1-1-2011

Sleep, Memory, and Aging: Effects of Pre- and Post-Sleep Delays and Interference on Memory in Younger and Older Adults

Michael Scullin
Washington University in St. Louis

WASHINGTON UNIVERSITY IN ST. LOUIS

Department of Psychology

Dissertation Examination Committee:
Mark McDaniel, Chair
Sandy Hale
Larry Jacoby
Henry Roediger, III
Paul Shaw
James Wertsch

Sleep, Memory, and Aging: Effects of Pre- and Post-Sleep Delays and Interference on Memory in Younger and Older Adults

by

Michael K. Scullin

A dissertation presented to the
Graduate School of Arts and Sciences
of Washington University in
partial fulfillment of the
requirements for the degree
of Doctor of Philosophy

December 2011

Saint Louis, Missouri

Abstract

The present research investigated the relationship between sleep and memory in younger and older adults. Previous research has demonstrated that during the deep sleep stage (i.e., slow wave sleep), recently learned memories are reactivated and consolidated in younger adults. However, little research has examined whether memory consolidation occurs during deep sleep in older adults. Younger adults and older adults encoded word pairs (e.g., channel – result) in the morning or evening and then returned 12 hours or 24 hours later for a final test (three groups: 12-hr wake, 12-hr sleep, 24-hr PM-PM sleep). Sleep stage scoring was obtained by having participants use a home sleep monitoring system (Zeo, Inc.) between experimental sessions. In the younger adult group, memory retention was greater in the 12-hr sleep condition than in the 12-hr wake condition (the 24-hr sleep condition produced results similar to, though nominally greater than, the 12-hr wake group), and these younger adult participants demonstrated a positive correlation between memory retention and amount of deep sleep. In contrast, in the older adult group, no effect of delay condition was observed and deep sleep did not significantly correlate with memory retention. Furthermore, for one measure of post-sleep delay learning, the older adults but not the younger adults demonstrated a significant *negative* correlation between deep sleep and memory performance. These findings suggest that the relationship between memory and deep sleep that is typically observed in younger adults, is weakened or changed in older adults.

Acknowledgements

Support for this research was provided by the NIH Aging Training Grant 5T32AG00030, NIH Grant 01-AG-102, the APF/COGDOP Clarence J. Rosencrans Scholarship, and a Psi Chi Graduate Research Grant. Philips Respironics, Inc., loaned the Actiwatches and Actiware-5 analysis software for the use of this dissertation project. Zeo, Inc., awarded the Wireless Monitoring Devices as part of a Zeo Sleep Research Grant.

The development of this experiment benefited from conversations with members of the dissertation committee (Mark McDaniel, Roddy Roediger, Larry Jacoby, and Sandy Hale), members of the McDaniel Laboratory (Jill Shelton, Cindy Fadler, Michael Cahill, Ji Hae Lee, amongst others), as well as Don Bliwise, Sean Drummond, Matt Walker, Bryce Mandler, and Bob Stickgold. I am highly appreciative of Mark McDaniel who allowed me the flexibility to pursue a line of sleep research in graduate school when such research was not already occurring in the lab or in the department. I am also very grateful to Larry Jacoby, Roddy Roediger, and Sandy Hale, who generously offered to help expedite the dissertation reading and defense process when it appeared that my NRSA might be contingent on it. In addition, I would like to thank Sophie Goloff for her help with data analyses as well as Ji Hae Lee, Michael Cahill, and Cindy Fadler for their helpful comments on an earlier version of this dissertation. Finally, perhaps no one is more deserving of acknowledgment than my wife Rachel who was extremely supportive of me throughout this dissertation project (and graduate school) even when it meant being away many nights to run participants.

Table of Contents

List of Tables

List of Figures

List of Appendices

List of Abbreviations

AB′ pairs	Session 1 pairs that were followed by *AC′* pairs in Session 2
AB pairs	Session 1 pairs that were *not* followed by *AC′* pairs in Session 2
AC′ pairs	Session 2 pairs that used the same *A*-word as a pair from Session 1
AMPA	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor
ANCOVA	analysis of covariance
ANOVA:	analysis of variance
DE pairs	Session 2 pairs that were unrelated to other word pairs
EEG:	electroencephalography
hr:	hour
fMRI:	functional magnetic resonance imaging
min:	minute
MEQ	Morningness-Eveningness Questionnaire
MMFR	modified modified free recall
MSE	mean squared error
NREM:	non-rapid eye movement (sleep) (i.e., Stages 1-4, or light and deep sleep)
OA:	older adult
PET:	positron emission tomography
PSG:	polysomnography
PSQI	Pittsburg Sleep Quality Index
REM:	rapid eye movement (sleep)
SD card:	secure digital card
tDCS:	transcranial direct current stimulation

WAIS: Wechsler Adult Intelligence Scale

WASO: wake after sleep onset

YA: younger adult

Sleep, Memory, and Aging: Effects of Pre- and Post-Sleep Delays And Interference on Memory in Younger and Older Adults

Humans spend approximately one-third of their lives sleeping but scientists have yet to reach a consensus as to why sleep occurs. One likely explanation is that, like waking behavior, sleep serves multiple purposes ranging from tissue restoration (Adam & Oswald, 1977) and energy conservation (Berger & Phillips, 1995) to maintaining synaptic homeostasis (Tononi & Cirelli, 2003). In recent years scientists have discovered an additional function of sleep: sleep benefits the consolidation of memories (Karni, Tanne, Rubenstein, Askenasy, & Sagi, 1994; Wilson & McNaughton, 1994).

The history of sleep benefits to memory can be traced back to Ebbinghaus's (1885/1964) seminal study of memory. Though Ebbinghaus concluded that forgetting was a function of time, the association between time and memory recall was imperfect. The primary discrepancy in his forgetting curve was the reduced forgetting rate between the delay of 8.8 and 24 hours, in which only 2.1% of information was forgotten, which can be compared to the higher forgetting rates prior to sleep onset (8.4% between 1 and 8.8 hours) and following the first night of sleep (6.1% between 24 and 48 hours). Although the reduced forgetting occurred during a period that would include the first full night of sleep following learning, Ebbinghaus argued that the observed reduction "[was] not credible" (p. 77).

Subsequent research revealed that Ebbinghaus's (1885/1964) results were not accidental. In a classic study, Jenkins and Dallenbach (1924) examined memory recall across sleep and wake delays of 1, 2, 4, or 8 hours. Memory was better overall following

sleep delays (59%) than wake delays (26%). Interestingly, in the wake condition, memory consistently declined from the 1-hour delay to the 8-hour delay, whereas in the sleep condition, there was a decline in recall from 1 to 2 hours, but additional sleep delays showed no further decrease in recall. Even though this last pattern suggests that there may be a complex relationship between sleep and memory, Jenkins and Dallenbach concluded that sleep only benefits memory by (passively) protecting it from daytime interference.

Advances in Sleep Technology and in Understanding Sleep Physiology

Jenkins and Dallenbach's (1924) theory that sleep-related memory benefits result entirely from the protection of memory traces from interference was partially based upon the assumption that sleep is a homogenous state in which the brain essentially "shuts down." With the development of polysomnography [including electroencephalography (EEG)] in the 1950s and the subsequent study of neural activity during sleep, the assumption of a "quiet" brain during sleep was falsified. Aserinsky and Kleitman's (1953) discovery of rapid eye movement (REM) sleep demonstrated that the sleeping brain is not a homogenous state, but instead cycles through qualitatively different stages of activity. In following years, sleep researchers distinguished between REM sleep and Stages 1-4 of non-REM sleep. I elaborate on these stages below.

Humans cycle through five to six 90-minute-long non-REM/REM stages per night, and the amount of time spent in each stage changes across time spent asleep. Humans first enter Stage 1 of non-REM sleep, which is considered to be a transitional state between sleeping and waking. Stage 2 of non-REM is considered to be "true" sleep

(Martin, Shochat, & Ancoli-Israel, 2000), and is marked by slower EEG activity relative to waking rest periods. Because individuals are fairly easily awakened during Stages 1 and 2, these stages are often collectively referred to as *light sleep*. Following Stage 2, individuals enter into Stage 3 and then Stage 4 of non-REM sleep. Stages 3 and 4 are characterized on the EEG by delta activity (1-4 Hz) and slow oscillations (< 1 Hz). Slow oscillations are generated in the neocortex (particularly frontal regions such as the medial prefrontal cortex), and are believed to orchestrate the firing of thalamo-cortical neurons (sleep spindles) and hippocampal-cortical neurons (sharp wave ripples)(Buzsaki, 1998; Diekelmann & Born, 2010). In contrast to the specific activity related to slow oscillations, spindles, and sharp wave ripples, positron emission tomography (PET) studies (Maquet, 1997) have shown that the brain is, in general, at its quietest during Stages 3 and 4. Because Stages 3 and 4 are marked by very slow EEG activity and individuals are not easily woken during these stages, researchers often refer to these stages as slow-wave sleep or *deep sleep* (heretofore referred to as deep sleep).

Following deep sleep, the sleeping brain enters into REM sleep. EEG activity during REM sleep shows similar levels of activity to that observed during wake and PET studies (Maquet, 1996) have revealed increased cerebral blood flow (relative to deep sleep and wakeful states) in several regions (e.g., the amygdala). The first REM sleep stage is relatively short and then the cycle starts over. Humans spend the majority of the first half of the night in deep sleep whereas the second half of the night is dominated by REM sleep. When humans are deprived of deep sleep or REM sleep, on following nights, younger adults will show less light sleep and a rebound (recovery) effect to the stage(s) for which they were deprived (i.e., REM and/or deep sleep; Kollar, Pasnau, Rubin,

Naitoh, Slater, & Kales, 1969). Older adults (>55 years of age) will show a rebound to deep sleep (though more for Stage 3 than for Stage 4, whereas younger adults show the reverse), but may not show a rebound effect for REM sleep (Bonnet & Arand, 1989).

The Relationship Between Deep Sleep and Episodic Memory

Following the developments in sleep technology and gaining a fuller understanding of the different stages of sleep, Ekstrand and colleagues (Barrett & Ekstrand, 1972; Ekstrand, 1967; Fowler, Sullivan, & Ekstrand, 1973; Yaroush, Sullivan, & Ekstrand, 1971) conducted a series of experiments to test Jenkins and Dallenbach's (1924) original conclusion that simply being asleep preserves memories. Ekstrand and colleagues were particularly interested in whether episodic memory is similarly benefited by deep sleep and REM sleep stages. In one study (Yaroush et al., 1971), participants learned a paired-associate word list (e.g., Train – Black) and were tested 4 hours later. There were three conditions: daytime awake, deep sleep, or REM sleep. In the deep sleep condition, participants learned word pairs in the evening (to a criterion of 10 out of 15 correct) and were woken after 4 hours of sleep for testing (first 4 hours of sleep are rich in deep sleep); in the REM sleep condition, participants first slept for 4 hours, then were woken to learn the word pairs to criterion, and then following 4 more hours of sleep (last 4 hours are rich in REM sleep) they were given a final test. Though this design is confounded by whether participants have slept or not immediately prior to learning, it is worth noting that performance on the learning task did not differ between groups. On the final test, Yaroush et al. observed better recall in the deep sleep condition than in the REM condition, which was no better than a 4-hour daytime awake condition. The pattern

of better episodic memory following deep sleep than REM sleep has been replicated several times (Barrett & Ekstrand, 1972; Fowler, Sullivan, & Ekstrand, 1973; Plihal & Born, 1997) and suggests that Jenkins and Dallenbach's early account of why sleep benefits episodic memory may not be wholly correct.

Just as technological developments preceded Ekstrand and colleagues' work in the 1970s, developments in single cell recordings (often used in non-human animal studies) and human neuroimaging (e.g., functional magnetic resonance imaging, or fMRI) have recently led to a resurgence in interest in sleep-related benefits to memory (Stickgold, 2005; Wilson & McNaughton, 1994). One of the most intriguing scientific discoveries of the last two decades has been that recent memories are reactivated and "replayed" during sleep. In a seminal study, Wilson and McNaughton showed that the same hippocampal neurons that fire while a rodent is learning a maze fire again while the rodent sleeps. This hippocampal ensemble replay (sharp wave ripples) has sometimes been observed during REM sleep (Poe, Nitz, McNaughton, & Barnes, 2000). But, the more consistent finding is that hippocampal replay occurs during deep sleep (Ji & Wilson 2007; Lee & Wilson, 2002; Nadasdy, Hirase, Czurko, Csicsvari, & Buzsaki, 1999; Skaggs & McNaughton 1996). In humans, sharp wave ripples have been observed during deep sleep but not during REM sleep (Staba, Wilson, Fried, & Engel, 2002). The hippocampus does not simply replay memories; single-cell recording studies have demonstrated an orchestrated pattern of firing between hippocampal and neocortical cells—often referred to as the hippocampal-neocortical "dialogue" (Euston, Tatsuno, & McNaughton, 2007; Wierzynski et al., 2009)—in which memories are theorized to be reactivated and transferred from short-term hippocampal storage to long-term neocortical

storage (Buszaki, 1996; Marr, 1971; McClelland, McNaughton, & O'Reilly, 1995). This transfer, or consolidation, process is hypothesized to promote long-term recollection.

Though hippocampally-generated sharp wave ripples are suggestive of memory reactivation and consolidation, stronger evidence for this claim would come from research connecting the presumed memory reactivations to later memory performance. In two recent animal studies (Ego-Stengel & Wilson, 2009; Girardeau, Benchenane, Wiener, Buzsaki, & Zugaro, 2009), sharp wave ripples were experimentally suppressed using an electrical stimulation procedure following a spatial memory task. The suppression of sharp wave ripples blocked memory consolidation, as demonstrated by worse spatial memory performance in the suppression group relative to a no-suppression (normal sleep) control group.

The importance of hippocampal reactivation to memory consolidation has also been demonstrated in humans. Peigneux et al. (2004) had human participants learn routes in a virtual town while undergoing PET scanning. After learning, the participants slept in the PET scanner. Peigneux et al. reported that the hippocampus was activated both during learning and during deep sleep. Importantly, the degree of hippocampal (re)activation during deep sleep correlated positively with route retrieval the following day.

Marshall, Molle, Hallschmid, and Born (2004) attempted to experimentally control memory reactivation during sleep. They had subjects learn word pairs and then tested them 3 hours later after either a sleep delay (rich in deep sleep) or a wake delay. The critical manipulation was whether participants were given a transcranial direct current stimulation (tDCS) or placebo stimulation during the wake interval or during deep sleep. The tDCS technology can be employed to increase natural patterns of firing in the

human brain. For example, Marshall et al. used the tDCS to experimentally increase the number of slow oscillations (which coincide with hippocampal sharp wave ripples) observed during deep sleep. Final cued recall was better when tDCS was applied during deep sleep (but not when applied during the wake interval) relative to the placebo stimulation. Furthermore, the degree of memory benefit was significantly associated with the degree of increase in slow oscillations. Thus, experimentally increasing the neural activity that is theorized to underlie reactivation and consolidation benefited later memory recall.

Rasch, Buschel, Gais, and Born (2007) further demonstrated the relationship between reactivation during sleep and memory enhancement. Participants learned an object-location task (the game "Concentration") that involved recalling the location of card pairs following a sleep or wake interval. During learning, a rose scent (or an odorless control) was repeatedly delivered and participants were (re)exposed to that scent (or odorless control) during either deep sleep or REM sleep. Memory performance was enhanced when the rose scent (relative to the odorless control group) was presented during learning and during deep sleep. No memory enhancement was observed (relative to the odorless control group) if the rose scent was presented during deep sleep but not during learning, if the rose scent was presented during both learning and REM sleep, or if the rose scent was presented at learning and again during a wake delay. Compelling the conclusion that the rose scent was reactivating the object-location pairs during deep sleep, Rasch et al. used fMRI to show greater hippocampal activation during rose-scent-on periods than rose-scent-off periods in a sleep condition, relative to a wake condition. Diekelmann, Buchel, Born, and Rasch (2011) recently replicated these findings.

Using a similar approach, Rudoy, Voss, Westerberg, and Paller (2009) paired sounds (e.g., cat meow) with object-location pairs (e.g., picture of a cat) during learning. Then participants slept and some of the sounds were (re)presented during the deep sleep stage. Memory performance was better for the cued items than for the non-cued items thereby demonstrating selective consolidation of experimentally reactivated memories. Thus, in addition to protecting against daytime interference (Jenkins & Dallenbach, 1924), sleep can benefit memory by reactivating and consolidating recently-learned information.

In addition to studies demonstrating hippocampal reactivation of memories during deep sleep, two studies (Gais et al., 2007; Takashima et al., 2006) have further suggested that these reactivations are indicative of a transfer of memory representations to neocortical regions (Buzsaki, 1996; Marr, 1971; McClelland et al., 1995). Takashima et al. (2006) had participants memorize visual stimuli (e.g., photographs) and then gave them recognition tests in the fMRI scanner for these items at four time points over a 3-month span. The results demonstrated that, across the 3 months, memory retrieval was progressively associated with less hippocampal activation and more ventral medial prefrontal cortex activation.

Gais et al. (2007) had participants learn word pairs, and then allowed the participants to sleep or deprived them of nighttime sleep. The participants returned after 48 hours and recalled the word pairs while undergoing fMRI scanning. Functional connectivity analyses revealed greater connectivity between the hippocampus and the medial prefrontal cortex in the normal sleep group than in the sleep deprivation group. When tested again 6 months later, participants in the normal sleep group demonstrated

greater medial prefrontal cortex activation than those originally deprived of sleep. The changes across time suggested that initial sleep is critical for consolidating new memories into neocortical storage regions.

Sleep, Memory, and Aging

The recent surge of interest in deep sleep and memory consolidation has led some researchers to theorize that sleep disturbances may account for some cognitive declines in older adults (Buckley & Schatzberg, 2005; Hornung, Danker-Hopfe, & Heuser, 2005). Cognitive declines, and especially episodic memory declines, are prominent in older adults (e.g., Park et al., 2002). The root of age-related cognitive declines is a source of debate, but probably involves influences related to general slowing of speed of processing (Salthouse, 1996), inhibitory deficits (Hasher & Zacks, 1988), encoding deficits (Naveh-Benjamin, 2000), controlled processing declines (Jennings & Jacoby, 1993), and cognitive control declines (Braver & Barch, 2002), each of which have also been demonstrated to be symptoms of impaired sleep (Drummond, Meloy, Yanagi, Orff, & Brown, 2005; Killgore, 2010; Yoo, Hu, Gujar, Jolesz, & Walker, 2007). The neural underpinnings of these age-related cognitive declines may include dopamine depletion (Backman, Nyberg, Lindenberger, Li, & Farde, 2006), gray matter declines (Resnick et al., 2003), white matter abnormalities (Gunning-Dixon, & Raz, 2000), cortical thinning (Salat et al., 2004), frontal lobe dysfunction (West, 1996), and decreased hippocampus—prefrontal cortex connectivity (Grady, 2006).

Preceding, or at least paralleling, declines in cognitive functioning are declines in sleep quality (Van Cauter, Leproult, & Plat, 2000). As can be seen in Figure 1, older

adults get more light sleep than younger adults, but there is a large age-related decline in deep sleep (for a review, see Bliwise, 1993; for a meta-analysis, see Ohayon, Carskadon, Guilleminault, & Vitiello, 2004). Older adults get fewer deep sleep minutes, even when accounting for total sleep time (i.e., examining percentage of deep sleep). Not only is there nominally less deep sleep in older adults, but there is also a profound age-related decrease in the amplitude of slow waves typically observed during deep sleep (Carrier, Monk, Buysse, & Kupfer, 1997; Martin et al. 2000). In addition to consistent age-related changes in deep sleep and light sleep, older adults typically show decreased total sleep time, increased sleep latency (i.e., time in bed until person falls asleep), and increased waking after sleep onset (both in number of awakenings and minutes awake at night) (Bliwise, 1993; Ohayon et al., 2004). Though there are large age-related changes in objective sleep quality, older adults tend to under-estimate the severity of these changes (Hood, Bruck, & Kennedy, 2004; Vitiello, Larsen, & Moe, 2004).

Given the critical importance of deep sleep and slow waves to episodic memory (Marshall et al., 2004; Rasch et al., 2007; Walker, 2009), the implication of studies demonstrating changes in deep sleep across the lifespan is that some memory impairments in older adults are due to not adequately consolidating memories during sleep. Declines in sleep quality might have a direct influence on age-related cognitive declines or may be a co-factor along with other known covariates of age-related memory declines such as changes in hippocampal—neocortical functional connectivity (Grady, McIntosh, & Craik, 2003; Grady, 2006).

Research on episodic memory consolidation during sleep in older adults is minimal. Before elaborating on the episodic memory, sleep, and aging literature (which is

the most pertinent to the present research), I will first describe research on *procedural* memory consolidation in younger and older adults. The distinction between episodic memory (explicit recollection of learned information) and procedural memory (motor memory) is relevant because different neural networks support these different kinds of memory (see Gabrieli, 1998, for a review) and sleep research has demonstrated that different sleep physiology facilitates consolidation of episodic versus procedural memory (see Plihal & Born, 1997, for the classic paper, and Diekelmann & Born, 2010, for a review). Whereas episodic memories are usually consolidated during deep sleep (e.g., Rasch et al., 2007), procedural memory consolidation is linked to Stage 2 sleep (Fogel & Smith, 2006; Nishida & Walker, 2007; Walker, Brakefield, Morgan, Hobson, & Stickgold, 2002) and REM sleep (Fisher, Hallschmid, Elsner, & Born, 2002; Plihal & Born, 1997). REM sleep shows relatively minimal declines with aging and Stage 2 sleep may actually increase with aging (see Figure 1); therefore, if sleep directly contributes to procedural memory consolidation in older adults then one would predict procedural memory consolidation effects (across sleep) to be similar, if not better, in older adults relative to younger adults.

Spencer, Gouw, and Ivry (2007) examined procedural memory consolidation behaviorally (i.e., without concurrently measuring sleep physiology) in younger and older adults by having participants perform a 10-element sequence serial reaction time task following wake versus sleep intervals. The younger adults demonstrated large improvements (i.e., quicker responding, fewer errors) on this procedural memory task following sleep versus wake intervals. The older adults showed an improvement when sleep immediately followed initial learning, but similar improvements were found

following a wake delay. Because the improvement in the older adults may not have been sleep-dependent (i.e., only reflected a practice effect), the authors concluded that consolidation declines with increasing age. Siengsukon and Boyd (2009) later extended Spencer et al.'s general finding of no sleep-dependent memory improvements in older adults with a different procedural memory task (use a joy stick to track a cursor moving in a sine wave through a sequence with 10 direction reversals).

Tucker, McKinley, and Stickgold (2011) most recently investigated whether procedural memory consolidation can occur in older adults. They gave younger and older participants a 5-element motor sequence task and tested them following sleep versus wake delays. Following sleep (but not wake), the younger adults and the older adults performed the procedural memory task faster than during training. However, whereas the younger adults demonstrated improvement on the procedural memory task immediately following sleep, the older adults only demonstrated such benefits following repeated testing. That is, in an immediate test (trials 1-3) there was a strong age effect but in the last trials (trials 10-12) there was no age effect. These behavioral data suggested relative preservation of procedural memory consolidation in the older adults. To account for the discrepancy in their findings and previous work, these authors argued that the serial reaction time task used by Spencer et al. (2007) was too challenging for the older adults, and that if a certain level of initial learning (motor skill proficiency) were not reached then consolidation would be unlikely to occur. While intriguing, this interpretation appears to be inconsistent with the finding of a practice effect across wake delays in Spencer et al.'s study.

In addition to their motor sequence test, Tucker et al. (2011) had the older adults (but not the younger adults) undergo polysomnography recording the night between training and testing. Whereas their behavioral data suggested that procedural memory consolidation might be somewhat preserved in the older adults, the conclusion that a *sleep* mechanism drove these effects was not strongly supported by polysomnography data: older adults' procedural memory improvements did not significantly correlate with percentage of Stage 2 sleep ($r = -.15$), REM sleep ($r = .38$, $p = .14$), deep sleep ($r = -.15$), or any other sleep parameter.

The lack of a correlation between procedural memory and sleep parameters in older adults has been observed in other studies. Following motor skill learning, younger adults often demonstrate an increase in spindle density during Stage 2 sleep (i.e., an associate of procedural memory consolidation; Walker, 2009). Peters, Ray, Smith, and Smith (2008) demonstrated a significant boost in spindle density following motor skill learning in a younger adult group but not in an older adult group. Thus, procedural memory might not be strongly linked to sleep processes in older adults.

Age-Related Changes in the Sleep—Cognition Link

Tucker et al. (2011) interpreted their (and Peters et al.'s, 2008) nonsignificant sleep parameter—memory performance correlations to mean that "yet-unidentified age-related changes in the sleep-wake cycle may limit ability to observe the effect of specific sleep characteristics on motor skill enhancement" (p. 6). Their claim is intriguing, but difficult to disprove (due to the vagueness of the proposed limitation), and a reasonable alternative interpretation of the literature is that the relationship between *sleep physiology*

and cognition has broken, weakened, or otherwise changed in older age. This idea dovetails with Spiegel, Koberle, and Allen's (1986) idea that "[deep sleep] changes its functional significance during ontogenesis…to a functionally meaningless remnant in old age" (p. 77). Three lines of research—rodent research, sleep and vigilance research, and sleep deprivation research—provide evidence that the link between sleep and cognition diminishes with increasing age.

Two studies from the rodent literature suggested that the sleep—memory link might weaken or change with increasing age. Gerrard, Burke, McNaughton, and Barnes (2008) found that the hippocampal memory reactivation ("replay") normally observed in rodent models (e.g., Wilson & McNaughton, 1994) is reduced or eliminated in older rats. In addition, Buechel, Popovic, Searcy, Porter, Thibault, and Blalock (2011) examined performance on the Morris Water Maze task in older rats (Fischer 344 rat model of aging). These older rats demonstrated either no significant correlation between deep sleep and memory performance or even a *negative* correlation whereby more deep sleep was associated with worse memory performance. The Gerrard et al. and Buechel et al. studies demonstrated that the relationship between sleep and memory might differ between younger and older rodents.

Research on deep sleep and vigilance in humans provides further evidence for the possible erosion of the sleep—cognition link in older adults. In younger adults, increasing amounts of deep sleep are related to reductions in daytime fatigue, as measured by the ability to sustain attention on vigilance tasks. For example, Jurado, Luna-Villegas, and Buela-Casal (1989) observed that poorer performance (slower reaction times) on a vigilance task was associated with less deep sleep the prior night. In contrast, Crenshaw

and Edinger (1999) reported no such correlation in a group of healthy older adults. These findings recently led Pace-Schott and Spencer (2011) to theorize that "the relationship between [deep sleep] and cognitive performance may weaken as the amount of [deep sleep] diminishes with aging" (p. 82; cf. Spiegel et al., 1986).

The sleep deprivation and aging literature provides a third line of evidence that the relationship between sleep and cognition might change with increasing age. In this literature, younger and older adults are either partially or completely deprived of one or more nights of sleep and then they take cognitive tests (usually the psychomotor vigilance test) following various lengths of time spent awake. Whereas younger adults are usually dramatically impaired by sleep deprivation, older adults either show no effects of sleep deprivation or lesser effects than younger adults (Adam, Retey, Khatami, & Landolt, 2006; Bonnet, 1989; Philip et al., 2004; Stenuit & Kerkhofs, 2005; Webb, 1985; Webb & Levey, 1982). One potential concern with this literature is that older adults may already show large cognitive impairments and further impairments would therefore be impossible to observe due to floor effects. While this concern is valid for some of the early sleep deprivation studies (e.g., Bonnet & Rosa, 1987), floor effects do not limit the results of other studies in which baseline performance is similar between age groups and older adults end up performing better than their younger counterparts following sleep deprivation (Duffy, Willson, Wang, & Czeisler, 2009; Stenuit & Kerkhofs, 2005). These studies illustrate that sleep is closely related to cognition in younger adults but less so in older adults.

Sleep and Episodic Memory Consolidation in Older Adults

The question of whether sleep is functionally related to episodic memory consolidation in older adults has rarely been investigated. There are only a few papers examining sleep and episodic memory in an older adult population (Hornung, Regen, Danker-Hopfe, Schredl, & Heuser, 2007; Mazzoni et al., 1999; Schredl, Weber, Leins, & Heuser, 2001), and only three published studies comparing episodic memory between age groups across sleep delays (Aly & Moscovitch, 2010; Backhaus et al., 2007; Rauchs et al., 2008).

Early sleep, memory, and aging studies attempted to correlate sleep physiology measures with word pair recall *within* an older adult sample. These studies tended to find no correlations between sleep parameters and memory recall. Though Mazzoni et al. (1999) reported a significant correlation between word recall and total number of NREM/REM cycles (perhaps indicating preserved sleep architecture), they did not observe any significant correlations between memory recall and specific sleep stages (e.g., deep sleep). Further, Schredl et al. (2001) used a pharmacological manipulation to augment REM sleep in older adults (n = 8) and observed that the degree of increase in REM sleep was positively associated with later cued recall performance; however, Hornung et al. (2007) used a much larger sample size (n = 107) and found that pharmacologically boosting or minimizing REM sleep had no effect on recall of word pairs in an older adult group. Thus, sleep and memory might not be intimately interwoven in older adults.

More recent studies have investigated sleep, memory, and aging associations cross-sectionally. Backhaus et al. (2007) compared younger adults (18-25 years old) and

middle-aged adults (48-55 years old) on cued recall of word pairs following sleep delays, and they reported that cued recall performance and deep sleep declined with increasing age. Importantly, the cued recall declines were mediated by deep sleep declines such that time spent in deep sleep correlated positively with cued recall performance, and controlling for age-related changes in deep sleep eliminated the age-related cued recall difference. In addition, middle-aged adults with high levels of deep sleep demonstrated evidence for episodic memory consolidation. These results suggest that sleep—memory processes might begin to decline in middle age but that the functional relationship between deep sleep and episodic memory might still be preserved in *middle*-aged adults.

Rauchs et al. (2007) gave younger adults, healthy older adults, and Alzheimer's disease patients a very strong encoding task (semantic encoding strategy, frequent tests) and a less-strong encoding task (single reading of a story). Encoding took place at night and participants were tested the next morning. They reported ceiling-level performance on the very strong encoding task for the younger and healthy older adults (100% versus 99%), but a reduction in performance for the Alzheimer's disease patients (68%). For the less-strong encoding task, there was a significant difference between the younger adults (72%), healthy older adults (59%), and Alzheimer's disease patients (floor levels of performance). Although the authors used EEG to collect sleep architecture data, they did not report any correlations with the memory measures in the younger adults or the healthy older adults, citing ceiling effects as the reason. Rauchs et al.'s results suggested that sleep-dependent episodic memory consolidation might decline in healthy older adults, at least for less-strong encoding memory tasks.

Aly and Moscovitch (2010) compared recall in younger and older adults following wake versus sleep delays. In the first session (morning or evening), the experimenter read stories (WAIS III) to participants over the phone and gave them an immediate test. Older adults who could not recall sufficient details of the story were read the story again. After a sleep or wake delay, participants were asked to recall the stories. They found that there was a roughly equivalent sleep-related benefit to story recall for both younger and older adults (i.e., there was no sleep/wake by age interaction, but note that Cohen's *d* for the sleep/wake comparison was numerically larger for the younger adults—1.48—than for the older adults—1.14). The experimenters also assessed for "personal memories" (e.g., Who was the last person you spoke to the previous night? What was he/she wearing?). For this measure, the sleep-related benefit was significantly reduced in the older adults relative to the younger adults. Though Aly and Moscovitch's experiment was the first to compare episodic memory following sleep versus wake delays in younger and older adults, the study was not conducted in a controlled environment and measures of sleep physiology were not recorded. Thus, the quantity and quality of sleep-dependent memory consolidation in older adults is still unknown.

The Present Research

The most compelling sleep and memory consolidation studies have employed experimental manipulations and collected measures of sleep physiology, but these procedures have not been used together in a sleep, aging, and episodic memory study. In addition to manipulating sleep versus wake delays, one experimental procedure that previous researchers (Ellenbogen, Hulbert, Stickgold, Dinges, & Thompson-Schill, 2006;

Ellenbogen, Hulbert, Jiang, & Stickgold, 2009) have suggested would lend itself well to behavioral detection of consolidation processes involves the classic *AB′/AC′* list-learning paradigm (Barnes & Underwood, 1959). In this paradigm, participants learn a list of paired word associates (e.g., Train—Black) called the *AB* list (or *AB′* list). Then, participants may be required to learn an *AC′* list (e.g., Train—Keyboard), which is designed to interfere with memory of the previous word pairs. Note that the ′ symbol refers to pairs that are interfering (*AC′*) or receiving specific interference (*AB′*). On a final cued recall test (e.g, Train— ____?), participants typically show greater forgetting of *AB′* pairs which have been followed by *AC′* pairs than *AB* pairs which are not followed by interfering material (for a review, see Crowder, 1976).

The *AB′/AC′* paradigm has been employed by sleep researchers to illustrate that sleep might promote memory consolidation (Drosopoulos, Schulze, Fischer, & Born, 2007; Ekstrand, 1967; Ellenbogen et al., 2006; Ellenbogen et al., 2009). For example, Ellenbogen and colleagues (2006; 2009) had participants learn an *AB′* list or *AB* list (of word pairs), and then following a sleep or wake delay, half of the participants learned an *AC′* list whereas the other half did not learn the interfering list. Ellenbogen et al. argued that without consolidation the *AC′* word pairs should greatly interfere with recall of the *AB′* pairs. But, if the *AB′* pairs were consolidated, then recall of those words should be similar to recall of *AB* pairs (i.e., pairs which were not followed by interference learning). As illustrated in Figure 2, Ellenbogen et al. found a pronounced sleep benefit for *AB′* words (i.e., in the condition that also learned the *AC′* pairs). Furthermore, whereas the wake group showed high levels of *AB′* forgetting following *AC′* learning (relative to the no-interference condition), such forgetting was minimal in the sleep group. Ellenbogen et

al. concluded that these results were consistent with the account that sleep promotes memory consolidation.

One goal of the present research was to extend Ellenbogen et al.'s (2006) paradigm to compare younger and older adult groups. Because this interference paradigm has previously produced large effect sizes, I expected there to be sufficient range from which to detect possible age-related declines in consolidation. I modified their interference manipulation to be conducted within subjects so that data collection would be more efficient. In addition, I extended their paradigm by employing actigraphy (to identify participants who napped excessively) and included a cued multiple-choice recognition test following the cued recall test. Some research has suggested that smaller sleep benefits obtain when a recognition test, rather than a recall test, is employed (for a review, see Diekelmann, Wilhelm, & Born, 2009), but this pattern has not yet been investigated in older adults. Most importantly, I collected measures of sleep physiology by using the Zeo, Inc., home monitoring device, which distinguishes between wake, light sleep, deep sleep, and REM sleep. The Zeo sleep-stage scoring was recently demonstrated to agree highly (according to standard definitions; Landis & Koch, 1977) with polysomnography sleep scoring across an adult population that ranged in age from 19 to 60 (Shambroom, Fabregas, & Johnstone, in press). If there are age-related differences in memory retention following sleep then the measures of sleep physiology might help pinpoint why there are age-related differences. Thus, I used both experimental and correlational approaches to test whether age-related differences in consolidation processes (during sleep) exist.

One possible concern when comparing younger and older adults across sleep and wake delays is age-related circadian rhythm differences. Though much of the research on age-related circadian rhythm changes has been done using animal models, empirical research with humans documents age-related changes in the circadian rhythms of body temperature, sleep—wake times, various hormones, as well as other changes (for a review, see Bliwise, 1993). Despite clear evidence for some physiological changes in circadian rhythms from younger to older adults, there are at least three empirical findings that suggest that circadian influences (caused by morning versus night testing) would not be a critical moderator of human cognitive performance, or at least not disproportionately impair the older adults. First, morning versus evening testing typically produces no significant differences in cognitive performance in younger adult sleep studies (e.g., Dumay & Gaskell, 2007; Ellenbogen et al., 2006; Payne, Stickgold, Swanberg, & Kensinger, 2008; Scullin & McDaniel, 2010). Second, though early work (May, Hasher, & Stolzfus, 1993) found that time-of-testing was important in determining whether age-differences are observed in cognitive tests, follow-up work (including my own unpublished data) has failed to replicate this finding (Brown, Goddard, Lahar, & Mosley, 1999). Third, forced circadian desynchrony studies (e.g., Silva, Wang, Ronda, Wyatt, & Duffy, 2010) have found that shifting the timing of the wake-sleep cycle leads to greater cognitive impairments in younger adults than in older adults.

Though there is ample evidence that age-related circadian rhythm changes should not undermine the present investigation of age-related changes in memory consolidation, I took several approaches to examine/control for circadian influences in the younger and older adult participants. First, during recruitment, participants were scheduled to

participate during their self-reported optimal time within a 7-10 AM/PM range. Second, participants completed the Morningness-Eveningness Questionnaire (Horne & Ostberg, 1976) so that I could assess the relationship between optimal time of day and performance on learning and memory recall. Third, I compared learning phase performance between the morning learning sessions and the evening learning sessions.

In the current experiment, in addition to the 12-hr wake and 12-hr sleep groups, I used a 24-hour, PM-to-PM group as utilized by Ellenbogen et al. (2006). Ellenbogen et al. hypothesized that because the 24-hour retention interval contained sleep, the results of the 24-hour group should be similar to those in the 12-hour sleep group if the observed memory benefits reflected consolidation processes. In contrast, classic interference theory (Jenkins & Dallenbach, 1924) anticipates memory performance to be worse in a 24-hr sleep group than a 12-hr wake group because the 24-hr group has spent more time awake (i.e., been subjected to greater daytime interference). Ellenbogen et al. found similar levels of AC' recall between the 24-hr sleep (71%) and 12-hr sleep (76%) groups. Consistent with this finding, I predicted that performance in the 24-hr sleep group would fall in between the 12-hr sleep and 12-hr wake levels, but that performance levels would be closer to the sleep group. Furthermore, because the 24-hour and 12-hour sleep groups both contained nighttime sleep, these conditions may be collapsed to increase power for detecting significant correlations between sleep measures and memory performance.

Based upon literatures suggesting a relationship between deep sleep and episodic memory retention (for reviews see Diekelmann & Born, 2010; Walker, 2009), as well as age-related declines in deep sleep, I predicted that older adults would demonstrate less evidence for memory consolidation than the younger adults, and that this would be

observed in levels of memory retention across delay conditions. If deep sleep is still functionally related to memory in older adults then there should be a positive correlation between deep sleep and memory retention (e.g., Buckley & Schatzberg, 2005); if the sleep—memory relationship is weakened or changed in older adults then deep sleep and memory should not be related (e.g., Spiegel et al., 1986; Pace-Schott & Spencer, 2011).

Method

Participants

I recruited fifty-seven younger adults (M_{Age} = 19.73; *SD* = 1.09; Range: 18-22; 55.4% females) and forty-one older adults (M_{Age} = 70.66; *SD* = 5.41; Range: 60-84; 70.7% females), which is comparable to, if not larger than, the typical sample size employed in most sleep, memory, and aging studies (cf. Peters et al., 2008; Rauchs et al., 2008; Tucker et al., 2011). The sample size across conditions can be viewed in Table 1. Younger adults were Washington University undergraduates and older adults were community-dwelling individuals who are part of the Psychology Department's Older Adult Participant Pool. Participants were pre-screened for age (18-30 for younger adults, 60-85 for older adults), history of taking medications that are known to affect sleep architecture (benzodiazepines, melatonin, antidepressants, antipsychotics, nicotine, and any sleep medication; Conn & Madan, 2006), and history of diagnosed sleep disorders (e.g., restless legs syndrome), neurodegenerative disorders (e.g., Alzheimer's disease; Rauchs et al., 2008), or mental health disorders (e.g., depression or anxiety; Wolkove, Elkholy, Baltzan, & Palayew, 2007). Three younger adults did not complete the second experimental session (e.g., due to a winter ice storm and campus closure); their (Session 1) data will not be included in any analyses.

Recruitment

The younger adults were recruited using an online study advertisement (Washington University's Psychology Department's Experimetrix.com scheduling system). The pre-screening (age, medications, disorders/diseases) was done via email. Younger adults who met the above inclusion criteria (i.e., they do not have any of the above histories) were randomly assigned to the 12-hr wake, 12-hr sleep, or 24-hr sleep conditions and the experimenter scheduled them to participate at the corresponding time.

Approximately half of the older adult participants in the present study filled out a paper pre-screening form (age, medications, disorder/disease history) after completing a different study in the laboratory. If they met inclusion criteria then the experimenter called to recruit them. The remaining older adult participants were determined to be eligible and recruited by "cold calling" them. Prior to calling each older adult the experimenter randomly determined the condition for which the individual would be recruited (12-hr wake, 12-hr sleep, 24-hr sleep). In a few circumstances (approximately 3-5), the older adult had a schedule conflict such that they could not participant in the randomly assigned condition. These individuals were still scheduled for a time (and condition) for which they could participate.

Consistent with common recruitment methodology in the sleep literature, participants were instructed not to consume alcohol or to take naps during the interval in which they were participating in the experiment.

Design

Younger and older adults were recruited and then, with few exceptions (see above), they were randomly assigned to one of three groups: 12-hour wake, 12-hour sleep, and 24-hour (PM-PM) sleep groups. I manipulated word pair type in the paired associative learning tasks (*AB* pairs, *AB′* pairs, *AC′* pairs, *DE* pairs) within subjects.

Materials

The *AB′*/*AC′* learning paradigm is a classic paradigm in psychology (Barnes & Underwood, 1959). Word lists were generated from a lexicon database (e.g., Balota et al., 2007; and also the MRC Psycholinguistic Database: Coltheart, 1981; Wilson, 1988) according to specifications described by Ellenbogen et al. (2006). Two-syllable nouns were drawn from the lexicon database and randomly assigned to word sets, with the exception that the sets had to be similar (i.e., not statistically different) in average word length, imageability, frequency, and concreteness. Words were paired together randomly, with the exception that obvious semantic association between the paired words was avoided; the goal was to have unrelated word pairs. Each word pair set contained 10 *AB* pairs (i.e., Session 1 pairs that were *not* followed by *AC′* pairs in Session 2), 10 *AB′* pairs (i.e., Session 1 pairs that were followed by *AC′* pairs in Session 2), 10 *AC′* pairs (Session 2 pairs that used an *A*-word from Session 1), and 10 *DE* pairs (Session 2 pairs that were unrelated to other pairs). I created 8 different word pair sets (e.g., counterbalancing which word served as *A* versus *B* versus *C* across participants) so that any observed results could be generalized beyond a particular set of words.

The influence of optimal time of day and typical sleep habits was examined by administering the Morningness-Eveningness Questionnaire (Horne & Ostberg, 1976) and the Pittsburg Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989),

respectively. The Pittsburg Sleep Quality Index was considered to be useful in establishing that the experimental groups did not differ in their sleep habits in the weeks preceding the experiment.

Sleep measurement

To measure sleep architecture I used a wireless home sleep-stage monitoring device (Zeo, Inc.). This system includes a clock base station and a headband that is worn on the forehead (at approximately the Fp1-Fp2 locations). The size of the headband is adjusted to each individual so that it is tight but not uncomfortable. The headband includes sensors that collect electrophysiological data from a single channel, pre-process the data (amplify signal and filter noise), and transmit the data wirelessly to the clock base station. A microprocessor in the base station then uses the signal to calculate sleep stages in real time, in accordance with standard Rechtschaffen and Kales (1968) polysomnography scoring norms. It produces four possible stages: light sleep (Stages 1 and 2 combined), deep sleep (Stages 3 and 4 combined), REM sleep, and wakefulness. For full details of this device, see Shambroom, Fabregas, and Johnstone (in press).

Polysomnography (PSG) is considered the gold standard for distinguishing sleep stages but it is not always cost-effective and its use requires participants to sleep in the laboratory rather than at home, which can alter sleep efficiency (Bruyneel et al., in press). In contrast, the Zeo is inexpensive, can be used easily at home, and a recent validation study that used adults ranging in age from 19-60 demonstrated high agreement between Zeo and PSG in sleep stage scoring (light sleep, deep sleep, and REM sleep) (Shambroom et al., in press). This study included author affiliates of Zeo, Inc., but preliminary results from an independent lab also suggest that Zeo is a good indicator of

sleep stages, especially deep sleep (Dr. Bryce Mandler, personal communication, August 24, 2010).

I also employed actigraphy (Actiwatch 2, Philips Respironics, Inc.), which is regularly used in sleep studies. Actiwatches use accelerometer technology to track motor activity and they also detect amount and duration of ambient white light luminance so as to measure light-on/light-off periods. These motor and light measures allow for reliable discrimination of sleep versus wake states (Littner et al., 2002; Van de Water, Holmes, & Hurley, in press). The advantage of actiwatches is that they can be worn on the wrist continuously throughout the day and are therefore convenient measures of napping, total sleep time, sleep latency, and wake after sleep onset. Participants who napped extensively (determined *a priori* to be naps lasting greater than 1 hour) were excluded from the study. Two younger adult participants (no older adults) in the 24-hr sleep condition met this exclusion criterion. Actigraphy data also suggested that short (<1 hour) naps occurred in six younger adults ($n_{12\text{-hr wake}} = 2$, $n_{24\text{-hr sleep}} = 4$) and one older adult (wake condition) but these naps did not meet the exclusion criterion established during the research proposal.

Procedure

The first experimental session took place in the morning (7am-10am) or in the evening (7pm-10pm). The morning/evening ranges were larger than normal to minimize the influence of circadian rhythm changes: older adults typically wake up earlier and go to bed earlier than younger adults (Ancoli-Israel, 2005; Bliwise, 1993). During recruitment, participants were asked to come in at their most optimal time of day within the 7-10 am/pm range.

Following reading and signing an informed consent sheet, participants were given the actiwatches and asked to wear them until they returned for the second experimental session. Then participants were asked to fill out two questionnaires: the Morningness-Eveningness Questionnaire which asks 19 questions regarding optimal time of day (e.g., "At what time of the day do you think that you reach your "feeling best" peak?") and the Pittsburg Sleep Quality Index which includes 10 questions that pertain to typical sleep habits (e.g., "During the past month, what time have you usually gone to bed at night?).

The experimenter next loaded an E-Prime 2.0 program on the computer to administer the *AB*/ *AB′* learning procedure. Participants were instructed that they would see pairs of words on the computer screen and that they should try to remember them for a later test. They were also instructed that they would sometimes have to solve simple math problems. After reading these instructions the participant began the study phase. During the study phase, participants saw word pairs on the computer screen, one-at-a-time for 7 seconds per pair (presentation was randomized each cycle). After studying all 20 pairs—10 *AB* pairs and 10 *AB′* pairs—the participants were asked to solve simple math problems (Is 7 X 3 = 23? Press Y for yes and N for no). The math phase lasted two minutes and was included to act as a delay between study and test phases (i.e., so that participants would have to recall the pairs from secondary memory rather than rehearsing the pairs in short-term memory).

Following the math phase, participants were given a cued recall test in which they were provided with the *A* word and had to type in the associated *B* (*B′*) word (e.g., Channel – _____?). If the participant recalled less than 80% of the pairs (i.e., 15 or fewer) then the program returned to the study phase. The study-math-recall cycle repeated until

the participant recalled at least 80% of the pairs correctly in a given recall phase. If 30 minutes of the learning procedure elapsed without the participant reaching the 80% learning criterion then the experimenter terminated the program once they concluded the current cycle (i.e., to avoid exceeding time limits approved by the Institutional Review Board). Because I aimed to assess *retention* of learned word pairs and such a measure was still possible in these participants (i.e., examine final recall of word pairs after controlling for number of pairs initially learned), these participants were included in the analyses. After the learning phase, participants in the 12-hr wake condition were excused whereas those in the sleep conditions were given the Zeo device and instructed how to use it. The experimenter fit the Zeo headband size to participants and provided them with a printed instruction sheet in case they forgot any of the verbal instructions.

The second experimental session occurred 12 or 24 hours later. When participants returned they were seated at the same computer station as before and they underwent another learning phase that was identical in structure to the Session 1 learning phase. However, in the Session 2 learning phase, the word pairs consisted of 10 AC' pairs and 10 *DE* pairs. After completing the Session 2 learning phase, participants were required to take a 5-minute break during which they could use the restroom, drink water, rest, etc. Then, participants were given a final cued recall test (see Appendix A for one example) that followed Barnes and Underwood's (1959) modified modified free recall (MMFR) procedure. The *A* words and *D* words were provided to the participants who were given space to write whichever word or words were previously associated (to the *A* or *D* cue word). This final test was provided on paper and was untimed (see Tucker et al., 2011, for evidence that sleep effects may not be observed in older adults immediately). Recall

of Session 2 pairs was considered to be an additional measure of learning, though ceiling effects might limit such analyses because participants were expected to have just learned these lists to an 80% criterion.

Following the cued recall test, participants were given a cued multiple-choice recognition test of the Session 1 pairs (see Appendix B for one example). The *A* words were paired on the left side of a sheet of paper and participants were asked to circle which of four words appearing to the right of the cue word was originally paired with it. The *B* (or *B′*) word appeared amongst 3 new lure words which were semantically related to the *B* (or *B′*) word. Semantically related lures were included to attempt to get performance off of ceiling.

Results

An alpha of .05 was set *a priori* for all statistical analyses. P values between .05 and .10 were considered marginally significant and would be treated with some caution.

Treatment of Missing Zeo Data

Thirteen participants (nine younger adults, four older adults) had full behavioral datasets but missing Zeo sleep stage data. The primary reason for missing data was that if the headband is not placed in the Zeo station dock before unplugging the clock device then no data is saved. This bug was discovered to be the source of missing data approximately ¼ of the way through data collection after doing troubleshooting with Zeo, Inc. staff. Afterward, I emphasized to participants to make sure to dock the headband device in the morning and I also taped a highlighted reminder on the Zeo clock base station. Though the rate of missing data decreased, it was not eliminated, and it is unclear (to Zeo, Inc., staff) why additional data are missing; potential reasons include a poor

wireless connection between the headband and base station, SD card malfunction, and battery failure. Given the presence of missing data, and the interest in relating behavioral data to sleep stage data, when reporting the behavioral data I separately conducted inclusive (i.e., all participants) and exclusive (i.e., those who have complete Zeo datasets) analyses.

Questionnaire Data

Table 1 lists descriptive data for the Pittsburg Sleep Quality Index, Morningness-Eveningness Questionnaire, and chronological age across age groups and conditions. Chronological age did not significantly differ across conditions *within* the older adult group regardless of whether all subjects were included in the analysis (F (2, 41) = 2.17, MSE = 27.67) or the sample was restricted to those with Zeo data (F (2, 37) = 2.14, MSE = 26.25). Likewise, there was no condition effect on chronological age within the younger adult samples (Fs < 1).

For the sleep quality score (higher scores denote worse habitual sleep quality) and morningness-eveningness score (higher scores denote morning preferences), I conducted separate 2 x 3 analyses of variance (ANOVAs) that included the between subjects variables of age group (younger, older) and condition (12-hr wake, 12-hr sleep, 24-hr sleep). When considering all subjects (i.e., regardless of whether they had missing Zeo data), there were no significant main effects or interactions for sleep quality index scores (largest F (1, 93) = 3.42, MSE = 9.20, p = .068 for age main effect); when restricting the sample to only those with complete (Zeo) data, the older adults demonstrated significantly worse subjective sleep quality than the younger adults, F (1, 81) = 4.06,

MSE = 8.90, $p = .048$ (next largest F (2, 81) = 1.37, *MSE* = 8.90, for the interaction). The lack of a condition main effect or age group by condition interaction suggests that participants (i.e., across delay conditions) maintained similar levels of sleep quality in the weeks prior to the experiment.

For the Morningness-Eveningness Questionnaire, both younger (M = 42.33) and older adults' (M = 56.27) overall means fell within the "neutral" range (42-58), though the higher scores in the older adult group suggested a greater tendency toward morning preferences. The age group difference was statistically significant regardless of whether all subjects were included, F (1, 93) = 50.23, *MSE* = 87.21, $p < .001$, or if participants who had missing Zeo data were excluded, F (1, 81) = 42.78, *MSE* = 90.06, $p < .001$. Neither the condition main effect nor the condition by age group interaction was significant (largest F (2, 93) = 2.11).

Sleep Parameters

Table 2 presents Zeo and actigraphy means and inferential statistics for younger adults and older adults (collapsed across 12-hr and 24-hr sleep conditions). The results were consistent with several general findings in the sleep and aging literature (Bliwise, 1993; Ohayon et al., 2004): older adults spent a greater proportion of their sleep in light sleep than younger adults, but there was a substantial age-related reduction in deep sleep. Other expected outcomes included an age-related increase in the number of awakenings from sleep as well as greater time spent awake during normal sleeping hours (Table 2; also see Bliwise, 1993, for review). No significant age differences were observed for

REM sleep. As noted by Bliwise (1993), there is considerable variability in the REM sleep and aging literature, with many studies finding no age differences in REM sleep.

Table 3 separates the Zeo and actigraphy data for 12-hr and 24-hr sleep conditions and across younger adults and older adults. These results were highly congruent with the collapsed data (above), with only a few minor discrepancies which I will highlight here. First, whereas percent of time spent in light sleep showed a significant age-related increase in the 12-hr condition, this increase was not significant in the 24-hr condition. In addition, though REM sleep showed no declines in the collapsed analysis above or in the 24-hr condition, there was a significant age-related decline in the 12-hr group (see Bliwise, 1993, for discussion of age-related variability in REM sleep). The third discrepancy was that a significant age-related decrease in total sleep time was observed in the 12-hr condition but not in the 24-hr condition. The final discrepancy was that every measure of waking time at night was significant except that the actigraphy-measured wake after sleep onset measure did not reach statistical significance in the 24-hr group. Importantly, there were no discrepancies in the age-related impairment in deep sleep.

Another potentially interesting question was whether sleep differed between the 12-hr and 24-hr conditions. One plausible prediction is that individuals in the 24-hr condition may have slept longer because they did not have to wake up to come to the laboratory in the morning. The only significant differences between the 12-hr and 24-hr conditions (collapsed across age groups) were for percentage of sleeping hours spent awake, t (52) = 2.44, and for actigraphy-measured total sleep time, t (63) = 2.32 (marginally significant effects for Zeo-measured total sleep time, t (52) = 1.78, p = .081, REM minutes, t (52) = 1.86, p = .068, and wake after sleep onset, t (52) = 1.92, p = .060).

Participants in the 24-hr group slept longer ($M_{\text{Total Sleep}}$ = 383.71 min) and spent a lower proportion of their nighttime hours awake ($M_{\text{Wake \%}}$ = .04) than participants in the 12-hr group ($M_{\text{Total Sleep}}$ = 325.47 min; $M_{\text{Wake \%}}$ = .13). Though total sleep time differed between the groups, most critically, the 12-hr and 24-hr sleep groups were similar in percent of deep sleep (both *M*s = .21; $t < 1$).

AB′/AC′ Interference Manipulation Check

The *AB′/AC′* interference paradigm typically produces robust effects (Barnes & Underwood, 1959). The hypothesis posed in the introduction section, which followed from Ellenbogen et al.'s (2006; 2009) work, was that final cued recall of *AB′* pairs (i.e., pairs for which *AC′* pairs were subsequently learned) would be worse than recall of *AB* pairs (i.e., no subsequent *specific* interference), and that such effects would be particularly potent in the 12-hr wake condition. Table 4 presents the recall means across word type and condition. Surprisingly, when conducting the 2 (*AB*, *AB′*) x 2 (younger, older) x 3 (12-hr wake, 12-hr sleep, 24-hr sleep) ANOVA with all subjects included, word pair type failed to reach conventional levels of significance (F (1, 87) = 3.01, MSE = 2.39, p = .087) and word pair type did not interact significantly with the other variables (largest F = 1.80 for the word pair type by condition interaction).

Because the theoretical interest was not in general ability to recall, but in *retention* of words learned during Session 1, a more theoretically precise (and sensitive) test was to run the above analysis after controlling for the number of *AB* and *AB′* pairs learned (i.e., the number of pairs correctly recalled during the final Session 1 learning cycle). Yet, this analysis of covariance (ANCOVA) demonstrated that the word pair type main effect was

still not significant, $F < 1$ (see Table 4). The above analyses produced similar, but even more dampened, results when they were restricted to the younger adult group, older adult group, or to only participants who had full Zeo (and behavioral) datasets.

Because Ellenbogen et al. (2006) demonstrated the largest retroactive interference effects in their 12-hr wake group, I next restricted the analyses to the 12-hr wake condition and conducted an ANOVA and an ANCOVA (controlling for Session 1 final learning cycle recall) that included the within subjects variable of word pair type (*AB*, *AB′*) and the between subjects variable of age group (younger, older). Both analyses failed to produce a significant main effect of word pair type or interaction with age group (all *F*s < 1).

Another idea is that retroactive interference might be evidenced by a negative correlation between final recall of *AB* and *AB′* items or a negative correlation between final recall of *AB′* and *AC′* items (i.e., if retroactive interference is dependent on how well the interfering information was learned; e.g., see Crowder, 1976; Postman & Underwood, 1973). But, both correlations were *positive* and significant in the younger adults ($r_{AB—AB'}$ (52) =.428, $p = .002$; $r_{AB'-AC'} = .284$, $p = .04$) and in the older adults ($r_{AB—AB'}$ (41) = .578, $p < .001$; $r_{AB'-AC'}$ (41) = .428, $p = .005$). The above correlations were also conducted after restricting the analysis to only participants with full (Zeo + behavioral) data sets, and the correlations remained positive and significant (expect only marginally significant for the $AB'-AC'$ correlation in the younger adults).

The one remaining effect that the *AB′*/*AC′* manipulation may have had was to produce *proactive* interference—originally learning *AB′* pairs might subsequently impair the ability to learn and recall the *AC′* pairs (relative to *DE* words). But, learning phase

performance was similar for *AC′* pairs and *DE* pairs (i.e., no significant word-pair-type differences in final learning cycle, $F < 1$) and final cued recall of the *AC′* pairs also did not significantly differ from final recall of *DE* pairs ($F < 1$). These collective results converge on the conclusion that the *AB′/AC′* manipulation was not effective in the present research. Though surprising, the advantage moving forward is that because word pair type is not an informative variable it can be collapsed to provide a potentially more sensitive measure (twice the number of test items) of associative learning and recall.

Learning Phases

During both sessions, all younger adults were able to reach the learning criterion of 80% or more word pairs correctly recalled. However, the learning task proved challenging for older adult participants and nearly 1/2 of them failed to reach the learning criterion in Session 1 ($n_{12\text{-hr wake}} = 9$, $n_{12\text{-hr sleep}} = 5$, $n_{24\text{-hr sleep}} = 6$) and approximately 1/3 of them failed to reach the learning criterion in Session 2 ($n_{12\text{-hr wake}} = 5$, $n_{12\text{-hr sleep}} = 4$, $n_{24\text{-hr sleep}} = 6$). The learning procedure was terminated for these participants after approximately 30 minutes.

Encoding performance on the list learning procedures during Sessions 1 and 2 (see Table 5) was assessed as the number of learning cycle (study-math-recall) repetitions—which is unfortunately a flawed measure because many participants never reached the 80% learning criterion—as well as the number of pairs correctly recalled during the final learning cycle. For each variable I conducted a 2 x 3 ANOVA in which age group (younger, older) and condition (12-hr wake, 12-hr sleep, 24-hr sleep) varied between subjects.

I first examined the Session 1 learning phase in all subjects (i.e., regardless of whether they had Zeo data). As anticipated by the encoding deficit hypothesis of cognitive aging (e.g., Naveh-Benjamin, 2000), the older adults had to repeat the learning cycles a significantly greater number of times than the younger adults, F (1, 87) = 41.47, MSE = 1.19, $p < .001$, and they also recalled significantly fewer word pairs on the final learning cycle, F (1, 87) = 44.42, MSE = 9.91, $p < .001$ (see Table 5). Whereas there was no condition main effect for the number of word pairs recalled ($F < 1$), there was a significant condition effect on the number of cycles completed, F (2, 87) = 3.51, $p = .034$. But, follow-up tests demonstrated no condition main effect in the younger adults ($F < 1$) or in the older adults (F (2, 38) = 2.48, $p = .10$). Importantly, this result was in the opposite direction of the age-related circadian rhythm change prediction (see Table 5); learning appeared to be slightly easier for the older adults in the evening than in the morning. Moreover, the lack of a significant age group by condition interaction for either measure of Session 1 learning (both Fs < 1) was inconsistent with the idea that age-related circadian shifts would impact cognitive performance. The above statistics are maintained when restricting the sample to those who have Zeo data.

I next examined Session 2 learning-phase performance (all participants included). The results were highly similar to the Session 1 learning results and the means and standard deviations are presented in Table 5. For the dependent variable of number of pairs correctly recalled during the last Session 2 learning cycle, there was a main effect of age group, F (1, 87) = 30.77, MSE = 10.48, $p < .001$ (all other Fs < 1). For the dependent variable of Session 2 learning cycles completed, there was a significant age group main effect, F (1, 87) = 47.38, MSE = 1.10, $p < .001$, and a significant condition main effect, F

(2, 87) = 3.78, p = .027, but no interaction (F < 1). However, the condition main effect was not significant when the analysis was restricted to the younger adult group (F (2, 49) = 1.48, MSE = 0.77), the older adult group (F (2, 38) = 2.33, MSE = 1.53, p = .11), or when excluding participants who did not have full Zeo datasets (F (2, 75) = 2.78, MSE = 1.18, p = .068). Further, because differences across conditions were not observed for number of pairs correctly recalled during the final learning cycle, the above effect should probably be treated with some caution.

One possible prediction is that sleep could facilitate encoding of word pairs during the Session 2 learning phase (e.g., restoring learning efficiency; Tononi & Cirelli, 2003). To examine whether sleep facilitated learning during Session 2 beyond what would be expected of baseline learning ability, I conducted a 2 (younger, older) x 3 (12-hr wake, 12-hr, sleep, 24-hr sleep) ANCOVA for the dependent measure of Session 2 cycles completed, after controlling for Session 1 cycles completed. There were no significant effects (largest F (2, 86) = 1.73, MSE = 0.73, p = .18, for the condition main effect). In addition, I repeated the above ANCOVA but substituted the dependent measure of number of pairs correctly recalled in the final Session 2 learning cycle (and controlled for the corresponding Session 1 variable). Neither the condition main effect (F (2, 86) = 1.01, MSE = 4.61) or the condition by age group interaction (F < 1) were significant. These analyses produced similar results when restricting the sample to only those participants with Zeo data.

Final Cued Recall and Cued Recognition Tests

Table 6 and Table 7 present the means (proportion correct) for final cued recognition and final cued recall, respectively, for Session 1 and Session 2 word pairs. The analyses in this section were consistent regardless of whether analyzing data from all subjects or just those who had Zeo data (with one exception for Session 2 recall, noted below), and so to be more fluent with the next section on sleep—memory correlations I will just present the statistics for those with both behavioral and Zeo sleep data.

Despite using semantically related lures in the cued recognition test, performance approached ceiling levels in the younger adults (M = .98), and therefore statistical analyses across conditions were uninterpretable in this group (see Table 6). However, performance was off of ceiling in the older adults (M = .82), and this age difference in recognition test performance was captured by a significant main effect of age group, F (2, 81) = 16.09, MSE = .040, p < .001. Interestingly, the condition main effect was not significant in the older adult group (F < 1), suggesting that sleep might not benefit memory in older adults.

I next examined final cued recall, and those means can be viewed in Table 7. Session 1 word pair retention was assessed by conducting a 2 x 3 ANCOVA that included the between subjects variables of age group (younger, older) and condition (12-hr wake, 12-hr sleep, 24-hr sleep) while controlling for initial learning of those items (i.e., number correctly recalled during final Session 1 learning cycle). There was a significant age group main effect, F (1, 81) = 11.61, MSE = .022, p = .001, such that the younger adults retained more word pairs than the older adults. There was also a significant main effect of condition, F (2, 81) = 4.42, MSE = .022, p = .015, and the follow-up tests showed that cued recall was greater in the 12-hr sleep condition (M_{adjusted}

= .48) than the 12-hr wake condition ($M_{adjusted}$ = .37), F (1, 58) = 7.10, MSE = .025, p = .01, and the 24-hr sleep condition ($M_{adjusted}$ = .39), F (1, 63) = 6.16, MSE = .029, p =.016 (the latter two conditions did not differ statistically, F < 1). The condition by age interaction was not significant (F (2, 81) = 2.10, MSE = .022, p = .13).

Because a primary focus of this research was to examine whether age differences emerged in memory retention across sleep delays, I next tested for the condition main effect (by repeating the above ANCOVA) in the younger adult and older adult groups separately. The younger adults demonstrated a significant condition main effect, F (2, 44) = 6.17, MSE = .023, p = .005, with the effect largely being driven by greater retention of word pairs in the 12-hr sleep condition ($M_{adjusted}$ = .66) relative to the 24-hr sleep condition ($M_{adjusted}$ = .50), F (1, 30) = 8.112, MSE = .025, p = .008, and the 12-hr wake condition ($M_{adjusted}$ = .48), F (1, 29) = 9.516, MSE = .023, p = .005 (the latter two did not differ, F < 1). In the older adult group, no significant delay condition differences emerged (Fs < 1 for main effect and each individual contrast; adjusted means: $M_{12\text{-hr Sleep}}$ = .29, $M_{24\text{-hr Sleep}}$ = .27, $M_{12\text{-hr Wake}}$ = .24). This pattern suggests that delay (quality and/or quantity) may not moderate memory retention as strongly in older adults as in younger adults.

To assess final cued recall of Session 2 pairs, I conducted a 2 (younger, older) x 3 (12-hr wake, 12-hr sleep, 24-hr sleep) ANCOVA that controlled for levels of recall during the final Session 2 learning cycle. Because these pairs had been learned only a few minutes earlier, ceiling effects were expected to limit this statistical analysis, at least in the younger adult group (Ellenbogen et al., 2006). Indeed, there were no significant effects (largest F (2, 81) = 2.32, MSE = .007, p = .11; see Table 7 for means and standard

deviations). To be consistent with the Session 1 final cued recall analysis, I further tested for the condition main effect in the younger and older adults separately. There was a marginally significant condition main effect in the younger adult restricted sample (i.e., those with full Zeo and behavioral datasets), F (2, 44) = 2.96, MSE = .008, p = .06 (adjusted means: $M_{12\text{-hr Sleep}}$ = .94, $M_{24\text{-hr Sleep}}$ = .89, $M_{12\text{-hr Wake}}$ = .85), and this main effect was significant when the analysis was inclusive of all younger adult participants, F (2, 52) = 3.35, MSE = .007, p = .043. The condition effect obtained because Session 2 word retention was greater in the 12-hr sleep group (M_{adjusted} = .93) than the 12-hr wake group (M_{adjusted} = .86), F (1, 34) = 5.33, MSE = .009, p = .028, and the 24-hr sleep group (M_{adjusted} = .88), F (1, 38) = 6.26, MSE = .003, p =.017 (the latter two did not significantly differ, F < 1). In contrast, the condition main effect was not significant for the older adults, regardless of whether those with Zeo data were included or excluded (both Fs < 1; adjusted means: $M_{12\text{-hr Sleep}}$ = .73, $M_{24\text{-hr Sleep}}$ = .74, $M_{12\text{-hr Wake}}$ = .75). These findings suggest that a sleep delay may have provided some, albeit weak, benefits to subsequent learning in the younger adults but not in the older adults (e.g., via synaptic downscaling which promotes efficiency of new learning; Tononi & Cirelli, 2003).

Sleep—Behavior Correlations

A primary interest of this research regarded whether deep sleep benefited memory consolidation in both younger and older adults. The results thus far have demonstrated age differences in amount of deep sleep as well as evidence that sleep delays are less likely to benefit memory retention in older adults than in younger adults. The next critical question is whether the association between deep sleep and memory retention is upheld in

both younger and older adults. Scatterplots are presented in Figure 3 to illustrate the relationship between deep sleep and memory retention (Session 1 pairs) for younger versus older adults. I conducted a partial correlation between percent deep sleep and final cued recall of Session 1 word pairs, after controlling for delay condition (12-hr sleep, 24-hr sleep) and number of word pairs learned during Session 1 learning. This correlation was strong and statistically significant in the younger adults, r (26) = .500, p = .007, but not significant and near zero in the older adults (r (20) = .016, p = .926). A Fisher r-to-z transformation test demonstrated that the magnitude of the correlation differed between younger and older adults, Z = 1.83, p = .033 (one-tailed test; two tailed test yields marginally significant p = .067). The magnitude of these correlations was generally stable when separately examining the 12-hr sleep condition (Younger: r (12) = .476, p = .085; Older: r (9) = -.018) and the 24-hr sleep condition (Younger: r (12) = .627, p = .016; Older: r (9) = .072), though doing so reduced power for detecting statistical significance (to marginal levels) in the 12-hr sleep group.

As can be seen in Table 8, Session 1 word pair retention significantly correlated with two other sleep variables in the younger adults (none in the older adults). First, there was a negative correlation with percent of time spent in light sleep in the younger adults. This correlation probably arose because there is an inverse correlation between deep sleep percent and light sleep percent in the younger adults, r (30) = -.784. One reason to favor the memory retention correlation with deep sleep over that with light sleep is that *number of minutes* spent in deep sleep significantly correlated with retention of Session 1 word pairs (in the younger adults), whereas light sleep minutes did not (see Table 8).

Another potentially interesting question is whether sleep variables correlated with learning phase performance (word pairs correctly recalled) and final recall of Session 2 word pairs (see Table 8). The only significant partial correlation (controlling for delay condition) between sleep variables and Session 1 learning phase performance was a negative correlation with total sleep time in the older adult group, r (21) = -.43, p = .04, suggesting that older participants who learn well also sleep less. This correlation did not reach statistical significance for Session 2 learning phase performance (r (21) = -.325, p = .13). There were also some significant correlations between sleep variables and retention of Session 2 word pairs in the older adults (but not the younger adults; see Table 8). Surprisingly, within the older adult group, there was a significant *negative* correlation between minutes in deep sleep and Session 2 word pair retention (the corresponding partial correlation with percent deep sleep was marginally significant). This finding was unexpected but it converges with Buechel et al.'s (2011) recent finding of a negative correlation between deep sleep and Morris Water Maze performance in older rodents. In addition to the correlation with deep sleep, percent light sleep correlated positively with retention of Session 2 items, though this correlation might need to be treated more cautiously because number of light sleep *minutes* did not significantly correlate with Session 2 word pair retention.

Table 9 presents the partial correlations between retention of Session 1 and Session 2 word pairs and the following measures: Pittsburg Sleep Quality Index, Morningness-Eveningness Questionnaire, and chronological age. None of these correlations was significant in the younger or older adults, thereby implying that memory retention, at least within the present research, was not significantly affected by age

differences in variables such as optimal test time, which is presumably a partial indication of age differences in circadian rhythms.

Sleep Fragmentation

One possibility is that sleep fragmentation, which is evident to a much greater degree in older adults than in younger adults throughout the literature (e.g., Bliwise, 1993) as well as in the present study (Table 2), could impair memory consolidation. To investigate this question I examined whether measures of wake after sleep onset (total awakenings and minutes awake after sleep onset) and sleep efficiency (i.e., percent of night spent asleep) correlated with Session 1 or Session 2 memory retention. As can be seen in Table 8, there were no significant correlations in the younger adults. The results were slightly more mixed in the older adults. There was a marginally significant negative correlation between Zeo-measured total awakenings and Session 2 word pair retention suggesting that greater nighttime awakenings leads to learning deficits in older adults. While tantalizing, the same correlation was not significant when utilizing actigraphy-measured (rather than Zeo-measured) awakenings. Furthermore, actigraphy-measured sleep efficiency demonstrated a marginally significant negative correlation with Session 1 memory retention (i.e., better sleep efficiency associated with worse memory consolidation), which also does not converge with the idea that sleep fragmentation is causing memory deficits in the older adults in the present study.

An additional, intriguing idea is that fragmentation of a particular stage of sleep could be associated with memory consolidation or learning deficits. To answer this question I examined number of awakenings that occurred during deep sleep, light sleep,

and REM sleep. This data was available for a subset of participants ($n_{Younger}$ = 20, n_{Older} = 21) due to additional Zeo device glitches in which minutes spent in each sleep stage, rather than the full polysomnogram, were available. There were no significant (partial) correlations with Session 1 memory retention in the younger or older adults, suggesting that sleep fragmentation might not be impairing memory consolidation in the present study. For Session 2 memory retention, there were no significant correlations in the younger adults; however, as illustrated in Figure 4, within the older adult group there was a significant negative correlation between number of deep sleep awakenings and Session 2 memory retention, r (17) = -.586, p = .008. This exciting finding suggests that an inability to sustain deep sleep might lead to next-day learning impairments in older adults (Van Der Werf et al., 2009); but, it is important to note that the Zeo provides a relatively insensitive measure of sleep arousals (averaged across 5 min intervals) and also that there was very little variability in number of deep sleep awakenings (see Figure 4).

Top Learners

Tucker et al. (2011) argued that memory consolidation might not occur in older adults if the learning test is too challenging. In the present study, there was variability in how difficult the learning task was for older adults; nearly 50% of older adult participants did not reach the learning criterion in Session 1. To investigate whether sleep benefits to memory retention were observed in a group that was successful on the initial learning task, I restricted the sample to only those older adults who reached the Session 1 learning criterion. An ANCOVA that included the between subjects variable of condition (12-hr wake, 12-hr sleep, 24-hr sleep) and controlled for number of items recalled during the

final Session 1 learning cycle, revealed a significant main effect of condition, F (2, 21) = 4.76, MSE = .019 (adjusted means: $M_{12\text{-hr Sleep}}$ = .498, $M_{24\text{-hr Sleep}}$ = .311, $M_{12\text{-hr Wake}}$ = .307). This behavioral finding was consistent with Tucker et al.'s claim that initial proficiency on a memory task is important for older adults to demonstrate sleep-related memory benefits. However, when I further restricted the analysis to only those participants who had Zeo data, the condition main effect was no longer significant (F (2, 18) = 2.42, MSE = .018, p = .126). Moreover, partial correlations between Session 1 word retention and deep sleep percent (r (10) = -.020) or minutes (r (10) = .137) were not significant. Furthermore, and consistent with the overall sample, there was still a marginally significant negative correlation between deep sleep minutes and Session 2 word pair retention (i.e., remembering items that were just learned), r (10) = -.560, p = .058.

One possibility is that the sleep—memory relationship age-group difference between might be explained by age-related differences in memory encoding. To help test this possibility, I examined mean final recall of weakly encoded items in the younger adults, which I operationally defined as word pairs that were correctly recalled only once during the Session 1 learning phase. A between-subjects ANOVA that included condition (12-hr wake, 12-hr, sleep, 24-hr sleep) revealed a significant main effect whether all younger participants were included, F (2, 49) = 4.23, MSE = .059, p = .020, or younger participants without Zeo data were excluded, F (2, 41) = 3.70, MSE = .055, p = .033. Final recall of weakly encoded word pairs was greater in the 12-hr sleep group (M = .59) than in the 12-hr wake group (M = .35), t (32) = 2.91, p = .007. Performance in the 24-hr sleep group (M = .47) did not differ significantly from either group (both ps > .13). These

patterns were stable when conducting ANCOVAs that controlled for the number of Session 1 learning cycles (i.e., how many times the younger adult attempted to recall the pair). In addition, despite the reduction in statistical power due to examining only items that were weakly encoded, there was a marginally significant partial correlation (controlling for condition) between final recall of weakly encoded pairs and deep sleep percent, r (27) = .35, p = .06 (r = .33 for correlation with deep sleep minutes). Similar marginally significant results obtained when also controlling for number of Session 1 learning cycles. Thus, when comparing performance on weakly encoded items in the younger adults to performance in older adults who were highly proficient at the learning task, there was less evidence for a positive relationship between deep sleep and memory in the older adult group than in the younger adult group.

Discussion

Overview of Findings

The overarching goal of the present research was to determine whether sleep, and deep sleep in particular, benefits memory in older adults, as it has been demonstrated to do so in younger adults (for a review, see Stickgold, 2005). To this end, I employed both correlational and experimental (delay type and word pair type manipulations) methods. In the younger adults, sleep benefits were observed as levels of memory retention being greater following an equal-length delay that included sleep versus wake (i.e., the 12-hr conditions) as well as a strong positive association between amounts of deep sleep and retention of Session 1 word pairs. In contrast, the older adults tended not to demonstrate these patterns (significantly), and even showed a significant negative correlation between deep sleep and Session 2 word retention. The present findings suggested that the sleep—

memory link may weaken or change with increasing age, but before diving deeper into the interpretation of the younger and older adult sleep—memory results, I will first attend to the unexpected finding of no *AB/AB′/AC′* interference effect.

AB′/AC′ Interference

The present research used the *AB′/AC′* interference procedure (Barnes & Underwood, 1959) because Ellenbogen et al. (2006) utilized this procedure to demonstrate memory consolidation across sleep intervals. A surprising finding of the present study was that the *AB/AB′/AC′* manipulation, which was expected to produce retroactive interference (at least in the wake condition), was ineffective. Below I describe how the current study's procedure differed from that used by Ellenbogen et al. with the aim of identifying why *AB′/AC′* interference did not occur.

During the *AB′* learning phase, Ellenbogen et al. (2006) had participants first study the full list of pairs (i.e., view each pair for 7 seconds), and then immediately afterward, participants began a retrieval—feedback phase (similar to the anticipation-plus-study procedure used by Bower, Thompson-Schill, & Tulving, 1994). In this second phase, participants saw the cue word, typed in the associated word, and then received immediate feedback regarding the correct answer. There were no additional study phases (other than the feedback screens) and participants were repeatedly tested on all word pairs until each pair was correctly recalled three times. *AC′* learning was conducted between subjects (i.e., some participants learned *AC′* pairs after the *AB′* pairs whereas other participants only learned the *AB* pairs).

There were three potentially relevant differences between the present methodology and Ellenbogen et al.'s (2006) methodology. First, whereas Ellenbogen et al. (2006) manipulated *AC′* learning between subjects, I manipulated word pair type (*AB′*/*AC′*) within subjects. Though this design change constitutes a large difference between the two studies, it is unlikely to explain the present study's null interference effects because other research has found significant interference effects using within-subjects manipulations of word pair type (Delprato, 1971; Kuhl, Shah, DuBrow, & Wagner, 2010). A second difference between the two studies was that Ellenbogen et al. (2006) provided *specific* feedback during the learning phase ("Correct answer is _____") whereas the present study only provided participants with *general* feedback during learning ("You recalled less than 80% of items correct"). There do not seem to be any published studies that have assessed the effects of specific versus general feedback on retroactive interference, but not all *AB′*/*AC′* interference studies have used specific feedback (e.g., Barnes & Underwood, 1959). Therefore, this methodological difference is also unlikely to explain the lack of *AB′*/*AC′* interference in the present study.

A third methodological difference between the present study and Ellenbogen et al.'s study (as well as other *AB′*/*AC′* studies) was that the present study employed a filler-task delay (two minutes of math problems) between study-test phases during learning whereas similar studies have not included a filler-task delay. The present study used a filler-task delay with the intention that participants would have to recall the word pairs from secondary (long-term) memory rather than just maintaining (e.g., rehearsing) the words in primary (short-term) memory. Not only does a filler-task delay increase the difficulty of the learning phase, it might also have affected the manner in which the word

pairs were encoded (e.g., hippocampal and other medial temporal lobe structures are more typically used to support long term versus short term memory).

There are a few reasons why including a filler-task delay and forcing participants to repeatedly recall word pairs (*AB*, *AB′*, *AC′*) from secondary memory might reduce or eliminate retroactive interference effects. One idea is that in learning and attempting to retrieve an *AC′* pair the participant might be reminded of the previous *AB′* pair. This idea follows from Walheim's (2011) recent work on remindings in a proactive interference paradigm and receives support from the finding that recall of *AB′* and *AC′* pairs correlated positively. Moreover, using neuroimaging (fMRI), Kuhl et al. (2010) found evidence that the hippocampus reactivated *AB′* memories during the learning of *AC′* word pairs. They also found that greater levels of hippocampal reactivation were associated with diminished forgetting of the *AB′* word pairs. If participants in the present study were relying more on hippocampal systems to encode and recall word pairs then that may have led to greater remindings during Session 2 (*AC′*) learning, thereby eliminating the classic *AB′/AC′* interference effect.

Effect of Delay on Memory in Younger Adults

Though the *AB′/AC′* manipulation was ineffective in the present study (cf. Ellenbogen et al., 2006), I was still able to examine the relationship between associative memory, delay type, and sleep measures. The results demonstrated that word pair retention (as measured on the final cued recall test) was better following a 12-hr sleep delay than a 12-hr wake delay. Though consistent with a memory consolidation account, the observation of better memory following sleep than wake delays is consistent with

other accounts such as protection against daytime interference (Jenkins & Dallenbach, 1924). In designing this experiment, I used the 24-hr sleep group, which includes greater daytime interference (~18 hours) than the 12-hr wake group but also a period of nighttime sleep, in part to try to distinguish between interference and consolidation interpretations. The consolidation account predicts that because both the 12-hr sleep and 24-hr sleep conditions received nighttime sleep, memory retention in the 24-hr sleep condition should approximate that of the 12-hr sleep condition. In contrast, the interference account predicts that performance in the 24-hr sleep group will be worse than performance in the 12-hr sleep group. The Session 1 memory retention results demonstrated a significant decrease from the 12-hr sleep condition to the 24-hr sleep condition, which was predicted by interference theory.

Whereas the contrast between the 12-hr sleep condition and the 24-hr sleep condition for the measure of Session 1 memory retention within the younger adult group supported the interference account (Jenkins & Dallenbach, 1924), other analyses were less consistent with interference theory. For example, interference theory predicts that greater daytime interference leads to worse memory performance, but Session 1 memory retention was statistically similar between the 12-hr wake group and the 24-hr sleep group (performance was nominally greater in the 24-hr sleep group). In addition, based upon the cognitive aging literature that has shown that older adults are more subject to interfering material than younger adults (e.g., Hasher & Zacks, 1988), by the interference theory, one would expect to find even larger effects of delay condition in the older adults than in the younger adults, but the reverse pattern was observed in the present study. One

tentative possibility is that both interference and consolidation contributed to the patterns of memory retention observed in the present study.

Total Sleep Time and Memory in the Younger Adults

Poor sleep the night before the final cued recall test might help explain why the sleep benefits to memory retention, especially in the 24-hr sleep condition, were weaker in this younger adult sample relative to other studies (e.g., Ellenbogen et al., 2006). Total sleep time was well below optimal (<6 hours on average) in the younger adults. Sleep deprivation impairs the functioning of the prefrontal cortex (Harrison, Horne, & Rothwell, 2000) and hippocampus (Yoo et al., 2007), as well as functional connectivity between these two regions (Gais et al., 2007); therefore, even if memories have been consolidated (deep sleep occurs early in the night and therefore was likely to be relatively preserved in the present study), these effects might be partially masked if prefrontal cortex and hippocampal impairments are causing disruptions in memory retrieval. It may also be important to point out that the partial sleep deprivation might disproportionately disadvantage the 24-hr sleep condition: Doran, Van Dongen, and Dinges (2001) demonstrated that the effects of total sleep deprivation accumulate increasingly with time remaining awake (see also Van Dongen & Belenky, 2009) and similar results have been observed in partial sleep deprivation studies (Belenky et al., 2003).

There are at least two reasons why total sleep time was reduced in the younger adult sample. First, undergraduate students generally sleep poorly due to living in dormitories, studying, stress, social events, and morning classes. One study found that only 11% of college undergraduates in the United States have good sleep quality

(Buboltz, Brown, & Soper, 2001). In addition, research at Washington University demonstrated that total sleep time declines in undergraduate students across the semester (Kathy Wildman, personal communication), and the majority of the younger adult data in the present study was collected during the latter half of the spring semester (months March and April). Despite clear evidence that total sleep time is not optimal in college students, most sleep and memory studies have demonstrated effects using college samples, and there is no reason to expect that impaired sleep due to being in college would affect the sleep and wake groups differently (Pittsburg Sleep Quality Index scores did not differ between groups). Therefore, there are likely additional factors that contribute to the low total sleep time (and weaker sleep-related memory benefits than might be expected) in the present study.

Another potential influence to the low level of total sleep time was that wearing the Zeo headband might have perturbed sleep. Though I did not record participants' subjective accounts systematically, there were some participants who commented that getting used to wearing the headband had some effect on their sleep (though others claimed that the headband did not interfere with their sleep). Sleep laboratory studies often include an adaptation night prior to the experiment in which participants get used to sleeping while connected to polysomnography equipment so as to decrease the probability of abnormal sleep during the experiment. An adaptation night was not included in the present study due to resource constraints and also because the Zeo headband was not considered to be as irksome as full-scale polysomnography recording. It is possible though that wearing the Zeo headband disturbed sleep enough to impair prefrontal cortex and hippocampal functioning and subsequently disadvantage the sleep

groups (especially the 24-hr sleep group; Doran et al., 2001), relative to the wake group, on the final cued recall test. Thus, future studies that use the Zeo device might employ an adaptation night to decrease concerns that getting used to the Zeo headband impacts sleep quantity and quality.

Relationship Between Deep Sleep and Memory in Younger Adults

Despite finding low levels of total sleep time, because deep sleep occurs early during nighttime sleep (i.e., it is presumably relatively preserved), one might still expect to find a relationship between amount of deep sleep and memory retention. Consistent with the hypothesis that deep sleep facilitates episodic memory consolidation in younger adults (e.g., Plihal & Born, 1997; Yaroush et al., 1971), the results revealed a strong correlation between time spent in deep sleep (both in percentage and total minutes) and retention of word pairs learned before sleeping (see Figure 3). These results were consistent with a large literature that has connected deep sleep physiology to memory reactivation and subsequent episodic memory behavioral benefits (for a review, see Diekelmann & Born, 2010). Whereas the consolidation prediction is that memory retention should correlate with deep sleep, the classic protection-against-daytime-interference account of sleep-related memory benefits (e.g., Jenkins & Dallenbach, 1924) anticipates that total sleep time moderates how well memories are retained; yet, there was not a significant partial correlation between Session 1 memory retention and total sleep time as measured by the Zeo ($r = .072$) or by actigraphy ($r = -.170$). Thus, the correlations between memory retention and sleep parameters tended to favor the consolidation account of sleep-related memory benefits in younger adults.

Sleep and Aging

The discussion thus far has focused on how sleep relates to memory in younger adults but the more novel question of the present research regards how sleep and memory may change with increasing age. The literature on sleep and aging (for a review, see Bliwise, 1993) suggests that older adults may demonstrate severe sleep disturbances and that aging is also associated with increased risk for many sleep disorders such as obstructive sleep apnea, restless legs syndrome, and REM-sleep behavior disorder. Each of these sleep disorders has been associated with later onset of neurodegenerative disorders (e.g., REM-sleep behavior disorder predicts onset of Parkinson's disease by 10 years; Postuma, Gagnon, & Montplaisir, 2008) as well as cognitive impairments (e.g., Bliwise, 1993; Bliwise, 2002; Bliwise, 2004).

Because the present study was concerned with how age-related sleep changes are associated with age-related cognitive declines in normal aging, the present research included screening for history of disorders and medications that affect sleep architecture. In *healthy* aging, one expects to find age-related increases in amounts of light sleep, but also age-related impairments in deep sleep, time until sleep onset, awakenings after sleep onset, and total sleep time (see Figure 1). Consistent with the literature on normal aging and sleep, I found evidence for age-related increases in light sleep, but also age-related impairments in time to fall asleep and nighttime awakenings. Some, but not all, studies have found age-related declines in REM sleep (Bliwise, 1993), but the present study did not demonstrate consistent age group differences in REM. Critically, I observed a consistent and sizeable decline in deep sleep in the older adult group (relative to the younger adult group).

Sleep and Memory Retention in Older Adults

If deep sleep is critical to memory consolidation, and older adults show declines in deep sleep, then one expectation is that increasing deep sleep in older adults (pharmacologically or via other methods) will augment their cognitive performance. However, this hypothesis is based on the assumption that deep sleep—though lesser in quantity in older age—is still functionally related to cognition in older adults. An alternative account (e.g., Spiegel et al., 1986) that receives support from memory research in older rodents (Gerrard et al., 2008; Buechel et al., 2011) as well as sleep deprivation studies in older adult humans (e.g., Bonnet, 1989), is that the sleep—cognition link is functionally weakened or otherwise changed in the elderly.

Sleep did not benefit episodic memory in older adults in the present study (cf. Aly & Moscovitch, 2010). Older adults failed to demonstrate a main effect of delay condition; memory retention was not statistically greater following a 12-hr sleep delay than a 12-hr wake delay. This finding, which could not be explained by age-related changes in circadian rhythms (e.g., optimal time of testing), was consistent with research on sleep and procedural memory consolidation in older adults (e.g., Spencer et al., 2007; Siengsukon & Boyd, 2008; but see Tucker et al., 2011, for more mixed findings). However, the present study's results were inconsistent with Aly and Moscovitch's (2010) finding of a sleep (relative to wake) benefit in older adults for story recall. The discrepancy between the present study and Aly and Moscovitch's study might be due to the difference in study environment (controlled laboratory versus over the phone), the ease of the memory task (encoding was nominally higher for the older adults than

younger adults in Aly & Moscovitch's study), or the use of sleep physiology measures (Zeo sleep stage scoring versus self-report questionnaires).

The lack of a delay condition main effect on memory retention in the older adult group in the present study suggested an age-related decline in memory consolidation during sleep. But, this finding does not legislate between whether sleep is still functionally related to memory in older adults. Because deep sleep was reduced but not eliminated in the older adults, it was possible that older adults who had relatively high levels of deep sleep would still demonstrate evidence for memory consolidation. However, in contrast to the younger adult finding of a strong association between deep sleep and memory consolidation, within the older adult group there was no evidence of a relationship between deep sleep and retention of word pairs learned prior to sleep. This is an important finding, because though some sleep, memory, and aging studies have examined sleep—memory correlations and failed to find them in older adults (e.g., Tucker et al., 2011), reporting divergent correlations in younger and older adults within the same study is a much more powerful demonstration of an age-related dissociation (cf. Peters et al., 2008). This sleep—memory dissociation in older adults is inconsistent with the claim that cognitive deficits in the elderly are directly linked to their lesser quantities of deep sleep, but dovetails with the theory that the sleep—cognition link is weakened, or otherwise changed, in older adults (Spiegel et al., 1986; Pace-Schott & Spencer, 2011).

Synaptic Downscaling, Deep Sleep, and Subsequent Learning

The major theorizing regarding the relationship between deep sleep and memory

has focused so far on memory reactivation and consolidation. Tonini and Cirelli (2003; 2006) proposed the synaptic downscaling theory, which has received increasing attention as a complementary theory to consolidation (e.g., Axmacher, Draguhn, Eler, & Fell, 2009; Walker, 2009). The synaptic downscaling theory argues that during waking hours an organism learns and encodes various experiences, which causes a net increase in synaptic weights. However, a continuous net increase in synaptic weights would tax grey matter space, be energetically unsustainable (e.g., maintaining AMPA receptors), and eventually lead to saturation of the synaptic networks (i.e., new learning would no longer be possible). In addition to noting that daytime experience should increase synaptic weights, Tononi and Cirelli also observed that the physiology of deep sleep could be conducive to decreasing synaptic weights. Specifically, they suggested that the slow oscillations (<1 Hz on the EEG), which are a hallmark of deep sleep, support long term depression and depotentiation of synaptic transmission (e.g., internalization of AMPA receptors). Consistent with synaptic downscaling theory, studies conducted in *Drosophila* (fruit flies)(Donlea, Ramanan, & Shaw, 2009; Gilestro, Tononi, & Cirelli, 2009) have demonstrated that markers of synaptic weights show increases with daytime experience and decreases with sleep.

Of particular interest to the present research focus on deep sleep and memory, synaptic downscaling theory claims that sleep-dependent memory effects might be a consequence of the proportional downscaling of synaptic weights. By Tononi and Cirelli's (2003; 2006) account, downscaling synaptic weights leads to an improved signal-to-noise ratio for strongly potentiated synapses leading to the "refinement and sharpening of previously acquired memories", especially those that have already been

reactivated during sleep (Axmacher et al., 2009, p. 2293). Thus, the results of the present study were consistent with synaptic downscaling theory in addition to consolidation theory (as well as hybrid reactivation—downscaling theories).

Another prediction of synaptic downscaling theory for cognitive functioning, which is the more often cited prediction, is that synaptic downscaling should set the stage for learning the next day. Consistent with this claim, Van Der Werf et al. (2009) found that specifically perturbing deep sleep (with total sleep time preserved) impairs subsequent learning. In the present study, I did not find any correlations between deep sleep and next-day learning in the younger adults. Interestingly, in the older adult group, there was a *negative* correlation between deep sleep and recall of Session 2 word pairs. Though unexpected, the negative correlation with deep sleep in older adults is actually consistent with Buechel et al.'s (2011) recent finding that older rats sometimes demonstrated negative correlations between deep sleep and performance on the Morris Water Maze task. Moreover, though the negative correlation seems to contradict synaptic downscaling theory, another possible explanation of this finding is that, in older adults, synaptic downscaling is increased *proportionally* relative to younger adults (e.g., similar levels of downscaling despite less daytime encoding in older adults) and that the age-related proportional increase in downscaling eventually becomes detrimental to cognitive functioning. Though only a preliminary hypothesis, this idea of "overactive downscaling" dovetails with Chang et al.'s (2006) finding that experimentally downscaling AMPA receptors in a rodent model contributed to Alzheimer's disease pathology (a disease that is prevalent in older adult humans).

Possible Mechanisms Driving Sleep—Cognition Weakening with Age

Presently, it is unclear at what point and why the sleep—cognition link should weaken. Research on deep sleep and memory consolidation in middle-aged adults (Backhaus et al. 2007) showed that memory consolidation was weaker in middle-aged adults than younger adults but also that middle-aged adults with high amounts of deep sleep still demonstrated memory retention effects similar to younger adults. Therefore, it is unlikely that a single event causes a sleep—memory dissociation, but rather, the sleep—memory link may gradually weaken with increasing age.

One possibility is that declines in sleep across the lifespan indirectly cause a weakening of the sleep—cognition link. For example, research conducted in rodents (Kang et al., 2009) and now in humans (Huang et al., in press) has demonstrated that amyloid beta levels (i.e., a biomarker strongly linked to Alzheimer's disease; e.g., Rabinovici & Jagust, 2009) accumulate with wakefulness and sleep deprivation but decrease with normal sleep. Increasing amyloid deposition might eventually cause neurological impairments that interfere with sleep (for a review of sleep in dementia see Bliwise, 1993) as well as cognitive processes occurring during sleep.

Another intriguing idea is that normal processes occurring during sleep, paradoxically, gradually cause the sleep—cognition link to weaken. For example, if synaptic downscaling occurs at rates greater than it should in older adults then that would lead to decreased neural connectivity which might subsequently impair processes such as memory consolidation. Consistent with this idea, fMRI research has demonstrated that functional connectivity between the hippocampus and prefrontal cortex (i.e., systems supposedly involved in memory consolidation; e.g., Gais et al., 2007) weaken with

increasing age (Grady, McIntosh, & Craik, 2003; Grady, 2006). Other, non-sleep factors such as neural atrophy (Raz et al., 2005; Resnick et al., 2003), white matter declines (Gunning-Dixon, & Raz, 2000), or changes in the hypothalamo-pituitary-adrenal axis (which might affect deep sleep quality; Buckley & Schatzberg, 2005), may contribute to this age-related change as well.

Implications for Sleep-Based Solutions to Cognitive Aging

The assumption most often expressed in sleep, memory, and aging papers is that if older adults gained more deep sleep then age-related cognitive deficits would be minimized (e.g., Buckley & Schatzberg, 2005). However, this hypothesis assumes that the sleep—cognition relationship that is prevalent in younger adults (e.g., Bonnet, 1989; Walker, 2009) is relatively maintained in older adults. Though one analysis (Figure 4) suggested that awakenings from deep sleep are associated with worse learning the following day in older adults, most of the results failed to produce evidence for a positive association between sleep stages and memory retention in older adults. Therefore, it may not be surprising that pharmacological interventions that simply bolster the amount of a particular stage of sleep have not been effective in improving memory in older adults (e.g., Hornung et al., 2007). However, if future studies use polysomnography to garner more precision in estimating arousals during sleep and still replicate the present study's finding of an association between learning deficits and awakenings from deep sleep in older adults, then pharmacological interventions that decrease (deep) sleep fragmentation may prove to be beneficial to cognitive functioning in older adults.

Though the best sleep-based treatment for cognitive declines in aging is likely to be derived by better knowledge of the mechanism(s) driving the weakening of the sleep—cognition link, one tentative possibility is to experimentally prime older adults to reactivate memories during sleep. Rasch et al. (2007) and Rudoy et al. (2009) found that when they forged an association between a memory (e.g., card locations on a grid) and a cue stimulus (e.g., a sound, an odor), later re-presenting that cue stimulus during deep sleep led to better (next-day) recall of the associated memory. This control over consolidation might be employed repeatedly in older adults in an attempt to prime them to consolidate memories during sleep. If effective, then that would suggest that older adults maintain the neural and cognitive structures/abilities to consolidate memories, and the next question would concern why they do not normally consolidate memories during sleep. In contrast, if a consolidation "training" procedure were *not* effective in older adults then that would suggest that they lack the ability to consolidate memories (e.g., due to functional connectivity changes; Grady, 2006). Pinpointing why the sleep—cognition link begins to weaken in older age and how such changes might be reversed could be one of the next great research questions for science.

References

Adam, K., & Oswald, I. (1977). Sleep is for tissue restoration. *Journal of the Royal College of Physicians of London*. *11*, 376-388.

Adam, M., Retey, J. V., Khatami, R., & Landolt, H-P. (2006). Age-related changes in the time course of vigilant attention during 40 hours without sleep in men. *Sleep*, *29*, 55-57.

Aly, M. & Moscovitch, M. (2010). The effects of sleep on episodic memory in older and younger adults. *Memory*, *18*, 327-334.

Ancoli-Israel, S. (2005). Sleep and aging: Prevalence of disturbed sleep and treatment considerations in older adults. *Journal of Clinical Psychiatry, 66,* 24-30.

Aserinsky, E., & Kleitman, N. (1953). Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. *Science*, *118*, 273-274.

Axmacher, N., Draguhn, A., Eler, C. E., & Fell, J. (2009). Memory processes during sleep: Beyond the standard consolidation theory. *Cellular and Molecular Life Sciences*, *66*, 2285-2297.

Backhaus, J., Born, J., Hoeckesfeld, R., Fokuhl, S., Hohagen, F., & Junghanns, K. (2008). Midlife decline in declarative memory consolidation is correlated with a decline in slow wave sleep. *Learning and Memory*, *14*, 336-341.

Backman, L., Nyberg, L., Lindenberger, U., Li, S-C., & Farde, L. (2006). The correlative triad among aging, dopamine, and cognition: Current status and future prospects. *Neuroscience and Biobehavioral Reviews*, *30*, 791-807.

Balota, D.A., Yap, M.J., Cortese, M.J., Hutchison, K.A., Kessler, B., Loftis, B., et al. (2007). The english lexicon project. *Behavior Research Methods*, *39*, 445-459.

Barnes, J. M. & Underwood, B. J. (1959). Fate of first-list association in transfer theory. *Journal of Experimental Psychology*, *58*, 97-105.

Barrett, T. R., & Ekstrand, B. R. (1972). Effect of sleep on memory. III. Controlling for time of day effects. *Journal of Experimental Psychology, 96*, 321–327.

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

Berger, R. J., & Phillips, N. H. (1995). Energy conservation and sleep. *Behavioral Brain Research, 69, 65-73.*

Blake, S., Pittman, S. D., MacDonald, M. M., Sun, K., Lanzi, B., Clark, D., Hueser. L., et al. (2009). Assessment of a wireless dry sensor to detect sleep in healthy volunteers and subjects with sleep disorders. *SLEEP Meeting*. Seattle, WA.

Bliwise, D. L. (1993). Sleep in normal aging and dementia. *Sleep*, *16*, 40-81.

Bliwise, D. L. (2002). Sleep apnea, APOE4 and Alzheimer's disease 20 years and counting? *Journal of Psychosomatic Research*, *53*, 539-46.

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

Bonnet, M. H. (1989). The effect of sleep fragmentation on sleep and performance in younger and older subjects. *Neurobiology of Aging*, *10*, 21-25.

Bonnet, M. H., & Arand, D. L. (1989). Sleep loss in aging. *Clinics in Geriatric Medicine*, *5*, 405-420.

Bonnet, M. H., & Rosa, R. R. (1987). Sleep and performance in young adults and older

normals and insomniacs during acute sleep loss and recovery. *Biological Psychology, 25,* 153-172.

Bower, G.H., Thompson-Schill, S.L., and Tulving, E. (1994). Reducing retroactive interference: An interference analysis. *Journal of Experimental Psychology: Learning, Memory, and Cognition*. *20,* 51–66.

Braver, T.S., & Barch, D. M. (2002). A theory of cognitive control, aging cognition, and neuromodulation. *Neuroscience Biobehavioral Review, 26,* 809–817.

Brown, L. N., Goddard, K. M., Lahar, C. J., & Mosley, J. L. (1999). Age-related deficits in cognitive functioning are not mediated by time of day. *Experimental Aging Research, 25,* 81–93.

Bruyneel, M., Sanida, C., Art, G., Libert, W., Cuvelier, L., Paesmans, M., Sergysels, R., et al. (in press). Sleep efficiency during sleep studies: Results of a prospective study comparing home-based and in-hospital polysomnograpy. *Journal of Sleep Research*.

Buboltz, W. C., Brown, F., & Soper, B. (2001). Sleep habits and patterns of college students: A preliminary study. *Journal of American College Health, 50,* 131-135.

Buckley, T. M., & Schatzberg, A. F. (2005). Aging and the role of the HPA axis and rhythm in sleep and memory-consolidation. *American Journal of Geriatric Psychiatry, 12,* 344-352.

Buechel, H. M., Popovic, J., Searcy, J. L., Porter, N. M., Thibault, O. & Blalock, E. M. (2011). Deep sleep and parietal cortex gene expression changes are related to cognitive deficits with age. *PLos One, 6,* e18387.

Buzsaki, G. (1996). The hippocampo-neocortical dialogue. *Cerebral Cortex, 6,* 81-92.

Buzsaki, G. (1998). Memory consolidation during sleep: A neurophysiological perspective. *Journal of Sleep Research, 7,* 17-23.

Buysse, D. J., Reynolds, C. F. III, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28*, 193-213.

Brown, L. N., Goddard, K. M., Lahar, C. J., & Mosley, J. L. (1999). Age-related deficits in cognitive functioning are not mediated by time of day. *Experimental Aging Research*, *25*, 81-93.

Carrier, J., Monk, T. H., Buysse, D. J., & Kupfer, D. J. (1997). Sleep and morningness-eveningness in the 'middle' years of life (20-59 y). *Journal of Sleep Research*, *6*, 230-237.

Carskadon MA, Rechtschaffen A. Monitoring and staging human sleep. In: Kryger MH, Roth TT, Dement WC, editors. Principles and Practice of Sleep Medicine. 4th ed. Philadelphia: Elsevier Saunders; 2005. pp. 1359–1377.

Chang, E. H., Savage, M. J., Flood, D. G., Thomas, J. M., Levy, R. B., Mahadomrongkul, V., et al. (2006). AMPA receptor downscaling at the onset of Alzheimer's disease pathology in double knockin mice. *Proceedings of the National Academy of Sciences, USA*, 103, 3410-3415.

Coltheart, M. (1981). The MRC Psycholinguistic Database. *Quarterly Journal of Experimental Psychology*, *33*, 497-505.

Conn, D. K., & Madan, R. (2006). Use of sleep-promoting medications in nursing home residents. *Drugs and Aging*, *23*, 271-287.

Crowder, R.G. (1976). Principles of learning and memory. Oxford, England: Lawrence

Erlbaum.

Delprato, D. J. (1971). Specific-pair interference on recall and associative-matching retention tests. *American Journal of Psychology, 84*, 185-193.

Diekelmann, S., & Born, J. (2010). The memory function of sleep. *Nature Reviews Neuroscience*, *11*, 114-126.

Diekelmann, S., Buchel, C., Born, J. & Rasch, B. (2011). Labile or stabile: Opposing consequences for memory when reactivated during waking and sleep. *Nature Neuroscience*, *14*, 381-388.

Diekelmann, S., Wilhelm, I., & Born, J. (2009). The whats and whens of sleep-dependent memory consolidation. *Sleep Medicine Reviews, 13*, 309-321.

Donlea, J. M., Ramanan, N., & Shaw, P. J. (2009). Use-dependent plasticity in clock neurons regulates sleep need in drosophila. *Science*, *324*, 105-108.

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

Drosopoulos, S., Schulze, C., Fischer, S., & Born, J. (2007). Sleep's function in the spontaneous recovery and consolidation of memories. *Journal of Experimental Psychology*: *General*, *136*, 169-183.

Drummond, S. P. A., Meloy, M. J., Yanagi, M. A., Orff, H. J., & Brown, G. G. (2005). Compensatory recruitment after sleep deprivation and the relationship with performance. *Psychiatry Research: Neuroimaging, 140*, 211-223.

Duffy, J. F., Willson, H. J., Wang, W., & Czeisler, C. A. (2009). Healthy older adults

better tolerate sleep deprivation than young adults. *Journal of the American Geriatrics Society, 57,* 1245-1251.

Dumay, N. & Gaskell, M. G. (2007). Sleep-associated changes in the mental representation of spoken words. *Psychological Science, 18,* 35-39.

Ebbinghaus, H. (1964). *Memory: A contribution to experimental psychology* (H. A. Ruger & C. E. Bussenius, Trans.). New York: Dover. (Original work published 1885).

Ego-Stengel, V., & Wilson, M. A. (2009). Disruption of ripple-associated hippocampal activity during rest impairs spatial learning in the rat. *Hippocampus, 20,* 1-10.

Ekstrand, B. R. (1967). Effect of sleep on memory. *Journal of Experimental Psychology, 75,* 64-72.

Ellenbogen, J. M., Hulbert, J. C., Stickgold, R., Dinges, D. F., & Thompson-Schill, S. L. (2006). Interfering with theories of sleep and memory: Sleep, declarative memory, and associative interference. *Current Biology, 16,* 1290-1294.

Ellenbogen, J. M., Hulbert, J. C., Jiang, Y., & Stickgold, R. (2009). The sleeping brain's influence on verbal memory: Boosting resistance to interference. *PLoS ONE, 4,* e4117.

Euston, D. R., Tatsuno, M., & McNaughton, B. L. (2007). Fast-forward playback of recent memory sequences in prefrontal cortex during sleep. *Science, 318,* 1147-1150.

Fisher, S., Hallschmid, M., Elsner, A. L., & Born, J. (2002). Sleep forms memory for finger skills. *Proceedings of the National Academy of Sciences, USA, 99,* 11987-11991.

Fogel, S. M., & Smith, C. T. (2006). Learning-dependent changes in sleep spindles and Stage 2 sleep. *Journal of Sleep Research, 15,* 250-255.

Fowler, M. J., Sullivan, M. J., Ekstrand, B.R. (1973). Sleep and memory. *Science, 179,* 302–304.

Gabrieli, J. D. (1998). Cognitive neuroscience of human memory. *Annual Reivew of Psychology, 49,* 87-115.

Gais, S., Albouy, G., Boly, M., Dang-Vu, T., Darsaud, A., Desseilles, M., Rauchs, G., et al. (2007). Sleep transforms the cerebral trace of declarative memories. *Proceedings of the National Academy of Sciences, USA, 104,* 18778-18783.

Gerrard, J. L., Burke, S. N., McNaughton, B. L., & Barnes, C. A. (2008). Sequence reactivation in the hippocampus is impaired in aged rats. *Journal of Neuroscience, 28,* 7883-7890.

Gilestro, G. F., Tononi, G., & Cirelli, C. (2009). Widespread changes in synaptic markers as a function of sleep and wakefulness in drosophila. *Science, 324,* 109-112.

Girardeau, G., Benchenane, K., Wiener, S. I., Buzsaki, G., & Zugaro, M. B. (2009). Selective suppression of hippocampal ripples impairs spatial memory. *Nature Neuroscience, 10,* 1222-1223.

Grady, C. L. (2006). Functional connectivity during memory tasks in healthy aging and dementia. In R. Cabeza, L. Nyberg, & D. Park (eds.) *Cognitive Neuroscience of Aging: Linking Cognitive and Cerebral Aging* (pp. 286-308). Oxford University Press.

Grady, C. L., McIntosh, A. R., & Craik, F. I. M. (2003). Age-related differences in the functional connectivity of the hippocampus during memory encoding.

Hippocampus, *13*, 572-586.

Gunning-Dixon, F. M., & Raz, N. (2000). The cognitive correlates of white matter abnormalities in normal aging: A quantitative review. *Neuropsychology*, *14*, 224-232.

Harrison, Y., Horne, J. A., & Rothwell, A. (2000). Prefrontal neuropsychological effects of sleep deprivation in young adults—A model for healthy aging? *Sleep*, *23*, 1-7.

Hasher, L. & Zacks, R. T. (1988). Working memory, comprehension, and aging: A review and a new view. In G. H. Bower (Ed.), *The psychology of learning and motivation* (pp. 193-224). New York: Academic Press.

Huang, Y., Potter, R., Sigurdson, W., Santacruz, A., Shih, S., Ju, Y-E., Kasten, T., et al. (in press). Effects of age and amyloid deposition on Aß dynamics in the human central nervous system. *Archives of Neurology*.

Hood, B., Bruck, D., & Kennedy, G. (2004). Determinants of sleep quality in the healthy aged: The role of physical, psychological, circadian and naturalistic light variables. *Age and Ageing*, *33*, 159-165.

Horne, J. A, & Ostberg, O. (1976). A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International Journal of Chrono-biology*, *4*, 97-110.

Hornung, O. P., Danker-Hopfe, H., & Heuser, I. (2005). Age-related changes in sleep and memory: Commonalities and interrelationships. *Experimental Gerontology*, *40*, 279-285.

Hornung, O. P., Regen, F., Danker-Hopfe, H., Schredl, M., & Heuser, I. (2007). The relationship between REM sleep and memory consolidation in old age and effects of cholinergic medication. *Biological Psychiatry*, *61*, 750-757.

Jenkins, J. G., & Dallenbach, K. M. (1924). Oblivescence during sleep and waking. *American Journal Psychology*, *35*, 605–612.

Jennings, J. M., & Jacoby, L. L. (1993). Automatic versus intention uses of memory: Aging, attention, and control. *Psychology and Aging*, *8*, 283-293.

Ji, D., & Wilson, M. A. (2007). Coordinated memory replay in the visual cortex and hippocampus during sleep. *Nature Neuroscience*, *10*, 13-15.

Jurado, J. L., Luna Villegas, G., & Buela–Casal, G. (1989). Normal human subjects with slow reaction times and larger time estimations after waking have diminished delta sleep. *Electroencephalography and Clinical Neurophysiology*, *73*, 124–128.

Kang, J-E., Lim, M. M., Bateman, R. J., Lee, J. J., Smyth, L. P., Cirrito, J. R., Fujiki, N. et al. (2009). Amyloid-ß dynamics are regulated by orexin and the sleep-wake cycle. *Science, 326*, 1005-1007.

Karni, A., Tanne, D., Rubenstein, B. S., Askenasy, J. J. M., & Sagi, D. (1994). Dependence on REM sleep of overnight improvement of a perceptual skill. *Science, 265*, 679-682.

Killgore, W. D. (2010). Effects of sleep deprivation on cognition. *Progress in Brain Research*, *185*, 105-29.

Kollar, E. J., Pasnau, R. O., Rubin, R. T., Naitoh, P., Slater, G. G., & Kales, A. (1969). Psychological, psychophysiological, and biochemical correlates of prolonged sleep deprivation.

Kuhl, B. A., Shah, A. T., DuBrow, S., & Wagner, A. D. (2010). Resistance to forgetting associated with hippocampus mediated reactivation during new learning. *Nature Neuroscience*, *13*, 501-508.

Landis, J. R., & Koch, G. G. (1977). The measurement of observer agreement for categorical data. *Biometrics*, *33*, 159-174.

Lee, A. K., & Wilson, M. A. (2002). Memory of sequential experience in the hippocampus during slow wave sleep. *Neuron*, *36*, 1183-1194.

Littner, M., Kushida, C. A., Anderson, W. M., Bailey, D., Berry, R. B., Davila, D. G., Hirshkowitz, M. et al. (2002). Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: An update for 2002. *SLEEP*, *26*, 337-341.

May, C. P., Hasher, L., Stoltzfus, E. R. (1993). Optimal time of day and the magnitude of age differences in memory. *Psychological Science, 4*, 326–330.

Maquet, P., Peters, J-M., Aerts, J., Delfiore, G., Degueldre, C., Luxen, A., & Franck, G. (1996). Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. *Nature, 383*, 163-166.

Maquet, P., Degueldre, C., Delfiore, G., Aerts, J., Peters, J-M., Luxen, A., Franck, G. (1997). Functional neuroanatomy of human slow wave sleep. *Journal of Neuroscience*, *17*, 2807-2812.

Marr, D. (1971). Simple memory: A theory for archicortex. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *262*, 23-81.

Marshall, L., Molle, M., Hallschmid, M., & Born, J. (2004). Transcranial direct current stimulation during sleep improves declarative memory. *The Journal of Neuroscience*, *24*, 9985-9992.

Martin, J., Shochat, T., & Ancoli-Israel, S. (2000). Assessment and treatment of sleep disturbances in older adults. *Clinical Psychology Review, 20,* 783-805.

Mazzoni, G., Gori, S., Formicola, G., Gneri, C., Massetani, R., Murri, L., & Salzarulo, P. (1999). Word recall correlates with sleep cycles in elderly subjects. *Journal of Sleep Research, 8,* 185-188.

McClelland, J.L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review, 102,* 419-457.

Nadasdy, Z., Hirase, H., Czurko, A., Csicsvari, J., & Buzsaki, G. (1999). Replay and time compression of recurring spike sequences in the hippocampus. *Journal of Neuroscience, 19,* 9497-9507.

Naveh-Benjamin, M. (2000). Adult age differences in memory performance: Tests of an associative deficit hypothesis. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 26,* 1170-1187.

Nishida, M., & Walker, M. P. (2007). Daytime naps, motor memory consolidation and regionally specific sleep spindles. *PloS One, 2,* e341.

Ohayon, M. M., Carskadon, M., A., Guilleminault, C., & Vitiello, M. V. (2004). Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: Developing normative sleep values across the human lifespan. *SLEEP, 27,* 1255-1273.

Park, D. C., Lautenschlager, G., Hedden, T., Davidson, N. S., Smith, A. D., & Smith, P. K. (2002). Models of visualspatial and verbal memory across the adult life span. *Psychology and Aging*, *17*, 299-320.

Payne, J. D., Stickgold, R., Swanberg, K., & Kensinger, E. A. (2008). Sleep preferentially enhances memory for emotional components of scenes. *Psychological Science*, *19*, 781-788.

Peigneux, P., Laureys, S., Fuchs, S., Collette, F., Perrin, F., Reggers, J., et al. (2004). Are spatial memories strengthened in the human hippocampus during slow wave sleep? *Neuron*, *44*, 535-545.

Peters, K. R., Ray, L., Smith, V., & Smith, C. (2008). Changes in the density of stage 2 sleep spindles following motor learning in young and older adults. *Journal of Sleep Research*, *17*, 23-33.

Philip, P., Taillard, J., Sagaspe, P., Valtat, C., Sanchez-Ortuno, M., Moore, N., Charles, A., et al. (2004). Age, performance and sleep deprivation. *Journal of Sleep Research*, *13*, 105-110.

Plihal, W., & Born, J. (1997). Effects of early and late nocturnal sleep on declarative and procedural memory. *Journal of Cognitive Neuroscience*, *9*, 534–547.

Poe, G. R., Nitz, D. A., McNaughton, B. L., & Barnes, C. A. (2000). Experience-dependent phase-reversal of hippocampal neuron firing during REM sleep. *Brain Research*, *855*, 176-180.

Postman, L., & Underwood, B. J. (1973). Critical issues in interference theory. *Memory & Cognition*, *1*, 19-40.

Postuma, R. B., Gagnon, J-F., & Montplaisir, J. (2008). Cognition in REM sleep behavior

disorder—A window into preclinical dementia? *Sleep Medicine, 9*, 341-342.

Rabinovici, G. D., & Jagust, W. J. (2009). Amyloid imaging in aging and dementia: Testing the amyloid hypothesis in vivo. *Behavioural Neurology, 21*, 117-128.

Rasch, B., Buchel, C., Gais, S., & Born, J. (2007). Odor cues during slow-wave sleep prompt declarative memory consolidation. *Science, 315*, 1426-1429.

Rauchs, G., Schabus, M., Parapatics, S., Bertran, F., Clochon, P., Hot P., Denise P., et al. (2008). Is there a link between sleep changes and memory in Alzheimer's disease? *NeuroReport, 19*, 1159-1162.

Raz, N., Lindenberger, U., Rodrigue, K. M., Kennedy, K. M., Head, D., et al. (2005). Regional brain changes in aging healthy adults: General trends, individual differences and modifiers. *Cerebral Cortex, 15*, 1676–1689.

Rechtschafen, A., & Kales, A. (1968). A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Brain Information Service/Brain Research Institute, Los Angeles: University of California at Los Angeles.

Resnick, S. M., Pham, D. L., Kraut, M. A., Zonderman, A. B., Davatzikos, C. (2003). Longitudinal magnetic resonance imaging studies of older adults: A shrinking brain. *Journal of Neuroscience, 23*, 3295–3301.

Rudoy, J. D., Voss, J. L., Westerberg, C. E., & Paller, K. A. (2009). Strengthening individual memories by reactivating them during sleep. *Science, 326*, 1079.

Salat, D. H., Buckner, R. L., Snyder, A. Z., Greve, D. N., Desikan, R. S., et al. (2004). Thinning of the cerebral cortex in aging. *Cerebral Cortex, 14*, 721–30.

Salthouse, T. A. (1996). The processing-speed theory of adult age differences in

cognition. *Psychological Review, 103*, 403-428.

Schredl, M., Weber, B., Leins, M. L., & Heuser, I. (2001). Donepezil-induced REM sleep augmentation enhances memory performance in elderly, healthy persons. *Experimental Gerontology*, *36*, 353-361.

Scullin, M. K., & McDaniel, M. A. (2010). Remembering to execute a goal: Sleep on it! *Psychological Science, 21,* 1028-1035.

Shambroom, J. R., & Fabregas, S. E. (2010). Age related changes in objectively measured sleep observed in a large population in the home. *SLEEP Meeting*, San Antonio, TX.

Shambroom, J.R., Fabregas, S.E., & Johnstone, J. (in press). Validation of an automated wireless system to monitor sleep in healthy adults. *Journal of Sleep Research*.

Siengsukon, C. F., & Boyd, L. A. (2009). Sleep to learn after stroke: Implicit and explicit off-line motor learning. *Neuroscience Letters*, *451,* 1–5.

Silva, E. J., Wang, W., Ronda, J. M., Wyatt, J. K., & Duffy, J. F. (2010). Circadian and wake-dependent influences on subjective sleepiness, cognitive throughput, and reaction time performance in older and young adults. *Sleep, 33*, 481-490.

Skaggs, W. E., & McNaughton, B. L. (1996). Replay of neuronal firing sequences in rat hippocampus during sleep following spatial experience. *Science, 271,* 1870-1873.

Spiegel, R. Koberle, S. & Allen, S. R. (1986). Significance of slow wave sleep: Considerations from a clinical viewpoint. *Sleep*, *9*, 66–79.

Staba, R. J., Wilson, C. L., Fried, I., & Engel, E. (2002). Single neuron burst firing in the human hippocampus during sleep. *Hippocampus, 12,* 724-734.

Stenuit, P., & Kerkhofs, M. (2005). Age modulates the effects of sleep restriction in

women. *Sleep, 28,* 1283-1288.

Stickgold, R. (2005). Sleep-dependent memory consolidation. *Nature, 437,* 1272-1278.

Takashima, A., Petersson, K. M., Rutters, F., Tendolkar, I., Jensen, O., Zwarts, M. J., McNaughton, B. L., et al. (2006). Declarative memory consolidation in humans: A prospective functional magnetic resonance imaging study. *Proceedings of the National Academy of Sciences, USA, 103,* 756-761.

Tononi, G., & Cirelli, C. (2003). Sleep and synaptic homeostasis: A hypothesis. *Brain Research Bulletin, 62,* 143-150.

Tononi, G., & Cirelli, C. (2006). Sleep function and synaptic homeostasis. *Sleep Medicine Reviews, 10,* 49-62.

Van Cauter, E., Leproult, R., & Plat, L. (2000). Age-related changes in slow wave sleep and REM sleep and relationship with growth hormone and cortisol levels in healthy men. *Journal of the American Medical Association, 284,* 861-868.

Van de Water, A. T., Holmes, A., & Hurley, D. A. (in press). Objective measurements of sleep for non-laboratory settings as alternatives to polysomnography – a systematic review. *Journal of Sleep Research.*

Van Dongen, H. P. A., & Belenky, G. (2009). Individual differences in vulnerability to sleep loss in the work environment. *Industrial Health, 47,* 518-526.

Vitiello, M. V., Larsen, L. H., & Moe, K. E. (2004). Age-related sleep change: Gender and estrogen effects on the subjective-objective sleep quality relationships of healthy, noncomplaining older men and women. *Journal of Psychosomatic Research, 56,* 503-510.

Walheim, C. N. (2011). Age differences in proactive interference and facilitation: The

role of remindings. *Dissertation presented at Washington University in St. Louis*.

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

Walker, M. P., Brakefield, T., Morgan, A., Hobson, J. A., & Stickgold, R. (2002). Practice with sleep makes perfect: Sleep-dependent motor skill learning. *Neuron, 35,* 205-211.

Webb, W. B. (1985). A further analysis of age and sleep deprivation effects. *Psychophysiology*, 1985, 22: 156–161.

Webb, W. B., & Levy, C. M. (1982). Age, sleep deprivation, and performance. *Psychophysiology*, *19,* 272–276.

West (1996). An application of prefrontal cortex function theory to cognitive aging. *Psychological Bulletin, 120,* 272-292.

Wierzynski, C. M., Lubenov, E. V., Gu, M., & Siapas, A. G. (2009). State-dependent spike-timing relationships between the hippocampal and prefrontal circuits during sleep. *Neuron, 26,* 587-596.

Wilson, M. D. (1988). The MRC psycholinguistic database: Machine readable dictionary, version 2. *Behavioural Research Methods, Instruments and Computers, 20,* 6-11.

Wilson, M. A., & McNaughton, B. L. (1994). Reactivation of hippocampal ensemble memories during sleep. *Science, 265,* 676-679.

Wolkove, N., Elkholy, O., Baltzan, M., & Palayew, M. (2007). Sleep and aging: 1. Sleep disorders commonly found in older people. *Canadian Medical Association Journal, 176,* 1299-1304.

Yaroush, R., Sullivan, M. J., & Ekstrand, B.R. (1971). Effect of sleep on memory. II: Differential effect of first and second half of the night. *Journal of Experimental Psychology, 88*, 361–366.

Yoo, S-S., Hu, P. T., Gujar, N., Jolesz, F. A., & Walker, M. P. (2007). A deficit in the ability to form new human memories without sleep. *Nature Neuroscience, 10*, 385-392.

Table 1

Means and standard deviations (in parentheses) for the PSQI, MEQ, and chronological age across age groups and conditions, separated by participants who do and do not have complete datasets (i.e., with Zeo data). PSQI: Pittsburgh Sleep Quality Index (Buysse et al., 1989); MEQ: Morningness-Eveningness Questionnaire (Horne & Ostberg, 1976).

Subjects with Behavioral Data

	N	PSQI	MEQ	Age
Younger: 12-hr Wake	14	4.57 (1.74)	43.50 (9.87)	19.86 (1.10)
Younger: 12-hr Sleep	20	5.38 (2.97)	40.50 (8.82)	19.80 (1.20)
Younger: 24-hr Sleep	18	5.06 (2.07)	43.44 (8.77)	19.56 (1.10)
Older: 12-hr Wake	13	7.46 (4.07)	60.85 (7.03)	73.15 (6.85)
Older: 12-hr Sleep	14	5.07 (2.92)	56.57 (9.45)	69.29 (4.03)
Older: 24-hr Sleep	14	6.00 (4.02)	51.71 (11.71)	69.71 (4.62)

Subjects with Complete Zeo and Behavioral Data

	N	PSQI	MEQ	Age
Younger: 12-hr Wake	14	4.57 (1.74)	43.50 (9.87)	19.86 (1.10)
Younger: 12-hr Sleep	15	4.87 (3.20)	41.40 (9.40)	19.67 (1.05)
Younger: 24-hr Sleep	15	5.00 (2.14)	44.13 (9.47)	19.67 (0.98)
Older: 12-hr Wake	13	7.46 (4.07)	60.85 (7.03)	73.15 (6.85)
Older: 12-hr Sleep	12	5.33 (2.90)	57.00 (9.88)	69.00 (3.74)
Older: 24-hr Sleep	12	5.67 (3.42)	52.75 (10.99)	70.42 (3.99)

Table 2
Zeo (n=54) and Actigraphy (n=65) data across younger and older adults for the sleep conditions (12-hr and 24-hr groups collapsed). Standard deviations are in parentheses.

	Younger Adults	Older Adults	*t*-test	*p*-value
Zeo Data Sample	n=30	n=24		
Light Sleep (%)	.49 (.12)	.61 (.15)	3.15	.003
Deep Sleep (%)	.26 (.12)	.15 (.09)	3.76	<.001
REM Sleep (%)	.26 (.08)	.25 (.12)	<1	*ns*
Wake (%)	.02 (.03)	.17 (.19)	4.40	<.001
Light Sleep (min)	164.43 (75.25)	200.92 (75.49)	1.77	.083
Deep Sleep (min)	83.17 (33.14)	46.54 (28.20)	4.31	<.001
REM Sleep (min)	90.23 (40.47)	84.13 (50.27)	<1	*ns*
WASO (min)	5.40 (7.82)	46.96 (45.27)	4.95	<.001
Sleep Latency (min)	19.73 (26.16)	17.38 (18.73)	<1	*ns*
Total Sleep Time (min)	337.20 (112.61)	331.13 (97.10)	<1	*ns*
Total Awakenings	1.43 (1.76)	4.88 (2.71)	5.64	<.001
	Younger Adults	Older Adults	*t*-test	*p*-value
Actigraphy Data Sample	n=37	n=28		
Sleep Latency (min)	14.11 (24.84)	17.32 (23.79)	<1	*ns*
Sleep Efficiency (%)	84.87 (8.92)	73.11 (18.24)	3.43	.001
WASO (min)	45.97 (60.89)	98.79 (88.90)	2.84	.006
Awakenings	29.00 (16.14)	29.11 (12.08)	<1	*ns*
Total Sleep Time (min)	375.33 (107.58)	326.14 (95.35)	1.92	.060

Table 3
Zeo (n=54) and Actigraphy (n=65) data across younger adults (YA) and older adults (OA) for the 12-hr and 24-hr sleep groups separately. Statistical discrepancies with Table 2 are bolded.

	12-hr Sleep Condition			24-hr Sleep Condition		
	Younger	Older	*p*-value	Younger	Older	*p*-value
Zeo Data Sample	n=15	n=12		n=15	n=12	
Light Sleep (%)	.48	.65	<.001	**.50**	**.57**	***ns***
Deep Sleep (%)	.27	.14	.005	.25	.15	.038
REM Sleep (%)	.26	.21	*ns*	.25	.28	*ns*
Wake (%)	.02	.27	<.001	.02	.07	.013
Light Sleep (min)	164.27	179.17	*ns*	164.60	222.67	*ns*
Deep Sleep (min)	85.20	37.08	<.001	81.13	56.00	.096
REM Sleep (min)	**89.60**	**60.50**	**.036**	90.87	107.75	*ns*
WASO (min)	5.40	67.58	<.001	5.40	26.33	.009
Sleep Latency (min)	28.27	17.83	*ns*	11.20	16.92	*ns*
Total Sleep (min)	**338.33**	**276.17**	**.022**	336.07	386.08	*ns*
Total Awakenings	1.13	5.47	<.001	1.73	4.08	.012
	Younger	Older	*p*-value	Younger	Older	*p*-value
Actigraphy Data Sample	n=19	n=14		n=18	n=14	
Sleep Latency (min)	16.97	7.07	*ns*	11.08	27.57	.057
Sleep Efficiency (%)	85.94	73.35	.009	83.76	72.88	.051
WASO (min)	29.21	100.91	.001	**63.65**	**96.67**	***ns***
Awakenings	24.84	28.21	*ns*	33.39	30.00	*ns*
Total Sleep Time (min)	338.05	308.40	*ns*	414.69	343.87	*ns*

Table 4

Final recall means (10 possible) for AB and AB′ word pair types (standard errors in parentheses). $AB_{adjusted}$ and $AB'_{adjusted}$ denote adjusted means (standard errors in parentheses) following controlling for levels of recall during the final learning phase study-test cycle. Data is for all subjects who have behavioral data.

	N	*AB*	*AB′*	$AB_{adjusted}$	$AB'_{adjusted}$
Younger: 12-hr Wake	14	4.79 (.59)	4.71 (.55)	4.12 (.53)	4.24 (.50)
Younger: 12-hr Sleep	20	6.55 (.50)	5.90 (.46)	5.93 (.45)	5.31 (.42)
Younger: 24-hr Sleep	18	5.56 (.52)	4.50 (.49)	4.74 (.48)	3.96 (.45)
Older: 12-hr Wake	13	2.38 (.62)	1.85 (.57)	3.72 (.59)	2.97 (.55)
Older: 12-hr Sleep	14	3.00 (.59)	3.79 (.55)	3.58 (.53)	4.40 (.50)
Older: 24-hr Sleep	14	3.21 (.59)	2.36 (.55)	4.00 (.54)	2.72 (.50)

Table 5

Number of pairs correctly recalled (20 possible) during the final learning phase cycle and number of study-test learning phase cycles completed across sessions, age groups, and conditions.

Subjects with Behavioral Data

	Session 1		Session 2	
	Cycles	Final	Cycles	Final
Younger: 12-hr Wake	2.64 (0.93)	17.86 (1.56)	2.57 (1.16)	18.50 (1.29)
Younger: 12-hr Sleep	2.25 (0.91)	17.80 (1.44)	2.05 (0.69)	18.20 (1.24)
Younger: 24-hr Sleep	2.50 (0.86)	18.22 (1.11)	2.22 (0.81)	18.17 (1.25)
Older: 12-hr Wake	4.54 (1.13)	12.31 (4.44)	4.38 (1.04)	13.77 (5.40)
Older: 12-hr Sleep	3.43 (1.02)	14.36 (4.40)	3.57 (1.34)	15.50 (3.88)
Older: 24-hr Sleep	3.86 (1.66)	14.00 (4.66)	3.43 (1.28)	14.29 (4.71)

Subjects with Complete Zeo and Behavioral Data

	Session 1		Session 2	
	Cycles	Final	Cycles	Final
Younger: 12-hr Wake	2.64 (0.93)	17.86 (1.56)	2.57 (1.16)	18.50 (1.29)
Younger: 12-hr Sleep	2.13 (0.92)	18.07 (1.39)	2.13 (0.74)	18.33 (1.23)
Younger: 24-hr Sleep	2.40 (0.91)	18.00 (1.00)	2.20 (0.86)	17.93 (1.22)
Older: 12-hr Wake	4.54 (1.13)	12.31 (4.44)	4.38 (1.04)	13.77 (5.40)
Older: 12-hr Sleep	3.42 (1.08)	14.00 (4.67)	3.67 (1.37)	15.25 (4.14)
Older: 24-hr Sleep	4.08 (1.68)	14.17 (4.57)	3.50 (1.31)	14.25 (4.75)

Table 6

Final cued recognition test performance (proportion correct out of 20) with standard deviations in parentheses.

	Subjects with Behavioral Data	Subjects with Zeo Data
Younger: 12-hr Wake	.982 (.037)	.982 (.037)
Younger: 12-hr Sleep	.988 (.028)	.990 (.028)
Younger: 24-hr Sleep	.969 (.042)	.963 (.044)
Older: 12-hr Wake	.787 (.248)	.787 (.248)
Older: 12-hr Sleep	.786 (.339)	.754 (.358)
Older: 24-hr Sleep	.877 (.246)	.860 (.264)

Table 7

Percent correctly recalled (number recalled divided by 20) on the final cued recall test.

Subjects with Behavioral Data

	Session 1	Session 2
Younger: 12-hr Wake	.475 (.176)	.868 (.167)
Younger: 12-hr Sleep	.623 (.187)	.930 (.057)
Younger: 24-hr Sleep	.503 (.158)	.883 (.079)
Older: 12-hr Wake	.208 (.108)	.723 (.244)
Older: 12-hr Sleep	.346 (.251)	.782 (.211)
Older: 24-hr Sleep	.279 (.187)	.754 (.225)

Subjects with Complete Zeo and Behavioral Data

	Session 1	Session 2
Younger: 12-hr Wake	.475 (.176)	.868 (.167)
Younger: 12-hr Sleep	.663 (.179)	.940 (.060)
Younger: 24-hr Sleep	.497 (.145)	.877 (.082)
Older: 12-hr Wake	.208 (.108)	.723 (.244)
Older: 12-hr Sleep	.304 (.242)	.771 (.226)
Older: 24-hr Sleep	.292 (.195)	.733 (.232)

Table 8

*Correlations between memory measures and sleep measures: ** indicates p < .01; * indicates p < .05; † indicates p < .10.*

	Session 1 Recall		Session 2 Recall	
	Younger	Older	Younger	Older
Zeo Data				
Light Sleep (%)	-.484**	.009	.322†	.424*
Deep Sleep (%)	.500**	.016	-.240	-.416†
REM Sleep (%)	-.015	-.027	-.129	-.230
Wake (%)	.209	.200	.082	.124
Light Sleep (min)	-.274	.157	.159	.171
Deep Sleep (min)	.457*	.116	-.191	-.507*
REM Sleep (min)	-.143	.021	-.054	-.326
WASO (min)	.165	.356	.147	-.002
Sleep Latency (min)	-.096	.143	.132	.135
Sleep Efficiency (%)	-.209	-.187	-.086	-.094
Total Sleep Time (min)	-.101	.206	.032	-.208
Total Awakenings	-.041	.333	.087	-.375†
Actigraphy Data				
Sleep Latency (min)	-.144	.171	.129	-.068
Sleep Efficiency (%)	-.073	-.409†	-.214	.116
WASO (min)	.129	.284	.158	-.252
Awakenings	-.190	.173	.262	-.193
Total Sleep Time (min)	-.087	-.259	.213	-.058

Table 9

Partial correlations of Session 1 and Session 2 correct word pair recall percent with the Morningness-Eveningness Questionnaire (MEQ), the Pittsburg Sleep Quality Index (PSQI), and chronological age (controlling for delay condition and corresponding learning phase performance). All p values were greater than .10.

	Session 1 Retention		Session 2 Retention	
	Younger	Older	Younger	Older
Questionnaire Data				
MEQ	.032	-.168	.194	-.073
PSQI	-.034	-.031	.027	.211
Chronological Age	-.095	.136	.061	-.041

Figure 1

Age-related sleep changes across the lifespan. Sleep latency: time in bed until individual falls asleep; WASO: wake after sleep onset (i.e., minutes spent awake at night after having initially fallen asleep and before rising for the day); REM: rapid eye movement (sleep); SWS: slow wave sleep (deep sleep); Stages 1 and 2 denote light sleep. (Carskadon & Rechtschaffen, 2005).

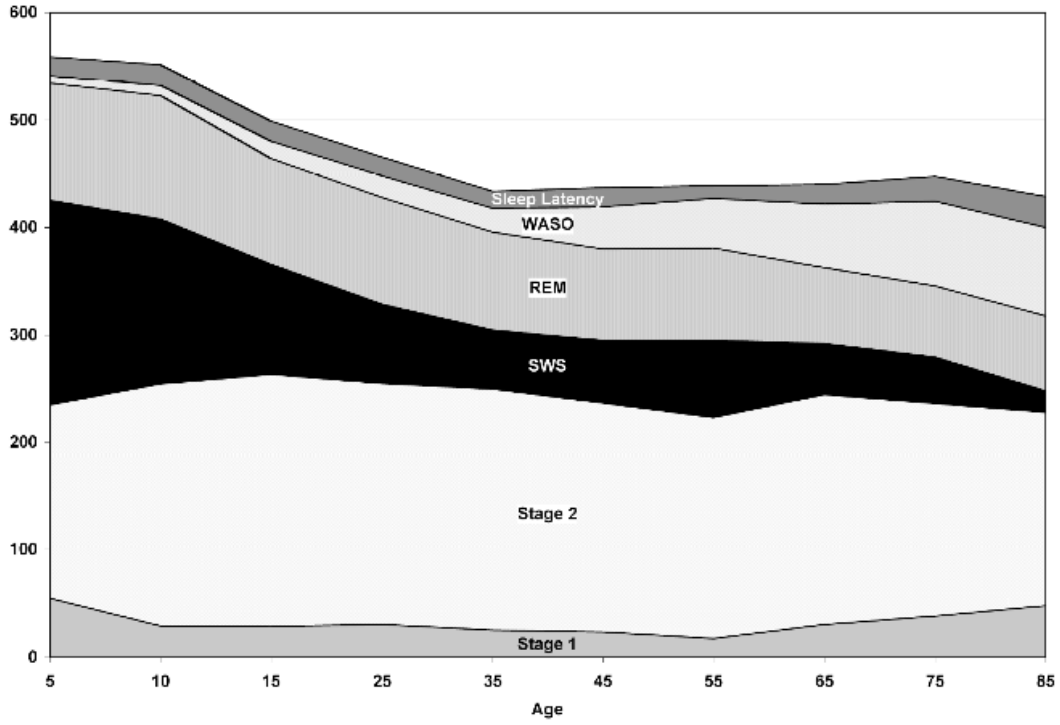


Figure 2

Results from the Ellenbogen et al. (2006, on the left; 2009, on the right) experiments. The AC′ groups are represented by the two bars (labeled interference) on the right.

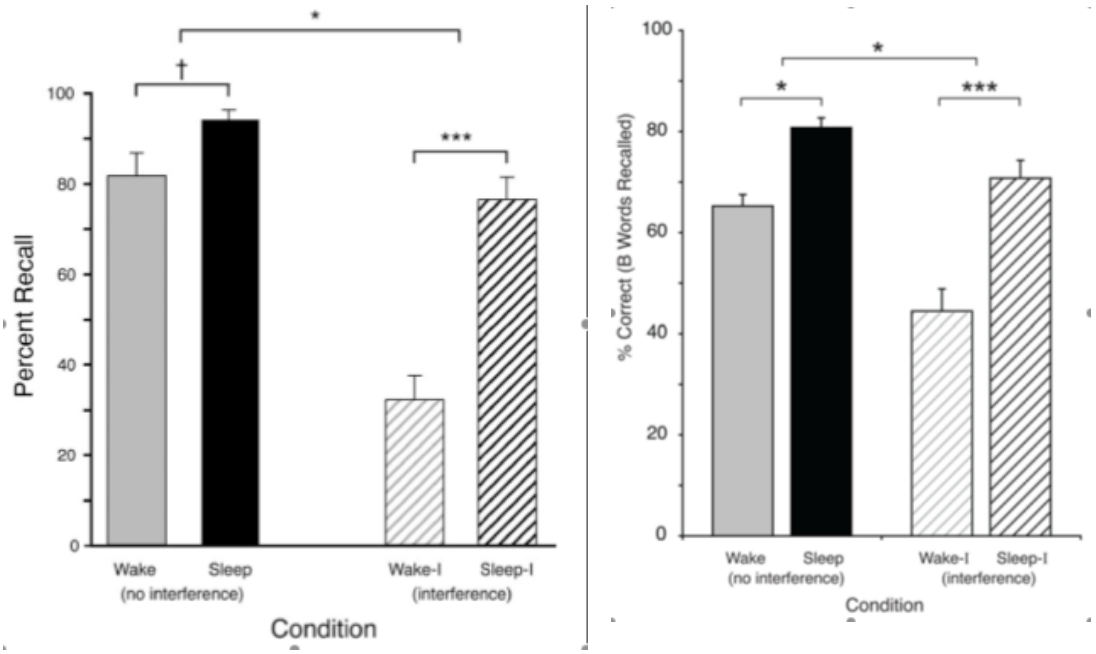
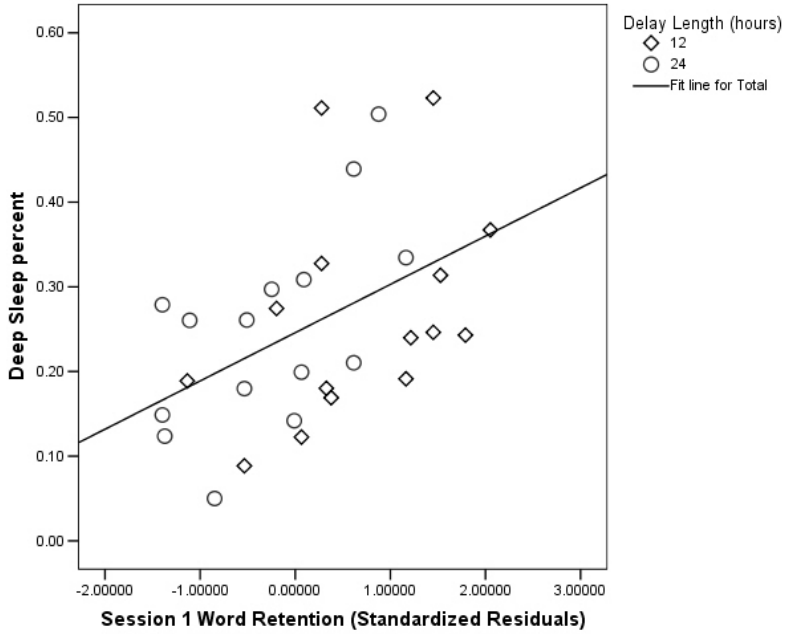


Figure 3

Scatterplots demonstrating the relationship between deep sleep percent and Session 1 memory retention in younger adults (top) and older adults (bottom). Standardized residuals were derived from regression analyses using Session 1 final recall (dependent variable) and number of items correctly recalled during the final Session 1 learning cycle. The partial correlation was significant for the younger, but not the older, adults.

Younger Adults



Older Adults

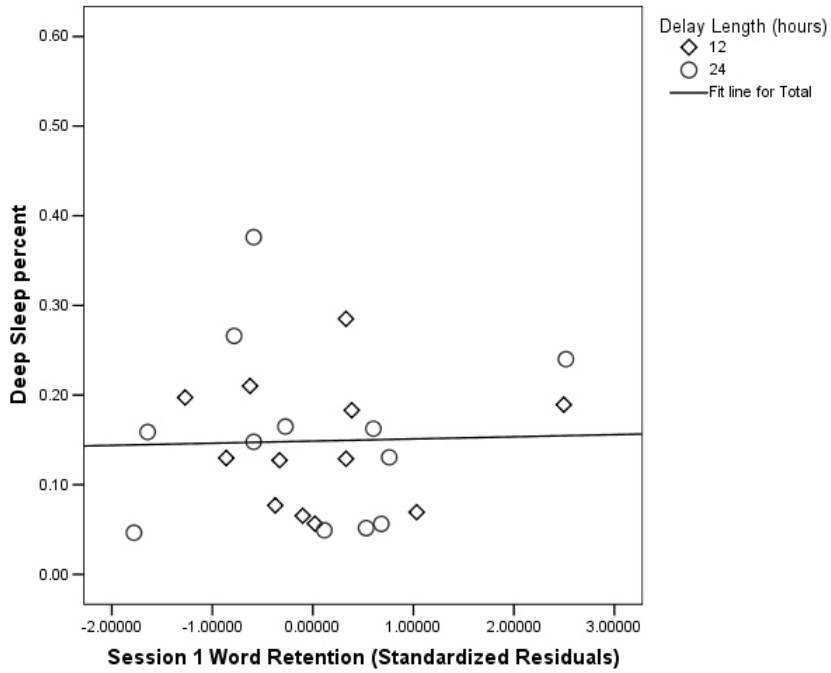
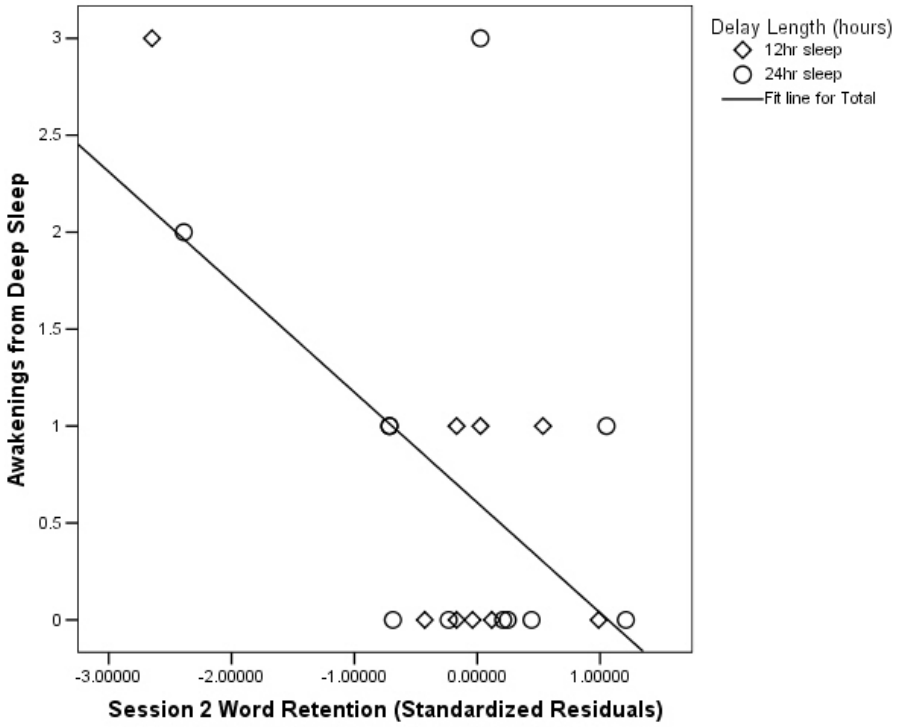


Figure 4

Scatterplot demonstrating the relationship between Session 2 memory retention and number of awakenings from deep sleep in the older adults.



Appendix A: *Example of the final cued recall test.*

Paired Associate Word Recall (version 1A)

Instructions: Recall and write down the word(s) that was previously associated with the word on the left side of the paper. The word(s) may have been learned in this experimental session or in the previous (the first) experimental session. If more than one word was associated with the word on the left then write down both words. Otherwise, leave one of the spots blank.

CHANNEL	_____	_____
TENNIS	_____	_____
LOAFER	_____	_____
CIRCUIT	_____	_____
ABYSS	_____	_____
RECEIPT	_____	_____
PUDDING	_____	_____
DEGREE	_____	_____
FORFEIT	_____	_____
BUILDER	_____	_____
VALUE	_____	_____
QUIVER	_____	_____
WHISKER	_____	_____
GRAPHITE	_____	_____
WIZARD	_____	_____
JACKET	_____	_____
RAILROAD	_____	_____
LINEN	_____	_____
TAILOR	_____	_____

SATIN	_____	_____
PAYMENT	_____	_____
SHADOW	_____	_____
MUSIC	_____	_____
ASPECT	_____	_____
TITLE	_____	_____
HERRING	_____	_____
ADVERB	_____	_____
PROGRAM	_____	_____
GARLIC	_____	_____
JOURNAL	_____	_____

Appendix B: *Example of the final cued recall recognition test.*

Paired Associate Word Recognition Test (version 1A)

Instructions: For each of the below words, there will be four options on the right. Circle the option that was previously learned to be associated with the word on the left.

1. CHANNEL: RESULT EFFECT CAUSE REACTION
2. TENNIS: STRAIGHT TALL UPRIGHT NARROW
3. CIRCUIT: KNOWLEDGE INSIGHT EXPERIENCE UNDERSTAND
4. ABYSS: FOOTBALL AUTUMN CALENDAR SEASON
5. RECEIPT: THIRST FOUNTAIN SPLASH WATER
6. FORFEIT: RESTRAINT PATIENCE TOLERANCE COMPOSURE
7. BUILDER: GRAVEL ROAD ROCKS STONES
8. QUIVER: CELERY REDUCE DIET WEIGHT
9. GRAPHITE: FUNCTION PURPOSE ROLE TASK
10. WIZARD: BABY CRADLE CRIB BASSINET
11. JACKET: REPAIR MAINTENANCE UPKEEP SERVICE
12. RAILROAD: CREVICE CRACK CLEFT FISSURE
13. TAILOR: CLUB RACQUET GLOVE STICK
14. SATIN: BUTTON CLASP FASTEN HOOK
15. MUSIC: REGION DIVIDE SECTOR QUARTER
16. ASPECT: SUBSTITUTE SURROGATE PROXY DELEGATE
17. HERRING: LOBBY HALL ENTRANCE FOYER
18. ADVERB: INTELLIGENCE SHREWD WISDOM LOGIC
19. PROGRAM: CHAIR SWING TABLE ROCKER
20. GARLIC: JOURNEY TRAVEL TOUR EXPLORE