37 CI[.02, .72], p = .04. After adjusting for age the results illustrated that source accuracy was marginally associated with slow wave power, β = .35 CI[-.006, .70], p = .054. No measure of accuracy from the item memory task such as recognition, hit rate, or false alarm rate was associated with slow wave power, ps > .2. Number of minutes in each stage of sleep such as slow wave sleep and rapid eye movement sleep (REM) were not associated with accuracy (see Table 4) or drift rate from either the source or item memory task, ps > .1. Similarly, basic sleep characteristics such as total sleep time, sleep efficiency, and wake after sleep onset were not associated with accuracy or drift rate from the source and item task, ps > .1. The basic sleep characteristics from the sleep diaries the night before the session were not associated with source or item memory performance, ps > .05. There was a negative association between slow wave power and sleep diary reported sleep quality (β = -.37 CI[-.70, -.04], p = .03) and total sleep time (β = -.34 CI[-.68, -.01], p = .04) the night before the session. This suggests that poorer sleep the night before was related to higher slow wave power during the in-lab sleep session. These findings illustrate that more slow wave power was linked to better source memory strength (drift rate) and not item memory strength. Minutes in each stage of sleep or overall sleep characteristics did not show any associations with memory performance.

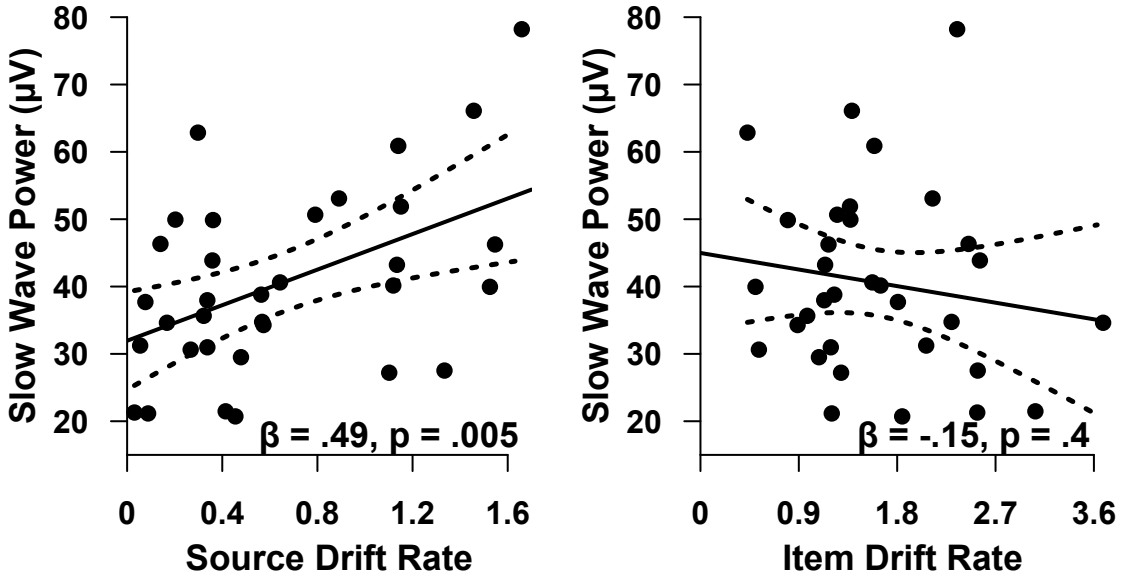

Figure 11. Slow Wave Power by Source and Item Drift Rate

Higher source but not item drift rate was linked to more slow wave power across the entire night of sleep. Dotted line represents 95% confidence intervals

Variable	Source Accuracy		Recognition	
	r value	p value	r value	p value
Total Sleep Time (min)	.07	.71	-.06	.74
Wake After Sleep Onset (min)	-.12	.53	.17	.34
Stage 1 (min)	-.15	.41	.10	.57
Stage 2 (min)	.01	.96	.02	.93
Slow Wave Sleep (min)	.10	.58	.01	.93
Rapid Eye Movement Sleep (min)	.01	.95	-.23	.20
Sleep Efficiency (%)	.14	.44	-.07	.69

Table 4. Sleep Characteristics by Source and Item Memory Task Performance

The correlations among basic sleep characteristics and accuracy on the source memory task (source accuracy) and the item memory task (recognition).

Word-Pair Recall

Memory change (morning – evening performance) was not related to slow wave power across the entire night of sleep, $\beta = .19$ CI[-.16, .56], $p = .27$. Similarly, morning memory performance was not associated with slow wave power, $\beta = .14$, CI[-.23, .51], $p = .44$. Memory change was not related to the number of minutes in each stage of sleep including stage 1, stage 2, slow wave sleep, rapid eye movement sleep, ps > .05. Although slow wave power was not associated with memory change, more minutes spent in slow wave sleep was related to better memory in the morning, $\beta = .38$ CI[.03, .73], $p = .03$ (see Figure 12). In addition, more minutes in stage 1 sleep was related to poorer morning memory performance, $\beta = -.36$ CI[-.71, -.01], $p = .04$. Memory change was not associated with total sleep time, sleep efficiency, or wake after sleep onset, ps > 1. Memory change was not associated with age ($\beta = .08$, $p = .64$) and did not differ across males and females ($F(1,33) = .64$, $p = .43$). Subjective ratings of sleepiness immediately before the encoding phase were not related to night performance on the immediate recall, $\beta = .13$, $p = .44$. These findings illustrate that change in memory performance across the night was not related to any measure of sleep. Performance on the morning portion of the task was positively related to the number of minutes spent in slow wave sleep and negatively related to the number of minutes spent in stage 1 sleep.

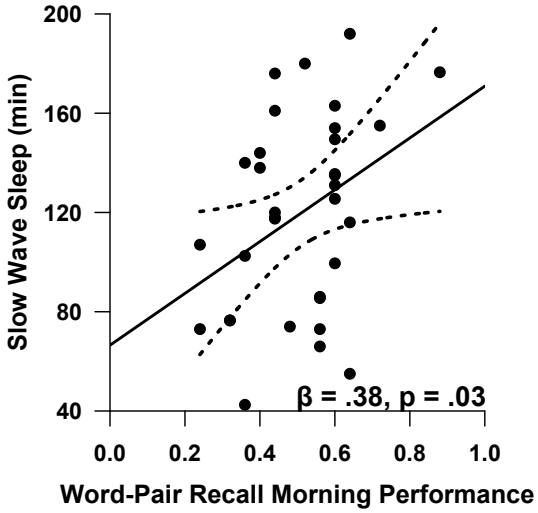

Figure 12. Word-Pair Recall Morning Performance by Slow Wave Sleep

The relationship between percent correct on the word-pair recall task during the morning and number of minutes spent in slow wave sleep. Dotted line represents 95% confidence intervals.

Psychomotor Vigilance Task

Mean reaction times from the PVT were not associated with slow wave power across the entire night of sleep, $\beta = .14$, $p = .43$. No other outcome measures from the PVT were associated with slow wave power, $ps > .2$. More minutes in REM had a trending association with faster mean reaction times, $\beta = -.31$ CI[-.67, .05], $p = .09$. Greater total sleep time was also marginally related to faster mean reaction times, $\beta = -.32$ CI[-.68, .04], $p = .08$.

Sleep Specifically Associated with Memory Function

To assess whether slow wave power was specifically associated with source memory strength we included mean reaction times in the model using slow wave power across sleep to predict source memory drift rate. Slow wave power significantly predicted source drift rate when adjusting for mean reaction times from the PVT, $\beta = .47$ CI[.13, .80], $p = .008$. Mean reaction times was not a significant predictor in the model, $\beta = .14$, $p = .38$. When examining whether slow wave power predicted source accuracy when adjusting for mean RT from the PVT, we found that slow wave power was a marginal predictor ($\beta = .33$ CI[-.01, .66], $p = .057$) along with mean RT from the PVT, $\beta = .30$ CI[-.03, .62], $p = .07$. By using the diffusion model we demonstrated that slow wave power across the entire night was specifically associated with source memory strength when adjusting for sustained attention performance (see Figure 13).

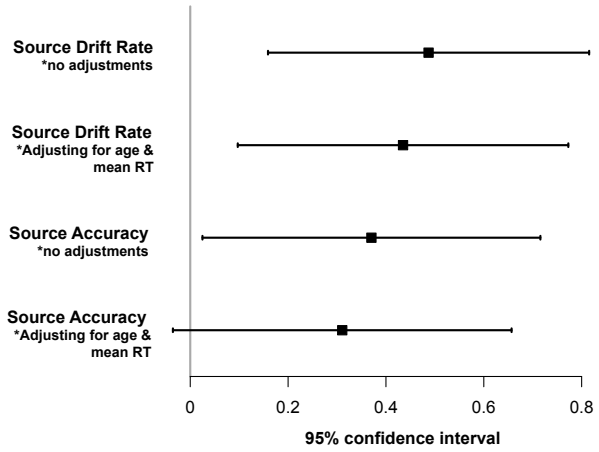

Figure 13. Source Memory Effect Size

This figure illustrates the extent to which slow wave power across the entire night of sleep predicts different measures of source memory performance. The 95% confidence intervals of the standardized betas (β) that cross 0 are non-significant. Source drift rate remains significant after adjusting for age and mean reaction time from the PVT while source accuracy does not.

DISCUSSION

Summary of the Results

Using the drift-diffusion model we discovered that higher source memory strength (drift rate) was associated with greater slow wave power (0.5 – 4 Hz) during sleep in healthy older adults. In contrast, there was no relationship between item memory strength and slow wave power. The relationship between slow wave power and source memory strength remained significant after adjusting for sustained attention performance from the Psychomotor Vigilance Task (PVT). Furthermore, sustained attention was not correlated with slow wave power and only marginally related to total sleep time and minutes spent in REM. These findings illustrated that slow wave power prior to learning was uniquely linked to enhanced source memory function. Slow wave power was not related to memory consolidation (memory change score) on the word-pair recall task. In contrast, the number of minutes spent in slow wave sleep was related to morning word-pair recall performance. These findings partially correspond to previous investigations of sleep-dependent memory consolidation (Westerberg et al., 2012). Overall our results support the synaptic homeostasis hypothesis (Tononi & Cirelli, 2003) suggesting that slow wave power is important for renormalizing synapses to prepare an individual to learn the following day. This hypothesis states that slow wave power led to synaptic downscaling which improved energy availability and subsequently increased learning (Olcese, Esser, & Tononi, 2010; Tononi & Cirelli, 2014). Additionally our results are in line with the memory consolidation hypothesis (Marshall & Born, 2007; Stickgold, 2005) suggesting that slow wave sleep promotes the transfer of short-term hippocampal-dependent memories to long-term memory storage in neocortical regions. This process is thought to

consolidate memory for subsequent retention and restore learning capacity for optimal hippocampal-dependent learning.

Advantage of Diffusion Modeling

This is the first study to use diffusion modeling to understand how memory performance is associated with sleep physiology. Applying the diffusion model to source and item memory performance incorporated both reaction times and accuracy to pinpoint which cognitive processes were related to aspects of sleep physiology. Although source accuracy was correlated with slow wave power, this relationship was partially accounted for by sustained attention (mean RT from the PVT). Including reaction times into the measure of source memory function was important for identifying the relationship between source memory strength and slow wave power. Other studies examining the association between sleep physiology and cognition that only utilized accuracy measures have yielded inconsistent results (for review see: Scullin & Bliwise, 2015). Using an auditory verbal learning task, one study did not find any association between immediate or delayed recall accuracy and slow wave power (Lafortune et al., 2013). In contrast, Van Der Werf and colleagues found that declarative memory performance declined when slow wave power was experimentally reduced. In addition to memory decline they also found increased lapses in vigilant attention (Van Der Werf, Altena, Vis, Koene, & Van Someren, 2011). Since memory accuracy was only examined, it is unclear whether including reaction times would have accounted for the same variance in reduced slow wave power as response lapses from the PVT. Future work should utilize the diffusion model to investigate whether modeling cognition provides more converging results.

Sleep Benefits Source Memory and Not Item Memory

Our findings indicate that greater slow wave power prior to learning was linked to better source memory strength while item memory did not show the same association. Although this is the first study to demonstrate that sleep containing more slow wave power prior to learning is differentially related to source and item memory, similar findings have been reported in investigations of sleep-dependent memory consolidation. Following a nap, young adults showed preserved associative memory but deficits in item memory performance (Studte, Bridger, & Mecklinger, 2015). Several studies have concluded that slow wave oscillations during sleep preferentially enhances hippocampal and prefrontal mediated memory function (Abel, Havekes, Saletin, & Walker, 2013). We expanded on this work by demonstrating that slow wave power prior to learning may also preferentially benefit memory for associations that involve hippocampal-mediated binding.

Source memory was assessed in this study because it benefits from sleep-related processes and it is sensitive to aging. Previous work suggests that memory for binding features such as an object with a context (source memory) is consistently impaired in older adults compared to young adults (Mitchell & Johnson, 2009). To further demonstrate the specificity of age-related memory decline, Ratcliff and colleagues applied the diffusion model to performance on an item and source memory task in young and older adults. When they compared memory strength (drift rate) in the two age groups they discovered no difference for item memory but drift rate for source memory was significantly lower in older individuals (Ratcliff & McKoon, 2015). Since source memory strength is sensitive to age-related decline, slow wave power may be a key indicator of the extent to which older individuals experience memory decline.

Does Slow Wave Power Cause Better Memory Function?

Due to the correlational nature of this study, it is unclear whether slow wave power causes better memory function in older adults. Two studies support a causal relationship between slow wave power and memory performance the following day. Using electrical transcranial slow oscillation stimulation (tSOS), slow wave power was increased in young adults during a nap. Those who received stimulation exhibited increased slow wave power and subsequently performed better on the episodic memory task (Antonenko et al., 2013). Instead of increasing slow wave power, one study experimentally reduced slow wave power in older individuals. They found that those who had reduced slow wave power showed impaired episodic memory performance (Van Der Werf et al., 2011). Together, these studies nicely demonstrate that slow wave power contributes to next-day memory function.

Although these studies present compelling evidence that changes in the amount of slow wave power cause changes in memory performance, some argue that without measuring sleep within individuals across multiple nights, it is unknown whether sleep physiology directly benefits cognition (Maurer et al., 2015). Especially because of work suggesting that the amount of minutes in each stage of sleep does not vary significantly within individuals across multiple nights (when under similar conditions; Maurer et al., 2015). Alternatively, earning high slow wave power and exhibiting intact memory function may be two independent components of good health in older individuals. Although Studte and colleagues found that greater sleep spindle density during slow wave sleep was related to better associative memory consolidation, they also demonstrated that associative memory performance measured prior to sleep yielded the

same relationship (Studte et al., 2015). These findings indicate that the contribution of sleep physiology to memory function may reflect a more stable aspect of behavior rather than uniquely benefit a person's present state. It is also possible that sleep the week before or even the month before is contributing to cognition (Seelye et al., 2015). Therefore future work should measure sleep physiology within individuals across multiple nights to discover whether changes in sleep translate to changes in memory performance.

Conclusion

Using the novel combination of diffusion modeling and sleep physiology measures, our results demonstrate that slow wave power prior to learning is linked to source memory strength. Since source memory strength is sensitive to age-related decline, slow wave power may be a key indicator of the extent to which older individuals experience memory decline. Future work should be done to understand whether experimentally increasing slow wave power uniquely increases next-day source memory especially in older individuals.

Chapter 4: General Discussion

SUMMARY

In this dissertation, we examined which components of episodic memory 1) changed following sleep loss and 2) correlated with aspects of sleep physiology in older adults. Our results demonstrated that memory functions that depend on processes associated with the prefrontal cortex were impaired following sleep deprivation. In addition, sleep loss caused a small but robust impairment in sustained attention. Since multiple cognitive processes were impaired by sleep loss in older adults, these findings were unable to provide definitive support for either the neuropsychological hypothesis or the vigilance hypothesis. Therefore we propose that sleep loss affects multiple cognitive processes in older adults. When examining sleep physiology, slow wave power during sleep was related to better next day source memory strength, dependent on processes associated with hippocampal function. These results support the synaptic homeostasis hypothesis (Tononi & Cirelli, 2003) which states that slow wave power renormalizes synapses to prepare an individual to learn the next day. Additionally, our results are in line with the memory consolidation hypothesis (Marshall & Born, 2007; Stickgold, 2005) suggesting that slow wave sleep promotes the transfer of hippocampal-dependent memories to long-term memory storage in neocortical regions. From our overall examination of sleep in older adults we conclude 1) strategic memory processes and sustained attention rely on sleep, 2) individuals who elicit more slow wave power are more likely to exhibit better episodic learning on the morning following sleep and 3) more minutes in slow wave sleep was related to higher morning recall. The implications of this work are that cognitive functions known to decline in aging depend on sleep behaviors and specific aspects of sleep physiology that show age-related declines are

associated with better cognitive function. In addition, understanding normal sleep in the elderly may ultimately lead to the identification of dysfunction that could serve a diagnostic purpose to detect early signs of neurocognitive disorders. These results support further efforts to investigate sleep as a general indicator of cognitive function across the lifespan and underscores the importance of reinforcing and supporting healthy sleep behaviors (Feld et. al., 2015) in order to preserve cognitive functioning in older adults.

POSSIBLE IMPLICATIONS

Sleep Loss

Our results suggest that sleep loss in older adults impairs strategic memory processes and sustained attention. Studies examining how sleep deprivation affects cognition in younger and older adults have revealed that older individuals are not as affected by sleep loss (for more explanation see Chapter 2, Discussion, Evidence for Hypotheses of Sleep Loss and Memory Performance; Adam et al., 2006; Duffy et al., 2009; Stenuit & Kerkhofs, 2005). This paradoxical finding has led researchers to conclude that older individuals do not need as much sleep, which has the potential of downplaying the consequences of sleep loss in aging. This is especially important because it is possible that lower sleep quality in older adults causes cognitive decline (Wilckens et al., 2012). Although changes in the association between sleep and cognition may occur during aging, our results revealed that sleep is still essential for optimal cognitive functioning. Even if the contribution of sleep to cognition is reduced, any beneficial effects of sleep on cognition is notable and may combat common age-related

declines in memory and attention. Therefore we conclude that examining sleep loss is important for understanding cognitive decline in older adults.

Sleep Physiology

Our results illustrated that slow wave power was associated with better next-day source memory strength during episodic learning. As discussed in Chapter 3, it is unclear whether slow wave power the night before directly causes better next-day learning. In other words, changes in slow wave power across nights may not be associated with changes in cognition the following day within individuals. Alternatively, amount of slow wave power could be an independent signature of cognitive health or associated with another component of health not measured in the current study. To examine whether slow wave power is more stable, we conducted an exploratory analysis to test whether source memory on the morning after the deprivation session was correlated with slow wave power during the sleep session (see Figure 14). The purpose of this analysis was to discover whether slow wave power and memory function measured on two separate occasions were associated. The results illustrated a trend showing that slow wave power during the sleep session was associated with better memory function during the deprivation session, $\beta = .26$, $p = .13$. These findings suggest that older individuals who generally have high memory functioning, even under conditions where sleep was deprived, show higher slow wave power on a night of sleep separated by a week or more from the testing time. The correlation provides some evidence that slow wave power is a sign of cognitive health since it is related to memory function measured following 24 hours without sleep (or slow wave power during sleep). Since sleep physiology was not measured the night before the deprivation session, the influence of prior slow wave

power cannot be ruled out. Future work should examine slow wave power during sleep within individuals across multiple nights to discover whether it is associated with general cognitive health or whether changes in slow wave power translate to changes in memory function.

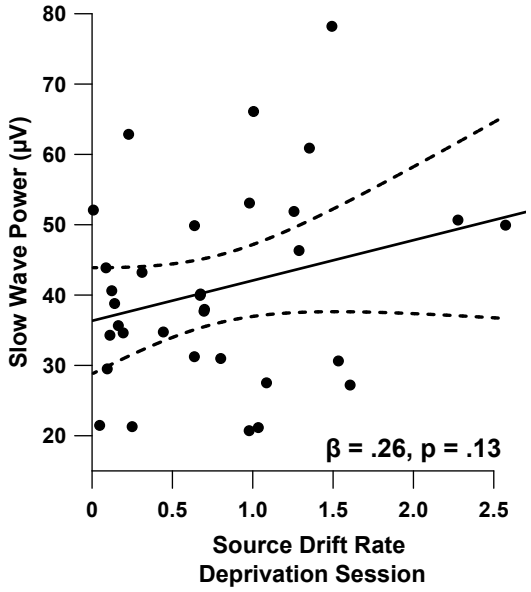

Figure 14. Slow Wave Power by Source Drift Rate during the Deprivation Session

The relationship between drift rate from the source memory task following sleep deprivation and slow wave power during the sleep session night. Dotted lines represent 95% confidence intervals.

FUTURE DIRECTIONS

Sleep Loss

This study utilized a sleep deprivation paradigm to directly manipulate sleep in order to understand which components of memory function rely on sleep. Although this paradigm has been successful in past studies at uncovering how sleep loss affects

physical and mental functioning (Killgore, 2010; J. Lim & Dinges, 2010), depriving an individual of sleep introduces other factors that impact cognition. Sleep deprivation is associated with increases in cortisol concentration (Wright et al., 2015), higher ratings of stress, and poorer mood (Dinges et al., 1997). In low stress conditions, participants who were sleep deprived exhibited greater stress, anxiety, and anger compared to fully rested participants (Minkel et al., 2012). Similar findings have been reported in studies of sleep restriction. Dinges and colleagues restricted young adults' sleep to about 4-5 hours per night and found that subjective ratings of mood were significantly lower the more days individuals' sleep was restricted (Dinges et al., 1997). Importantly, increases in cortisol and stress ratings influence memory function independent of sleep loss. In one study, older adults who were put into a stressful situation had impaired memory performance compared to those in a non-stressful condition (Lupien, Gaudreau, & Tchiteya, 2013). Since the current study did not measure stress, it is unclear how these processes may have interacted with the presented changes (or lack of changes) exhibited in cognitive functioning following sleep deprivation. Future work should examine how stress ratings and cortisol changes are associated with memory after sleep deprivation to better understand how sleep loss affects cognition in older adults.

Sleep Physiology

Our hypotheses focused on the association between slow wave power and episodic learning in older adults. There are other mechanisms of sleep besides slow wave power that may contribute to memory function that were not explored in the current study. Recent work has suggested that sleep spindles may play a role in episodic memory. Sleep spindles (10 -15 Hz) are one of the hallmarks of non-rapid eye movement (NREM)

sleep and are recognized by fast deflections that overall show an increase then decrease in amplitude (waxing and waning; De Gennaro & Ferrara, 2003; Luthi, 2014). Previous studies have proposed that sleep spindles are involved in episodic memory consolidation (Cairney, Durrant, Jackson, & Lewis, 2014) and new episodic learning (Lafortune et al., 2013; Mander, Rao, Lu, & Saletin, 2013a). While most of the research has focused on the role of sleep spindles in memory consolidation, Mander and colleagues discovered that fast spindles were associated with next day hippocampal-dependent learning in older adults (Mander, Rao, Lu, & Saletin, 2013a). In contrast to the current work, they did not find an association between slow wave power and episodic learning. Other investigations have revealed associations between episodic memory consolidation and slow wave power but not sleep spindles (Westerberg et al., 2012). In this study we made a priori predictions regarding slow wave power but not sleep spindles. Running exploratory analyses on different aspects of sleep physiology inflates the probability of false positive associations between sleep and memory function. Future work should make specific predictions to examine how the interaction between sleep spindles and slow wave power relate to episodic learning across the lifespan.

CONCLUSION

The work conducted here examined how sleep loss and sleep physiology are related to cognitive functioning in healthy older adults with a specific focus on new episodic learning. Our findings demonstrate that memory and attention rely on sleep behaviors and specific aspects of sleep physiology are associated with better episodic learning. Since older adults experience age-related changes in sleep and cognition, understanding how sleep contributes to cognitive function may explain why older

individuals experience varying levels of cognitive decline. In conclusion, we illustrated that sleep is important for cognition in older adults and monitoring changes in sleep may inform us about the changes that occur in memory across the lifespan.

Appendix: Health and Demographic Form

Health/Demographic Information

Please complete the survey below.

Thank you!

Birth Date

_____
(Use the calendar icon to add your birthdate or type it in using numbers in the Year-Month-Day format.)

Please enter the date you are completing the survey. CLICK THE "TODAY" BUTTON.

_____
(Click the "TODAY" button.)

Our system will record your age, in years, as:

_____
(This field will automatically be filled in as you move through the rest of the questions.)

Are you left handed, right handed or both?

- ◯ Left
- ◯ Right
- ◯ Both

Ethnicity (check all that apply)

- ☐ African American
- ☐ Asian
- ☐ Caucasian
- ☐ Hispanic
- ☐ Native American
- ☐ Other

If Other, please specify

_____

Gender

- ◯ male
- ◯ female

Occupation

_____

Have you been a shift-worker within the last year? (A shift worker is anyone who follows a work schedule that is outside of the typical business day)

- ◯ Yes
- ◯ No

What is the highest level of education you have completed?

- ◯ 12
- ◯ 13
- ◯ 14
- ◯ 15
- ◯ 16
- ◯ 17
- ◯ 18
- ◯ 19
- ◯ 20
- ◯ more than 20

(High school=12, college=16)

Name and place of school? What area of study?

_____

Is English your first language?

- ◯ Yes
- ◯ No

If no, what age did you begin formal education in English?

_____

Are you fluent in any languages other than English?

◯ Yes
◯ No

If yes, which ones? _____

How did you hear about this experiment? _____

Would you be willing to be contacted regarding participation in other experiments?

◯ Yes
◯ No

Have you ever had a stroke?

◯ Yes
◯ No

Do you have any history of epilepsy?

◯ Yes
◯ No

Have you used cocaine, ecstasy, or any IV drugs that were not for medical purposes?

◯ Yes
◯ No

If yes, when and for how long?

_____

Have you used LSD?

◯ Yes
◯ No

If yes, when and for how long?

_____

Have you ever had a seizure?

◯ Yes
◯ No

If yes, when did it occur? (month/day/year) _____

Do you still have them?

◯ Yes
◯ No

If so, how often? _____

Do you regularly consume alcohol?

◯ Yes
◯ No

How much alcohol do you drink at a time? _____
(number of glasses)

What type of alcohol do you typically consume? _____

Have you ever had a drinking problem?

◯ Yes
◯ No

If yes, please explain

_____

Do you have a learning disability?

◯ Yes
◯ No

If yes, did you need to be removed from the regular classroom and take special education classes? Please explain details.

_____

Do you have a heart condition?

◯ Yes
◯ No

If yes, when did the problems begin? What is your condition? Medications?

_____

Do you have hypertension?

◯ Yes
◯ No

If yes, when did the problems begin? What is your condition? Medications?

_____

Have you ever had a heart attack?

◯ Yes
◯ No

If yes, when? Have you noticed differences in what you can and cannot do since your heart attack?

_____

Have you ever been diagnosed with a psychiatric disorder?

◯ Yes
◯ No

When was it diagnosed? _____

Please specify _____

Are you currently depressed?

◯ Yes
◯ No

If yes, were you clinically diagnosed?

_____

Have you ever been diagnosed with a sleep disorder such as insomnia, sleep apnea, restless leg syndrome or narcolepsy?

◯ Yes
◯ No

If yes, please specify and explain

_____

When was it diagnosed? _____

Have you ever had a significant head injury?

◯ Yes
◯ No

Did it result in a loss of consciousness?

◯ Yes
◯ No

If yes, please list age, circumstances, if you were hospitalized and if there were and noticeable changes, including headaches.

_____

Have you ever had a neurological disorder or any other problems with your brain or head?

◯ Yes
◯ No

If yes, please explain

_____

Have you ever had any surgeries (especially on the heart or head?)

◯ Yes
◯ No

If yes, give dates, reasons and amount of time in the hospital.

_____

Do you have problems controlling your movements that would prevent you from being able to write or manipulate small objects?

◯ Yes
◯ No

If yes, explain

_____

Do you currently have diabetes?

◯ Yes
◯ No

If yes, please explain

_____

Do you have a vascular disease?

◯ Yes
◯ No

If yes, please explain

_____

Do you have any history of cancer that has been active in the last three years?

◯ Yes
◯ No

If yes, please explain

_____

Do you have arthritis?

◯ Yes
◯ No

If yes, please explain

_____

Do you have Alzheimer's?

◯ Yes
◯ No

If yes, please explain

_____

Do you have Parkinsons?

◯ Yes
◯ No

If yes, please explain

_____

Do you have any other serious illnesses?

◯ Yes
◯ No

If yes, please explain

_____

In the past 6 months, have there been any significant changes in your sleep habits?

◯ Yes
◯ No

If yes, please explain

_____

In the past 6 months, has there been any significant change in your level of physical activity?

◯ Yes
◯ No

If yes, please explain

_____

Do you smoke cigarettes/cigars/pipe?

◯ Yes
◯ No

Did you ever smoke?

◯ Yes
◯ No

If yes, how long have you/ did you smoke?

_____

Number of packs/cigars/pipes per day/week?

_____

When did you quit? (if applicable)

_____

Are you seeing a health care practitioner for any current medical or psychological problems?

◯ Yes
◯ No

If yes, please explain

_____

Are you taking any medications for any of the above problems or for any other reason (Including vitamins, aspirin, and other regularly taken medications)?

◯ Yes
◯ No

If yes, please list all medications you have not already mentioned (please include the dosage of each medication, whether or not it was prescribed, how long you have been taking it for, and the reason for the medication (i.e. which illness is it treating?))

_____

Are you now, or have you ever taken estrogen and/or used hormone replacement therapy?

◯ Yes
◯ No

Do you have normal or corrected to normal (i.e. glasses/contacts) vision?

◯ Yes
◯ No

Are you near-sighted or far-sighted?

◯ near-sighted
◯ far-sighted
◯ neither

Are you color blind?

◯ Yes
◯ No

Do you have cataracts?

◯ Yes
◯ No

If yes, please explain

_____

Do you have normal or corrected to normal (i.e. cochlear implant) hearing?	◯ Yes ◯ No
What is your height?	_____ ((in inches))
What is your weight?	_____ ((in lbs))
Can you think of anyone in your family (living or deceased) that has (or has had) a neurological disorder such as Alzheimer Disease, Dementia, Parkinson's or Huntington's?	◯ Yes ◯ No
If yes, please explain who it is and detail what type of disorder they have or have had	_____

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