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Sleep, Cognition, and Normal Aging: Integrating a Half-Century of Multidisciplinary Research

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Abstract

Sleep is implicated in cognitive functioning in young adults. With increasing age there are substantial changes to sleep quantity and quality including changes to slow wave sleep, spindle density, and sleep continuity/fragmentation. A provocative question for the field of cognitive aging is whether such changes in sleep physiology affect cognition (e.g., memory consolidation). We review nearly a half-century of research studies across 7 diverse correlational and experimental literature domains, which historically have had little crosstalk. Broadly speaking, sleep and cognitive functions are often related in advancing age, though the prevalence of null effects (including correlations in the unexpected, negative direction) in healthy older adults indicates that age may be an effect modifier of these associations. We interpret the literature as suggesting that maintaining good sleep quality, at least in young adulthood and middle age, promotes better cognitive functioning and serves to protect against age-related cognitive declines.

Keywords

memory consolidation; epidemiology; napping; sleep deprivation; actigraphy; polysomnography; neuropsychology; sleep pharmacology

Introduction

Across an 85-year lifespan, an individual may sleep nearly 250,000 hours, or over 10,000 full days. People often disparage time spent sleeping as "lost" time, but the persistent internal drive to sleep and its presumed universality across species would suggest that sleep is purposeful. Sleep science pioneer Allan Rechtschaffen put it most eloquently: "If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process ever made" (University of Chicago Sleep Laboratory, Smithsonian Institute, November, 1978).

Sleep does serve many functions, and these range from tissue restoration (Adam & Oswald, 1977) to brain metabolite clearance (Xie et al., 2013). Of particular interest to psychological scientists is sleep's role in cognitive functioning. Sleep loss has long been recognized to

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impair performance on attention and executive control tasks (see Bonnet, 2011, for a review). The more exciting possibility, however, is that normal sleep might *actively* promote memory stabilization and integration (see Table 1 for theories of the relation between sleep and memory) and this hypothesis has been supported across a diversity of psychological tests in *young adults* (Appendix). A topic of current interest is whether *aging* moderates the association between sleep and memory.

The present article focuses on sleep's implications for cognitive aging. Referring back to the estimate of 250,000 hours of sleep in a lifetime, a few assumptions become evident. First, this estimate assumed 8 hours of sleep per night, but sleep duration often declines across the lifespan (Bliwise, 1993). Furthermore, as depicted in Figure 1, sleep quality may change dramatically from young to older age: Sleep becomes more fragmented (i.e., older adults wake up more at night; e.g., Bliwise et al., 2009) and there is a decline in the quantity and quality of the "deep" stages of sleep such as slow-wave sleep and rapid eye movement sleep (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004).

If sleep functions to benefit memory and cognition in *young* adults, but is substantially altered in quantity/quality across the lifespan, then an alluring question is whether lifespan changes in sleep cause the widespread changes in cognitive functioning commonly observed in older adults (for overview of cognitive aging, see Cabeza, Nyberg, & Park, 2005). If so, then improving sleep might delay or reverse cognitive aging, as many authors have alluded (Altena, Ramautar, Van Der Werf, & Van Someren, 2010; Bruce & Aloia, 2006; Buckley & Schatzberg, 2005; Cipolli, Mazzetti, & Plazzi, 2013; Cirelli, 2012; Engel, 2011; Fogel et al., 2012; Goder & Born, 2013; Harand et al., 2012; Hornung, Danker-Hopfe, & Heuser, 2005; Kronholm, 2012; Pace-Schott & Spencer, 2011; Rauchs, Carrier, & Peigneux, 2012; Vance, Heaton, Eaves, & Fazeli, 2011; Wilckens, Erickson, & Wheeler, 2012). This "sleep—cognition hypothesis" (Feinberg & Evarts, 1969) has previously been challenging to verify because sleep, cognition, and aging represent three topics that are individually extremely rich, deeply broad, and diversely complex.

To fully address the question of whether age-related changes in sleep may be associated with age-related changes in cognition we have taken an integrative, multidisciplinary approach that incorporates experimental, clinical neuropsychological, and epidemiological literatures. Here we review 7 distinct and seldom cross-referenced domains, ranging from large-scale correlational studies that assessed self-reported sleep to experimental studies that deprived or extended sleep duration/quality. Table 2 provides an overview of the breadth of this review and the depth of each literature included. To foreshadow, some literatures produce curious findings (e.g., sleep deprivation affects young adults more than older adults) whereas other literatures highlight the potential for augmenting sleep (e.g., afternoon naps) to benefit cognitive functioning in middle-aged adults. We contend that these seven literatures provide complementary perspectives on how sleep and cognition interact as we age.

Wherever possible, we discuss findings separated across *young* (<30 years old), *middle-aged* (30–60 years old), and healthy *older* (\pm 0 years old) adult groups (Roebuck, 1979). By doing so we can begin to address whether age modifies sleep—cognition associations. Given

our focus on "normal" aging, we consider studies of abnormal aging (e.g., dementia, insomnia, sleep apnea; e.g., Cipolli et al., 2013) as well as developmental studies (e.g., Kopasz et al., 2010) to be beyond the scope of this review. Finally, to ensure that positive findings constitute strong supportive evidence, we have employed the conservative approach of reporting results following adjustment for demographics and comorbidities, whenever possible.

Self-Report Studies

We can begin to address sleep, cognition, and aging relationships by examining the most fully developed literature in this review: studies that simply asked adults how well they usually sleep. These self-report studies ask how many hours one typically sleeps, how long it takes one to fall asleep, how often one wakes up in the middle of the night, and how sleepy one feels during the day. The limitations of these studies will be evident in their reliance on subjective sleep measures and insensitive cognitive measures (e.g., mini mental state examination; MMSE), but their advantages in statistical power, attempts to capture habitual sleep patterns, adjustment for potentially confounding variables, and use of both cross-sectional and longitudinal designs are laudable.

Cross-Sectional Studies

Table 3 summarizes >40 studies that correlated self-reported sleep measures and cognitive functioning at a single time point. Studies conducted in *middle-aged* adults consistently linked sleep duration (e.g., short sleep) and waking up at night to poorer executive control (Regestein et al., 2004), working memory (Sternberg et al., 2013), episodic memory (Kronholm et al., 2009), attention (e.g., Krieg et al., 2001), and greater cognitive complaints (e.g., Roane et al., 2014). One explanation for these associations is that night-to-night sleep quality dictates day-to-day cognitive performance in middle-aged adults. For example, when maintaining a sleep diary and repeating a cognitive battery for 2–3 weeks, cognitive composite scores were lower the day after getting either less sleep or more sleep than normal (Gamaldo, Allaire, & Whitfield, 2010). Another interesting potential mechanism is that poor sleep in middle-aged adults could cause neurobiological impairments that summate over time. Consistent with this hypothesis, short sleep duration in cognitively-normal adults was recently linked to greater cortical β -amyloid burden (Spire et al., 2013), which is a precursor to cognitive declines (Bateman et al., 2012). We elaborate on this potential mechanism in the conclusions section.

Several cross-sectional studies have restricted their samples to *older* adults. Table 3 clearly shows that, as a whole, these studies have produced weaker results. First consider the evidence for short sleep duration. After controlling for demographic and/or health-related variables, most studies showed non-significant associations between cognitive measures and short sleep in *older* adults (see also Ramos et al., 2014). Interestingly, recent work indicates that the association between short sleep and episodic memory changes with increasing age such that *middle*-aged, but not *older*, adults showed this short-sleep—cognition association (Miller, Wright, Ji, & Cappuccio, 2014).

Perhaps sleep fragmentation rather than short sleep is the critical correlate of cognition in *older* adults. Increased nighttime awakenings were associated with poor memory in one small sample study (Mary, Schreiner, & Peigneux,, 2013; see also Sampaio, Sampaio, Yamada, Tsuboyama, & Arai, 2013), but puzzlingly, at least four studies have found the opposite pattern (Foley et al., 1995; Maggi et al., 1998; McCrae, Vatthauer, Dzierzewski, & Marsiske, 2012; Miller et al., 2014). The peculiar finding that greate wake time at night could be related to better cognitive performance in *older* adults is in notable contrast to the findings in *young* and middle-*aged* adults. Such unexpected results could be interpreted to mean: a) a hyperarousal mechanism (i.e., less sleep leads to hyperarousal which increases participant effort to perform the task); b) better self-awareness of sleep in adults who are more cognitively-intact (e.g., Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008), or c) Type I error in older adults. With regard to the above explanations, we note that some similar correlations emerge in studies that objectively-measured sleep.

One frequent cognitive association in *older* adults is with long sleep duration (e.g., ≥ 10 hours). Long sleep can indicate several diverse factors including underlying diseases and failing health (Grandner & Drummond, 2007). Additional consistent cognitive associations in older adults are difficulty falling asleep and daytime sleepiness (measured subjectively or as the frequency of needing to take daytime naps; but cf. Bliwise, Carskadon, Seidel, Nekich, & Dement, 1991). The conundrum here is how to cohesively explain such associations as *sleep-specific* effects when most supportive studies simultaneously found no correlation with short or fragmented sleep.

Sleep epidemiology studies typically incorporate 1–4 sleep questions, but the complexity and diversity of sleep symptoms might require more extensive questionnaires. The Pittsburgh Sleep Quality Index (PSOI: Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) is a 19-item questionnaire that uses a cutoff score to distinguish poor and good sleepers. In young adults, poorer executive function and attention performance is associated with poorer PSQI-defined sleep, independent of potentially confounding variables such as depression (Benitez, & Gunstad, 2012). In *older* adults, some provocative research suggests an association between PSQI and global cognition scores (e.g., MMSE; Amer, Hamza, El Akkad, & Abdel Galeel, 2013; Chang-Quan, Bi-Rong, & Yan, 2012; Lo, Loh, Zheng, Sim, & Chee, 2014; Potvin et al., 2012), executive control (Blackwell et al., 2014; Nebes, Buysse, Halligan, Houck, & Monk, 2009), and even spectroscopy estimates of glial functioning in brain regions associated with memory (hippocampus; Cross et al., 2013). However, some of the above studies did not control for cognitive status (i.e., combined healthy adults and patients), and a more perspicacious inspection of the literature reveals no shortage of null PSQI effects (≥ 10 studies) across a range of attention, executive control, working memory, problem solving, global cognition, and episodic memory tasks (Table 3). To presage a reoccurring theme in this review, Sutter, Zöllig, Allemand, and Martin (2012) concluded that, in *healthy older* adults, "poor sleep quality per se seems not to lead to changes in cognitive performance" (p. 773).

Longitudinal Studies

Does poor sleep in recent months predict cognitive decline years later? Table 4 summarizes the prospective epidemiological studies that have assessed self-reported sleep complaints as predictors of subsequent cognitive decline. At least eight such studies that included *middle-aged* adults have reported significant cognitive associations with short and/or fragmented sleep (e.g., waking up at night). Increased wake time at night predicted increased cognitive complaints and instrumental disabilities two years later (Stenfors, Hanson, Oxenstierna, Theorell, & Nilsson, 2013) and 28 years later (Kulmala et al., 2013), respectively. Moreover, short sleep duration predicted poorer performance on telephone-based cognitive tests 22 years later (Virta et al., 2013). Complementary and supportive evidence arises from four studies that indicated that poor sleep at baseline predicted development of cognitive disorders including mild cognitive impairment and Alzheimer's disease (Table 4; Lobo et al., 2008). These studies, however, did not always control for comorbidities.

The Whitehall II Study (Ferrie et al., 2011) provides some of the strongest evidence in support of a role for sleep in *middle-aged* adults as a protector against cognitive declines in *normal* aging. In this epidemiologically-famous longitudinal study, a shift from sleeping 6–8 hours/night at baseline to shorter sleep duration 5 years later was associated with lower cognitive performance on most cognitive measures (the surprising exception was episodic memory; cf. Devore et al., 2014). Thus, there is support for the hypothesis that sleeping well in *middle age* promotes sustained cognitive integrity.

Poor sleep may be a weaker predictor of declining cognition when baseline mesures were assessed in *older* adults. Similar to the cross-sectional studies, sleep fragmentation (i.e., nighttime awakenings) was not a strong correlate of cognitive performance in *older* adult samples, and two studies even reported that nighttime awakenings ("difficulty maintaining sleep") was associated with significantly *better* cognitive preservation (Jaussent et al., 2012; Pedraza, Al Snih, Ottenbacher, Markides, & Raji, 2012). Such findings are somewhat surprising given much of the zeitgeist of sleep—cognition findings in *young* adults (Rasch & Born, 2013; Rolls et al., 2011).

Though difficulty falling asleep correlated with cognitive functioning in *older* adults in cross-sectional studies (Table 3), 5 of 7 longitudinal studies in *older* adults suggested no association (see Table 4 column labeled "SOL"). Subjective sleepiness is a moderately consistent predictor of cognitive decline (see Table 4 column labeled "EDS"), but we would stress to the reader that even this finding becomes non-significant after controlling for depression (Quesnot & Alperovitch, 1999) and general health (Blackwell et al., 2014; Sterniczuk, Theou, Rusak, & Rockwood, 2013). The strongest evidence for short sleep duration in old age leading to speedier cognitive decline arises from the Nurses' Health Study (N>15,000; Devore et al., 2014), but readers might suspend judgment on this issue because at least five papers failed to show this effect (Table 4).

Summary, Critique, and Future Research Directions

In *middle-aged* adults, short and poor quality sleep is often associated with, and can even precede, cognitive declines. In *older* adults, self-reported sleep measures have been less

consistently linked to poorer cognitive functioning. This pattern sets the stage for predicting age-related modification of sleep—cognition associations, a theme that we consider in the remaining sections.

Some of the modest effects in this literature might reflect our conservative approach of emphasizing effects following correction for demographic and health-related variables, including depression. The interplay of sleep and depression is fascinating in that even though depression might independently explain cognitive effects (Lichtenberg, Ross, Millis, & Manning, 1995), sleep deprivation has sometimes been experimentally linked to increased depressive symptoms (Kahn-Greene, Killgore, Kamimori, Balkin, & Killgore, 2007). Therefore, future research in aging populations should attempt to disentangle causality (perhaps using structural equation modeling; Olaithe, Skinner, Hillman, Eastwood, & Bucks, 2014) amongst sleep, depression, and cognitive variables (cf. Vanderlind et al., 2014).

The sleep epidemiology literature provides a foundation for beginning to understand sleep, cognition, and aging associations. Despite its strengths, this literature is limited in several important ways. Cognitive psychologists will lament the overuse of the MMSE, which may be insensitive to cognitive variability in healthy adults. Furthermore, sleep neuroscientists are likely to question the validity of the subjective nature of the sleep measures. In the remaining sections we discuss attempts to more objectively measure sleep and more precisely measure cognitive performance.

Motor Activity (Actigraphy) and Neuropsychological Testing

Actigraphy is a small device that measures motor activity and is typically worn as a wristband (e.g., Fitbit®, Actiwatch®). Some sleep researchers have capitalized on actigraphy-defined periods of little or no movement as being a proxy for sleep. The benefits of actigraphy are it places minimal burden on the participant and researcher and it can be worn for weeks (i.e., to assess *habitual* sleep patterns). Though actigraphy estimates sleep/ wake state it cannot measure sleep stages, and importantly, as sleep quality gets worse the reliability and validity of actigraphy diminishes (de Souza et al., 2003; Paquet, Kawinska, & Carrier, 2007; Sivertsen et al., 2006). Put bluntly, it is possible to lie motionless for hours and still be unable to sleep (but actigraphy may score as sleep; e.g., Montgomery-Downs, Insana, & Bond, 2012). Nonetheless, actigraphy is an attractive option for attempting some objective measurement of sleep.

Studies with small-to-medium sized samples of cognitively-normal *older* adults have produced varied associations between actigraphy variables and episodic memory, problem solving, executive function, and processing speed performance (Cochrane, Robertson, & Coogan, 2012; Miyata et al., 2013; Oosterman, van Someren, Vogels, Van Harten, & Scherder, 2009; Parsey et al., 2012; Regestein et al., 2004; Scullin, 2013; Westerberg et al., 2010; Wilckens, Woo, Erickson, & Wheeler, 2014). These studies typically did not control for demographic or health-related variables (cf. Olaithe et al., 2014). In one study that controlled for age and depression, Cochrane et al. (2012) found one significant *unexpected* correlation (shorter sleep duration was associated with better episodic memory), one

Three epidemiology studies collectively involving thousands of participants—Rush Memory and Aging, Study of Osteoporotic Fractures, and the Osteoporotic Fractures in Men Studyhave reported several significant correlations (Blackwell et al., 2006; 2011a; 2014; Lim et al., 2012, 2013). Though their findings consistently demonstrated that individuals with poorer actigraphy-defined "sleep" (i.e., rest-activity variability) showed poorer cognitive performance (sometimes even using longitudinal data; Lim et al., 2013), these studies typically used very old age groups and they often included mild cognitive impairment and dementia patients. Thus, their meaning for "normal" aging is uncertain. On the one hand, these results could be viewed as supportive to findings that poor sleep is associated with β amyloid deposition (Spira et al., 2013). On the other hand, collapsing across control and dementia groups that are known to differ both on sleep and cognition (possibly due to a third unrecognized process) might bias one to find actigraphy-cognitive correlations, even if an association did not exist in the healthy controls. Consider, for example, that in the Osteoporotic Fractures in Men Study, age significantly moderated the cognitive association with nighttime awakenings such that these correlations were minimal/absent in 65–79 year old adults (i.e., the group more likely to include cognitively-normal adults; Blackwell et al., 2011a).

Summary, Critique, and Future Research Directions

The results of large-scale actigraphy studies suggest an association between motor activity ("sleep") and cognitive measures. Age modification of sleep—cognition associations was not a strong theme in this literature (cf. Section A), though many of the actigraphy studies focused on very old sample groups (cf. Blackwell et al., 2011a). Because most of the actigraphy studies were cross-sectional we need to consider direction of causation: Evidence that cognitive declines can precede changes in sleep (Yaffe, Blackwell, Barnes, Ancoli-Israel, & Stone, 2007) may indicate that a common neurobiological substrate (e.g., amyloid deposition; Ju et al., 2013) underlies both cognitive and sleep impairments in *older* adults. Thus, the major, unanswered question is whether common neurobiological underpinnings are caused by poor sleep, poor cognition, both factors, or a related "third" process.

Actigraphy is a low-cost and non-invasive tool for measuring sleep in population-based studies, but its use remains highly controversial. Correlations between actigraphy-and electroencephalography(EEG)-defined sleep variables in *older* adults are lamentably low (rs < .25) and may reflect underlying disorders (Mehra et al., 2008), which can independently explain poorer cognitive functioning (e.g., Kushida et al., 2012; Pearson et al., 2006). Prudence thus requires us to look for converging evidence for cognitive associations using the gold standard in sleep measurement, polysomnography.

Polysomnography and Neuropsychological Testing

Polysomnography (PSG) is the gold standard in capturing the complexity of sleep physiology. PSG measurement involves recording electrophysiological data from electrodes attached to the scalp (at frontal, central, and occipital EEG sites), beside the eyes (to identify

eye movements), and on the chin (to evaluate movements and muscle tone). More elaborate PSG recordings are possible, but even this simple approach allows one to measure sleep stages, microarchitecture (e.g., sleep spindles), and sleep continuity/fragmentation (Figure 1).

One might hypothesize that several PSG variables should correlate with cognitive functioning. First, sleep duration (and nighttime awakenings) can be precisely measured using PSG; if the subjective- and actigraphy-based reports (see the previous sections) validly reflect associations between sleep and cognition, then they should replicate with PSG. Second, PSG allows measurement of slow-wave sleep (SWS), which has a neurophysiological signature suggestive of cortical plasticity and memory processing in *young* adults. In SWS, brain regions that are recognized to be important to memory functioning (hippocampus, frontal cortex) are believed to "dialogue" against a quiet subcortical background (Buzsáki, 1996; Buzsáki & Peyrache, 2013; Logothetis et al., 2012; Massimini, Huber, Ferrarelli, Hill, & Tononi, 2004). Third, "sleep spindles," suggested to reflect synaptic plasticity mechanisms (Rosanova & Ulrich, 2005), are also detected with PSG. Fourth, one can isolate periods of rapid eye movement (REM) sleep, which is characterized by vivid dreaming, increased cerebral blood flow in several regions (e.g., the amygdala; Maquet et al., 1996), and increased cholinergic activity which might promote long term potentiation (Diekelmann & Born, 2010).

Table 5 summarizes studies that have evaluated overnight PSG in relation to neuropsychological testing in *older* adults. These studies sometimes included patients with dementia or psychiatric conditions and cross-sectional differences in PSG variables relative to healthy older adults are well recognized (e.g., Cipolli et al., 2013; Foley et al., 2003; Loewenstein et al., 1982; Palma, Urrestarazu, & Iriarte, 2013; Prinz et al., 1982a; Reynolds et al., 1985). In this section, we focus on normal aging and whether neuropsychological test performance—which is presumably "trait-like," but may incorporate some "state" effects is associated with PSG measures of sleep duration, SWS, REM sleep, or spindle density. To foreshadow, early studies (*First Wave*) did not consistently link PSG variables to cognitive measures, but more recent studies (*Second Wave*) have suggested a potential age-related modification of PSG—cognitive associations.

First Wave (1967–1999)

Feinberg, Koresko, and Heller (1967) pioneered the study of whether PSG variables correlate with performance on intelligence tests in *older* adults. They found that performance correlated positively with REM sleep (but also negatively with SWS). Most early PSG—cognition studies were limited by sample size. However, in one impressive early study, 119 middle-to-older-aged adults underwent five consecutive nights of PSG recording (Berry & Webb, 1985). Consistent with the conclusions from the Self-Reported Sleep literature (e.g., Sutter et al., 2012), "sleep and cognitive variables known to be sensitive to aging processes failed to intercorrelate robustly" (p. 334, Berry & Webb).

It is impressive that the "first wave" of PSG and neuropsychological studies included four longitudinal studies (Guazzelli et al., 1986; Hoch et al., 1994; Prinz, 1977; Spiegel, 1981). Two studies suggested that baseline cognitive levels, or longitudinal changes in cognition,

predicted poorer PSG-measured sleep (rather than vice versa; Hoch et al.; Prinz), but most studies reported very few significant effects with cognitive measures. For example, Feinberg and colleagues (1986) found that the correlations expected based on contemporary memory studies (Rasch & Born, 2013)—such as those between frontal spindle density and face recognition and memory for names—were consistently near zero or nominally negative (even in a 3-year follow-up; I. Feinberg, personal communication, June 23, 2013). Likewise, a 14-year study produced sporadic correlations (i.e., in both positive and negative directions) with REM measures (Spiegel, Herzog, & Koberle, 1999; Spiegel, Koberle, & Allen, 1986). Counterintuively, older adults who showed greater awakenings from sleep/SWS at baseline showed more preserved cognition.

Second Wave (1999-present)

With a few exceptions, interest in correlating PSG and neuropsychological measures in healthy *older* adults dwindled in the 1980s (Bliwise, 1989). The last decade, however, has seen a "second wave" (p. 135, Vertes, 2004) of interest. One advancement is the utilization of more technologically sophisticated analyses of PSG data. One approach is to calculate the number of microarousals (i.e., very brief awakenings) that occurred during SWS and REM sleep (Hita-Yañez, Atienza, Gil-Neciga, & Cantero, 2012), but these precise sleep fragmentation measures did not correlate with episodic memory in cognitively-normal *older* adults after controlling for age (J. Cantero, personal communication, February 15, 2013).

Another approach is to analyze EEG spectral power so as to capture not only the quantity, but presumably also the *quality*, of SWS. For example, analyzing spectral power in the *delta* range (0.5–4 Hz) provides a measure that conflates the incidence and amplitude of slow waves. Null effects are still sometimes observed (e.g., Seeck-Hirschner et al., 2012), however, in one study (Anderson & Horne, 2003) that analyzed spectral power in only the 0.5–1.0 Hz frequency range (motivated by Steriade, Nunez, & Amzica's, 1993, studies) during the first ~42 minutes of sleep, spectral power correlated positively with performance on many attention, executive function, and intelligence tests in older adults (cf. Mathias, Zihl, Steiger, & Lancel's, 2005, experimental study).

Similarly-focused attempts to extract precise components of sleep physiology include computer-automated analyses of sleep spindles. Sleep spindle counts have been associated with cognitive performance in young adults (Fogel & Smith, 2011; Nader & Smith, 2001), and two studies reported that episodic memory correlated with spindle density in aging adults (Table 5). Thus, early studies ("first wave") may have missed some PSG—cognition correlations because they primarily focused on sleep stage quantity, rather than on early-sleep delta spectral power or sleep spindles. Another worthwhile consideration is that many studies in this literature used broad age ranges. Returning to an overarching theme initially prompted by the findings of the self-report literature, could *age* be a modifier of the PSG—cognition relationship?

Three studies examined SWS correlates of a vigilance task in different age groups. In *young* adults, poorer vigilance task performance was associated with less SWS (Jurado, Luna-Villegas, & Buela-Casal, 1989), and similar findings emerged in *middle-aged* adults, albeit perhaps less consistently (Edinger, Glenn, Bastian, & Marsh, 2000). By contrast, in healthy

older adults, no such correlations were observed (Crenshaw & Edinger, 1999). These findings suggested that "the degree to which slow-wave sleep restores neurocognitive processes among normal sleepers changes as a function of aging" (p. 127, Edinger et al.).

An exciting possibility is that it is age-related physiological changes—and *not age per se* that modifies SWS—cognition relations. As an initial step toward addressing this possibility, one study measured cerebral oxygen reserve (or, more broadly, cerebrovascular risk) during SWS-rich sleep in 112 older adults without sleep apnea (Carlson, Neelon, Carlson, Hartman, & Bliwise, 2011). During early SWS, cerebral oxygenation increases in most *young* adults, but decreases or does not change in most *older* adults (Carlson, Neelon, Carlson, Hartman, & Dogra, 2008). Critically, *older* adults who showed a similar increase (as young adults) in cerebral oxygenation during SWS showed relatively preserved episodic memory performance.

Summary, Critique, and Future Research Directions

The PSG and neuropsychological testing literature has a rich, but often forgotten, history. Across nearly half a century of research, PSG studies have failed to provide converging evidence for self-report- and actigraphy-based findings that short sleep duration correlates with cognitive performance (Table 5). Furthermore, there was little evidence for specific relations between particular cognitive abilities and particular PSG variables in *older* adults. Consider, for example, studies that used tasks dependent on executive function (N-back, Wisconsin's Card Sorting Task, Trail Making Task B, switching attention): The predominant finding was no PSG correlation with executive function, and when significant correlations were observed, the particular PSG correlate was observed only in a single study.

Does preserved SWS correlate with preserved episodic memory in *older* adults? This popular hypothesis was not supported by the studies in Table 5 that included tests of visual memory, verbal memory, face-name pair learning, or the Wechsler Memory Scale (see Table 5 for correlations with spindle density, REM sleep, and nighttime awakenings, though null correlations were most common). Verbal fluency, which is presumably a measure of semantic memory that relies on frontal and temporal lobes (Baldo, Schwartz, Wilkins, & Dronkers, 2006), was the only cognitive ability to demonstrate any replicability in correlating with SWS measures in *older* adults.

One important technical consideration for SWS is that there is a strong reduction in slowwave EEG amplitude in *older* adults, and traditional SWS scoring criteria (Rechtschaffen & Kales, 1968) dictate that slow-wave amplitude must exceed 75μ V. Therefore, one might be concerned that SWS duration does not correlate with cognitive variables only because of the scoring method used (i.e., using amplitude rather than frequency). This explanation does not account for null SWS findings in studies in which the analyses ignored traditional amplitude criteria (e.g., Berry & Webb, 1985).

A weakness of the PSG literature is the overreliance on small sample sizes (except Blackwell et al., 2011b; Yaffe et al., 2011), which is commonly assumed to decrease statistical power, but also increases risk of Type I errors (Button et al., 2013; Yarkoni, 2009). Another limitation is that computer-automated spindle detection has been extensively

validated in healthy *young* adults, but only minimally in older adults. A third challenge for the field will be to demonstrate that spectral power correlations with cognitive measures represent *sleep-specific* effects, and not trait-based EEG correlations that could be observed during wakefulness (Finnigan & Robertson, 2011; Vlahou, Thurm, Kolassa, & Schlee, 2014).

Despite equivocal evidence for short sleep and SWS quantity, REM sleep often correlated with cognitive performance in older adults. Such findings seem to converge with early animal studies (Markowska et al., 1989; Stone, Altman, Berman, Caldwell, & Kilbey, 1989) and with reports of cross-sectional differences in REM sleep between healthy controls and dementia patients (Allen, Seiler, Stahelin, & Spiegel, 1987; Dykierek et al., 1998; Feinberg et al., 1967; Prinz et al., 1982a/b; Reynolds et al., 1985/1988; Vitiello et al., 1984). The crucial, unanswered question here is whether the reduction in REM and the development of dementia are both epiphenomenal to other mechanisms such as decreased cholinergic neurotransmission (cf. Stone, Rudd, Parsons, & Gold, 1997; Yaffe et al., 2007) or if loss of REM sleep drives cognitive changes (via, e.g., reduced long term potentiation).

Multiple studies suggested associations between cognitive measures and time awake after going to bed (Table 5; cf. Tables 3–4). The correlational findings with time awake converge with some of the actigraphy literature's findings. However, in the next section, readers will likely be surprised by the striking contrast between these correlational findings and the findings of the experimental sleep deprivation literature.

Experimental Sleep Deprivation Studies

A typical finding in healthy *young* adults is that sleep deprivation causes poorer cognitive performance (Williams, Lubin, & Goodnow, 1959; for reviews, see Durmer & Dinges, 2005; Killgore, 2010), which some have pointed out to be reminiscent of cognitive impairments with increasing age (Harrison, Horne, & Rothwell, 2000). Sleep deprivation has numerous neurobiological and psychological effects (e.g., stress) that could potentially mediate sleep—cognition associations (Bonnet, 2011), but the general approach in the literature is to view loss of sleep as a manipulation of sleep per se. The experimental sleep deprivation literature therefore provides a reasonable test of the hypothesis generated by the correlational studies in all three previous sections that short sleep (or increased wake time at night) causes poorer cognitive functioning in *older* adults.

Several behavioral studies examined sleep deprivation in only middle-aged or only older adult groups. These studies suggested some detrimental consequences of sleep deprivation/ fragmentation to "state" cognition (Bonnet, 1985; Carskadon & Dement, 1985; Froberg, Karlsson, Levi, & Lidberg, 1975; Webb; 1986; Williams et al., 1959; Williams, Gieseking, & Lubin, 1966). For example, Van Der Werf et al. (2009) reported that in 12 middle-toolder-aged adults that fragmenting SWS led to visual memory encoding impairments.

Table 6 lists experimental studies that compared *young* adults to *middle*-aged or healthy *older* adults following normal sleep versus sleep deprivation/fragmentation. Webb and colleagues' (1982; 1985) early studies conducted with *middle-aged* faculty members raised the possibility that the cognitive effects of sleep deprivation increase with age; yet the more

common theme that emerges from 30 years of experimental research is that sleep deprivation/fragmentation affects cognitive functioning in young adults, but *has less of an effect, no effect, or even a facilitating effect* on cognitive functioning in older adults (16 of the 20 studies in Table 6). It is possible that some of the reduced effects in *older* adults reflect diminished baseline performance in older adults (i.e., floor effects), but this explanation cannot account for studies in which older adults outperformed their younger counterparts following sleep deprivation (e.g., Duffy, Willson, Wang, & Czeisler, 2009; Stenuit & Kerkhofs, 2005). Another concern is the overreliance on vigilance tasks, but similar age modification effects have been observed with episodic memory (Bonnet & Rosa, 1987) and multitasking (Nesthus, Scarborough, & Schroeder, 1998).

Summary, Critique, and Future Research Directions

Sleep deprivation's minimalistic impact on cognition in *older* adults is somewhat surprising in light of the studies that correlated short sleep and/or increased time awake at night with poorer cognitive performance (Tables 3–5). First consider non-sleep-specific mechanisms for this age dissociation. Some argue that sleep deprivation primarily impairs cognitive performance in young adults at the nadir of their body temperature rhythm (i.e., a circadian, not a sleep, effect; Bonnet, 2011); the reduced change in cognitive performance in older adults might therefore reflect that the strength of such body temperature fluctuations diminishes with aging. A second possibility is that the cognitive repercussions of sleep deprivation are mediated by sleep-loss-induced cortisol elevations (Spiegel, Leproult, & Van Cauter, 1999). Elevated cortisol is a known correlate of cognitive impairments (McEwan & Sapolsky, 1995), but cortisol would be unlikely to explain the age interactions discussed herein (Maggio et al., 2013) because age does not moderate the cortisol and sleep-loss relationship or the cortisol—cognition relationship (Lee et al., 2007; Vgontzas et al., 2003).

Next consider sleep-specific interpretations. One possibility is that older adults are chronically sleep deprived and depriving of them of additional sleep will have minimal effects. However, age-dissociations are still present in studies that selected for good-sleeping older adults (e.g., Adam, Retey, Khatami, & Landolt, 2006). Additional possibilities are that older adults need less sleep than young adults (e.g., Bliwise, 2000; 2011) or that sleep is less restorative to cognitive functions (Edinger et al., 2000), and thus, less detrimental to cognition when lost. The behavioral results of the sleep deprivation and aging literature are clear, but the explanation for such effects requires further attention.

Experimental Napping and Sleep Extension Studies

Humans are encouraged to sleep 8 hours per night, but often fail to achieve this standard. If chronic sleep loss plagues modern American society, and if even mild sleep deprivation impairs cognition (Van Dongen, Maislin, Mullington, & Dinges, 2003), then extending sleep would be expected to improve cognitive functioning (cf. Buysse, Grunstein, Horne, & Lavie, 2010). *Could taking a daily nap be our society's solution*? The practice of regular napping has been observed in "Blue Zones" (Buettner, 2012), which are areas such as Ikaria, Greece where adults commonly live healthy lives into their 90s ("nonagenarians"; see also Asada, Motonaga, Yamagata, Uno, & Takahashi, 2000; cf. Table 3). Furthermore, in infants, children, adolescents, and young adults, daytime naps have been linked to improved

cognitive performance and memory consolidation (for reviews, see Kopasz et al., 2010; Mednick, 2006; Milner & Cote, 2009). Similar cognitive benefits of prophylactic naps (Schweitzer, Randazzo, Stone, Erman, & Walsh, 2006) and naps during a night shift (Purnell, Feyer, & Herbison, 2002) have been documented in *middle-aged* shift-workers (Ficca, Axelsson, Mollicone, Muto, & Vitiello, 2010). In this section, we evaluate experimental studies that investigated whether napping on a single day or across several weeks boosts cognitive functioning in (non-shift-worker) aging adults.

Nap Experiments (1–2 Days)

Some early napping, cognition, and aging work was well-designed but limited by ceiling effects (Tamaki, Shirota, Hayashi, & Hori, 2000; Tamaki, Shirota, Tanaka, Hayashi, & Hori, 1999). Subsequent work, however, has provided compelling evidence that an afternoon nap benefits middle-aged adults' cognitive functioning. When 32 healthy middle-to-older-aged adults were given a two-hour early afternoon nap or rest opportunity, napping led to improved reaction time and Stroop performance (Campbell, Murphy, & Stauble, 2005). Similarly, 10 young adults, 10 middle-aged adults, and 12 middle-to-older-aged adults completed cognitive testing before and after short naps (20-min), long naps (60-min), and no-nap reading conditions (Milner & Cote, 2008). Some nap-related cognitive benefits were observed (e.g., serial addition/subtraction performance), and these benefits did not significantly interact with age group. However, statistical power may have been a limiting factor; for example, in the 60-minute nap condition, serial addition/subtraction accuracy increased pre-to-post nap in the young adults and middle-aged adults, but decreased pre-topost nap in the *middle-to-older*-aged adults. In another study that focused only on *older* adults (N=24), there were no significant differences in episodic memory, attention, working memory, or procedural memory across 60-minute nap versus rest conditions (Wan, 2013). Thus, there is persuasive evidence for the cognitive value of napping in *young* and *middle*aged adults, but such benefits may decrease with increasing age.

Nap-based Sleep Extension Interventions (Weeks)

Some napping studies have been designed to increase 24-hour sleep across several days or weeks (Creighton, 1995). These studies have failed to demonstrate an experimental benefit of increased sleep on cognitive functioning. In one study, 21 middle-to-older-aged adults adhered to a month-long short- or long-nap regimen (there was not a no-nap control group; Campbell, Stanchina, Schlang, & Murphy, 2011), and in another study, nine healthy older adults took a 90-minute early afternoon nap or rested (no-nap) across 17 days (Monk, Buysse, Carrier, Billy, & Rose, 2001). The experimental manipulation increased 24-hour sleep duration in both studies, but no experimental group differences were observed across a range of executive control, intelligence, and attention tasks.

Summary, Critique, and Future Research Directions

Taking an afternoon nap improves cognitive functioning in *middle-aged* adults. Such benefits might not extend to *older* adults and this finding converges with evidence that older adults' cognitive functioning is minimally impacted by sleep deprivation. Future research should use no-nap control conditions and control the amount of nocturnal sleep prior to the

nap. This literature would also benefit from disentangling whether naps improve overall cognitive ability (transfer), or alternatively, consolidation of trained tasks, the topic to which we next turn our attention.

Experimental Studies of Memory Consolidation

The newest frontier in sleep, cognition, and aging research focuses on memory consolidation. There exist several theories of memory consolidation (see Table 1), but a consistent theme is that after a memory is encoded (i.e., learned or perceived) it must undergo a process of stabilization and integration (i.e., consolidation) if it is to later be retrieved (i.e., recollected). For at least 50 years, psychological scientists have hypothesized that memory consolidation declines with increasing age (Doty & Doty, 1964), but researchers have only recently focused on *sleep-dependent* memory consolidation and aging.

Sleep's role in memory consolidation has been elegantly demonstrated in human and animal studies that showed that memories are "replayed" and strengthened during sleep (Rasch, Buchel, Gais, & Born, 2007; Wilson & McNaughton, 1994; Yang et al., 2014). Though the sleep and memory consolidation field is not without some controversy and debate (Rickard, Cai, Rieth, Jones, & Ard, 2008; Siegel, 2001; Vertes, 2004; Vertes & Siegel, 2005) our interpretation is that the diversity of supportive empirical evidence (Appendix) is sufficiently compelling to conclude that there exists an active role for sleep in memory in *young* adults (Hennevin, Huetz, & Edeline, 2007; Oudiette & Paller, 2013; Rasch & Born, 2013).

In a typical memory consolidation study, participants study verbal materials or learn a motor memory task in the evening, then sleep and are re-tested in the morning. Memory consolidation is a "state-dependent" effect that is inferred following sleep relative to wake-only intervals when procedural (non-declarative) memory performance increases, when episodic (declarative) memory forgetting is reduced, or when a qualitative change in the memory trace is observed (e.g., integration). The procedures in the memory consolidation literature are typically derived from experimental psychology (Appendix) rather than from clinical neuropsychology or epidemiology.

The most straightforward prediction for *aging* is that as sleep becomes shortened, fragmented, and less "deep" (i.e., lower SWS), the sleeping brain may engage in less memory consolidation. If so, then the loss of memory consolidation during sleep might be one reason for the weakening evidence for sleep—cognition associations in *older* adults: If active cognitive processes are *not* occurring during sleep then sleep variables would not be expected to correlate with cognitive variables (Tables 3–6). Indeed, in animal studies, both *young* rodents and "*middle-aged*" rodents tend to show "replay" of memories during sleep (i.e., reactivation of learned hippocampal sequences; Huxter, Miranda, & Dias, 2012), but sleep-dependent memory replay is diminished in *older* rodents (Gerrard, Burke, McNaughton, & Barnes, 2008). Behavioral evidence from animal models also supports the idea of an age-related decline in memory consolidation (e.g., Hermann et al., 2007; Oler &

Markus, 1998; Ward, Oler, & Markus, 1999) In the following section, we address whether

there is an age-related change in sleep-dependent procedural memory (Table 7) and episodic memory (Table 8) consolidation in aging humans.

Procedural Memory Consolidation

In young adults, consolidation of procedural memories is most often linked to sleep spindles and REM sleep (Plihal & Born, 1997; Walker, 2009). These aspects of sleep change in quantity and quality across the lifespan (e.g., Martin et al., 2013; Ohayon et al., 2004). Therefore, one would predict less procedural memory consolidation during sleep in *older* adults.

One of the largest experimental studies on procedural memory consolidation in *older* adults, compared REM fragmentation, non-REM fragmentation, REM rebound (i.e., increased REM sleep following a night of REM deprivation), and pharmacologically-enhanced sleep (cholinesterase inhibitor) conditions to a placebo, normal-sleep control group (Hornung, Regen, Danker-Hopfe, Schredl, & Heuser, 2007). The major finding was that only the cholinergic medication accelerated overnight improvements in the procedural memory task. The characteristics of REM sleep certainly differed across experimental conditions (e.g., REM density), but it was still surprising that relative to the control condition, the sleep fragmentation groups did not affect procedural memory consolidation.

The early conclusion that "REM sleep does not critically affect procedural memory consolidation in old age" (p. 755; Hornung et al., 2007) has been generally supported by subsequent research. Consider Table 7. Whereas at least 10 studies in *middle-aged* adults showed behavioral evidence for overnight procedural memory improvements (but perhaps with an age-related decline; Dresler, Kluge, Genzel, Schussler, & Steiger, 2010; Roig, Ritterband-Rosenbaum, Lundbye-Jensen, & Nielsen, 2014; Wilson, Baran, Pace-Schott, Ivry, & Spencer, 2012), no sleep-specific improvements were observed in 7 of the 8 studies that experimentally contrasted sleep and wake retention intervals in *middle-to-older* adult groups. The studies that suggested relatively preserved procedural memory consolidation with aging either mixed wake and sleep over long time intervals or suggested that sleep-related benefits emerge only after repeated testing (i.e., "late/plateau" improvements; e.g., Tucker, McKinley, & Stickgold, 2011).

Current research focuses on *how* procedural memory consolidation changes with aging. One possibility is that procedural memory consolidation in older adults occurs equally across both wake and sleep intervals (Nemeth et al., 2010; 2013; Pace-Schott & Spencer, 2013). Though *young* adults are expected to display some consolidation across wake intervals (e.g., Dewar, Alber, Butler, Cowan, & Della Sala, 2012), the absence of additional benefits from sleep might reflect a failure of the sleeping brain to "replay" the procedural memory (cf. animal models; Gerrard et al., 2008). Supportive evidence in humans arises from two studies in which young and older adults were trained on a motor skill and then slept. In one study that used neuroimaging (Fogel et al., 2014), *young* adults showed post-training activation in frontal, parietal, and hippocampal regions during sleep; these patterns were not observed in *older* adults. In another study (Peters, Ray, Smith, & Smith, 2008), *young* adults demonstrated a significant boost in sleep spindle density following motor skill training, which is a reproducible finding (in young adults; Fogel & Smith, 2011). By contrast, *older*

adults did not demonstrate training-related increases in spindle density, but interestingly, they showed a significant increase in SWS quantity. SWS might therefore act as a compensatory mechanism in older adults, but additional work on this intriguing hypothesis is required because SWS did not correlate with memory measures (K. Peters, personal communication, March 6, 2013).

Episodic Memory Consolidation

Episodic memory refers to explicit memories for events, and is often distinguished from other forms of declarative memory such as semantic (general knowledge) memory (Tulving, 1972; 2002). In young adults, episodic memory consolidation has most often been linked to SWS (Diekelmann & Born, 2010) or to spindles (Fogel & Smith, 2011), both features of sleep that change in quantity and quality with aging (Carrier et al., 2011; Ehlers & Kupfer, 1989; Martin et al., 2013). Table 8 illustrates that most (aging) studies using young and *middle-aged* adults provided some behavioral evidence for sleep-dependent episodic memory consolidation. In older groups, one well-designed study suggested preserved sleepdependent episodic memory consolidation (Wilson et al., 2012) whereas at least five other studies indicated some age-related impairments for at least some episodic memory tests (Table 8). With few exceptions, these studies used simple verbal learning procedures rather than employing experimental psychology manipulations such as emotional memory tradeoff, directed forgetting, or contextual prospective memory procedures, methodologies which have been critical to convincingly demonstrating sleep-dependent memory consolidation in young adults (Appendix). Furthermore, these studies have generally not evaluated possible neurobiological, cardiovascular, or endocrine moderators of consolidation (but see Mander et al., 2013b), which when identified may explain variability across studies (cf. Carlson et al., 2011).

Identifying the PSG correlate(s) of episodic memory consolidation in aging adults has been challenging, perhaps because most work showed no behavioral evidence for consolidation in *older* adults (i.e., if there is no memory consolidation, then there should be no PSG correlate of the memory consolidation measure). Nevertheless, some work has connected overnight retention of episodic memories to spindle density (Seeck-Hirschner et al., 2012) and ability to maintain sleep (i.e., few awakenings; Conte, Carobbi, Errico, & Ficca, 2012; Mazzoni et al., 1999). Others have failed to observe correlations with spindles (and sigma spectral power; Hornung et al., 2007, 2009; C. Westerberg, personal communication, July 22, 2013) or reported a positive correlation between retention and time awake at night (Seeck-Hirschner et al., 2012).

Much work on episodic memory consolidation and aging has focused on the role of SWS. Table 8 indicates that in some *middle-aged* adult samples that memory consolidation correlated with SWS duration (Backhaus et al., 2006, 2007; Deak, Stickgold, Pietras, Nelson, & Bubrick, 2011). The SWS picture is still murky in *older* adults: SWS duration is typically not associated with overnight retention of episodic memories, but some have reported positive correlations with delta spectral power, which quantitatively blends the incidence and amplitude of slow waves (Mander et al., 2013b; Westerberg et al., 2012). These positive findings notwithstanding, we were again surprised to see that three studies

have observed *negative* correlations between SWS duration and retention of veridical memories (Mazzoni et al., 1999; Seeck-Hirschner et al., 2012) and lure (false memory) recognition (Lo et al., 2014b). Perhaps this literature can be cohesively explained by drawing a distinction between SWS quantity and SWS *quality* (operationalized as delta spectral power), but before drawing this conclusion we encourage researchers to consider the following evidence: a) delta power during *wakefulness* is associated with cognitive performance in older adults (Vlahou et al., 2014), b) overnight word pair retention was unaffected in older adults when Non-REM sleep was experimentally fragmented (Hornung et al., 2007), and c) overnight episodic memory retention was not affected by pharmacologically increasing delta power in SWS (Hornung et al., 2009).

Summary, Critique, and Future Research Directions

The burgeoning memory consolidation and aging literature is still developing, and therefore a few methodological weaknesses remain to be addressed. The reliance on small sample sizes and the absence of young-adult and wake-only control conditions are frequent limitations. We also must carefully consider the inferences drawn from studies that reported significant correlations between PSG and memory variables but demonstrated *no experimental benefit of sleep* (relative to wake). Correlating PSG variables with memory performance regardless of experimental effects is a very common practice (e.g., Scullin, 2013), but should we interpret such correlations as *sleep-specific* effects? Cognitive measures correlate with delta and theta spectral power during *wakefulness* in older adults (Finnigan & Robertson, 2011; Vlahou et al., 2014), and therefore, we caution against interpreting PSG—memory correlations as evidence for *sleep-dependent* memory consolidation in the absence of converging experimental evidence for consolidation.

Despite some limitations, several interesting themes are emerging in the aging and memory consolidation field. Middle-aged adults tend to demonstrate somewhat-dampened evidence for episodic and procedural sleep-dependent memory consolidation. In many (if not most) cases, *older* adults show reduced (or no) evidence for overnight memory consolidation. To the extent that memory consolidation forms the building blocks of optimal cognitive functioning (e.g., Mazzoni et al., 1999), the loss of sleep-dependent memory consolidation might accelerate cognitive aging and result in weaker sleep— cognition associations.

We were again surprised to see multiple reports of *negative* correlations between memory and SWS quantity (Lo, Sim, & Chee, 2014; Mazzoni et al., 1999; Seeck-Hirschner et al., 2012; refer back to Section C: Bastien et al., 2003; Buechel et al., 2011; Feinberg et al., 1967; Platt et al., 2011; Scullin, 2013; Spiegel, 1981), though some studies did not show a concomitant experimental sleep effect. One interpretation of negative SWS—cognition correlations is "overactive" synaptic downscaling (Table 1), whereby too much SWS might prune synapses that would otherwise support memory in older adults (Scullin, 2013; cf. Chang et al., 2006). Another interpretation is that slow EEG activity represents pathologic neural activity, as suggested by waking EEG data in severe cognitive disorders (Fernandez et al., 2002). Another conceivable alternative is that because SWS duration is negatively associated with REM duration, the negative correlations might potentially reflect a compensatory role for REM sleep in episodic memory consolidation in older adults (cf.

Table 5). A fourth interesting possibility is that negative SWS correlations might indicate more gist-like memory processing (e.g., Payne et al., 2009). According to this view, the negative SWS correlations may reflect the tendency for *older* adults to engage in gist-based rather than detail-based remembering (Adams, 1991; Castel, McGillivray, & Friedman, 2012).

It is important to recognize that not all SWS is created equal (fragmented SWS, low-density SWS, etc.). Understanding the individual and contextual conditions supporting *memory-promoting* SWS should therefore be a priority for future research on aging. For example, memory consolidation in *older* adults might depend on initial learning strength (Tucker & Fishbein, 2008), retrieval efficiency (Bizzozero et al., 2008), anxiety or arousal levels (Nielson, Wulff, & Arentsen, 2014; Platano, Fattoretti, Balietti, Bertoni-Freddari, & Aicardi, 2008), prefrontal cortex and hippocampal connectivity (Mander et al., 2013b), cerebral oxygenation (Carlson et al., 2011), cholinergic (e.g., Schredl, Weber, Leins, & Heuser, 2001) and/or dopaminergic modulation (Chowdhury, Guitart-Masip, Bunzeck, Dolan, & Duzel, 2012; Scullin, Trotti, Wilson, Greer, & Bliwise, 2012), but there are likely many other influential factors.

Nocturnal Sleep Interventions for Cognition

An important final question is whether interventions that improve the quantity and/or quality of overnight sleep also improve cognitive functioning (cf. napping). One approach to improving overnight sleep is to extend total time in bed or adjust sleep/nighttime habits (e.g., by routinizing bedtimes). These behavior-based sleep extension manipulations have been linked to positive cognitive outcomes in adolescents, young adults, and middle-aged adults (e.g., Dewald-Kaufmann, Oort, & Meijer, 2013; Lucassen et al., 2014; Mah, Mah, Kezirian, & Dement, 2011; but see Sadeh, Gruber, & Raviv, 2003). One study is suggestive of a similar benefit in healthy *older* adults (Klerman & Dijk, 2008), but this study did not control for practice effects (Shipstead, Redick, & Engle, 2012). In a similar vein, psychological therapies such as cognitive-behavioral therapy, can be applied to treat insomnia in older adults (Morin, Culbert, & Schwartz, 1994), but such clinical trials typically have not included cognitive performance or memory consolidation as an outcome (cf. Altena, Van Der Werf, Strijers, & Van Someren, 2008; Haimov & Shatil, 2013; Sun, Kang, Wang, & Zeng, 2013).

Another approach is to bolster sleep-dependent memory consolidation, for example, via targeted memory reactivation (Oudiette & Paller, 2013). One method for reactivating memories during sleep is to wait until the participant is in SWS and then play sounds over a speaker that were previously encoded during word learning, such as a "meow" sound if the word "cat" was previously studied (Rudoy, Voss, Westerberg, & Paller, 2009). Enhanced memory consolidation is inferred when recall is greater for cued words than for non-cued (counterbalanced) words. This procedure was successfully applied to increase memory consolidation in a small sample that included *middle-aged* adults (Fuentemilla et al., 2013), but no such study has been published in *older* adults. The only published attempt at increasing SWS-dependent episodic memory consolidation in *older* adults used transcranial current stimulation (Eggert et al., 2013), which when applied to *young adults* increases SWS

density and episodic memory consolidation (Marshall, Molle, Hallschmid, & Born, 2004). However, in *older* adults, the stimulation neither benefited SWS nor affected memory consolidation.

A fascinating, but controversial question is whether pharmacologically impairing or improving sleep impacts cognitive functioning. Antidepressants have been associated with REM suppression and their (lack of) impact on cognitive function was the subject of much debate a decade ago (Vertes, 2004; Walker & Stickgold, 2004; for a potential resolution, see Dresler, Kluge, Genzel, Schussler, & Steiger, 2010, and Goerke, Cohrs, Rodenbeck, & Kunz, 2014). Furthermore, there is a paradox that sleep hypnotics might improve memory consolidation (e.g., Mednick et al., 2013; but see Hall-Porter, Schweitzer, Eisenstein, Ahmed, & Walsh, 2013), while also causing anterograde amnesia or psychomotor slowing in *young* adults. Though clearly a complex and controversial area (Vermeeren & Coenen, 2011), we can currently ask whether common sleep medications demonstrate any benefits to memory consolidation or cognitive performance in *older* adults after the hypnotic effect of the medication has presumably dissipated.

In *young* adults, zolpidem (Ambien®) increases sleep spindles (Feinberg, Maloney, & Campbell, 2000) and possibly episodic memory consolidation (Mednick et al., 2013). Research is inconclusive regarding zolpidem's effect on delta spectral power (for review, see Monti, Spence, Pandi-Perumal, Langer, & Hardeland, 2009). In *older* adults, zolpidem can improve sleep continuity, REM sleep, and SWS duration (e.g., Kummer et al., 1993), but it does not improve next-day memory or cognitive performance (Allain, Bentué-Ferrer, Tarral, & Gandon, 2003; Fairweather, Kerr, & Hindmarch, 1992; Hindmarch, Legangneux, Stanley, Emegbo, & Dawson, 2006; Otmani et al., 2008; Scharf, Mayleben, Kaffeman, & Krall, 1991). Similar null effects (or even reserved direction effects) in *older* adults have been reported with eszopiclone (Lunesta®; Hemmeter, Müller, Bischof, Annen, & Holsboer-Trachsler, 2000; Leufkens & Vermeeren, 2009).

Pharmacological studies that specifically targeted SWS (tiagabine, sodium oxybate, gaboxodol) produced results consistent with age-modification of SWS—cognition associations. These SWS medications improved cognitive performance in *young* and *middle-aged* adults (Walsh et al., 2006, 2010), but did not impact episodic memory and working memory in healthy *older* adults, even when delta spectral power was enhanced (Mathias et al., 2005; also see Baker & Vitiello, 2013; Benedict, Chapman, & Schiöth, 2013). Finally, controversy surrounds whether melatonin is a "true" hypnotic (van den Heuvel, Ferguson, Mila Macchi, & Dawson, 2005; Zhdanova, 2005), but there is interesting pilot data that melatonin may benefit cognition in healthy older adults (Peck, LeGoff, Ahmed, & Goebert, 2004) and Alzheimer's disease patients (Cardinali, Furio, & Brusco, 2010).

Summary, Critique, and Future Research Directions

The extent to which increasing memory consolidation on a nightly basis could ameliorate cognitive declines and/or (re)strengthen sleep—cognition associations is an exciting avenue for further research. We expect this line of work to be challenging because the external stimulation techniques used to reactivate memories in *young* adults (e.g., playing a "meow" sound for the studied word "cat") might cause disruptions to sleep in *older* adults because

older adults are more likely to awaken in response to auditory stimuli (even in SWS; Zepelin, McDonald, & Zammit, 1984). Age-related neurobiological changes such as decreased hippocampal—neocortical connectivity (Grady, McIntosh, & Craik, 2003) and reduced brain derived neurotrophic factor (Calabrese, Guidotti, Racagni, & Riva, 2013) may also constitute significant barriers to increasing memory consolidation in older adults.

Current attempts at pharmacologically-enhancing sleep, which produce some positive outcomes in *young* adults, have nearly uniformly failed to improve memory and cognition in *older* adults. The null findings do not seem to be attributable only to lingering hypnotic effects or to failures to augment SWS duration or delta spectral power. These experimental studies might indicate that sleep physiology (e.g., SWS, sleep continuity) is not causally related to cognitive functioning in *older* adults; however, this literature still needs to evaluate whether sleep medications do not improve memory because they are not enhancing spindles in the "fast" spindle frequency range (Fogel & Smith, 2011) and whether melatonin can benefit cognitive functioning via improved sleep quality.

The most successful intervention for improving cognitive functioning in aging adults might combine treatments that target not only sleep, but also psychological health, the endocrine system, and exercise (among others; Benloucif et al., 2004; Dzierzewski et al., 2014; Horne, 2013; Naylor et al., 2000; Snigdha, de Rivera, Milgram, & Cotman, 2014; Tanaka & Shirakawa, 2004). Importantly, even if sleep interventions ultimately have no impact on memory in *older* adults, improving sleep may still have several non-cognitive benefits including improved quality of life (Arakawa, Tanaka, Toguchi, Shirakawa, & Taira, 2002; Faubel et al., 2009; Reid et al., 2010), mental health (Driscoll et al., 2008; Tanaka et al., 2001; 2002), and longevity (Dew et al., 2003; Marin, Carrizo, Vicente, & Agusti, 2005). Sleeping ~250,000 hours across the lifespan is time well-spent!

Conclusions and Interpretations

Nearly half a century of research has investigated sleep—cognition associations in normal aging (Feinberg et al., 1967). One of the most exciting trends in the self-report literature is that poor sleep in *middle*-age is linked to neurodegeneration-related biomarkers (e.g., amyloid deposition) and subsequent cognitive decline. Similar findings emerge when using movement-based actigraphy and EEG-based polysomnography, but the studies in these literatures often mixed healthy older adults with patient groups. Furthermore, healthy older adults did not always demonstrate clear associations between sleep and cognitive functioning.

In the experimental literatures, several thought-provoking themes have materialized: Sleep deprivation causes greater cognitive impairments in young adults than in older adults, sleep promotes memory consolidation in young adults more so than in older adults, and napping and enhancing nocturnal sleep benefit cognitive functioning in *young* and middle-aged adults but often not in *older* adults. Thus, the seven literatures reviewed herein indicate that in *older* adults inter- and intra-variability in sleep often do not relate to cognitive functioning, and solely improving sleep may not reverse cognitive impairments. We will consider five perspectives that might account for these findings.

The first explanation is that sleep does not relate to cognitive functions—in particular to memory consolidation—even in young adults (Rickard et al., 2008; Siegel, 2001; Vertes, 2004). Therefore, memory consolidation (and trait-like cognition) should not be associated with sleep in older adults. Though we acknowledge that memory consolidation studies sometimes suffer methodological weaknesses such as small sample sizes, analytical missteps, and inflated effect sizes (Button et al., 2013), the quantity and breadth of evidence for a role for sleep in memory consolidation in *young* adults is very strong (see Appendix and Rasch & Born, 2013). The mechanisms underlying this relationship, however, are still a matter of lively debate (Table 1).

A second explanation is that all sleep—cognition findings in older adults are complementary at a holistic level, and point to specific, preserved associations between particular cognitive domains and particular aspects of sleep quality. For example, one might only predict an association between SWS quality and episodic memory. The null findings in these 7 literatures may therefore be due to misguided selection of cognitive tests, imprecise measurements of cognitive functioning (e.g., MMSE), and/or inadequate measurement and analysis of sleep (self-report versus PSG, sleep quantity versus quality, etc.).

The two above explanations might be considered opposite ends of a spectrum ranging from no cognitive association with sleep *per se* in older adults to a wholly preserved association that is masked by measurement. We are inclined to believe that the truth lies somewhere in between. If we assume that sleep and cognitive functions are associated in *young* adults (Appendix), then the 7 sleep, cognition, and aging literatures we reviewed might indicate that there is an age-related change in sleep—cognition associations. The next three perspectives—reduced sleep need, compensation, and functional weakening—consider the possible nature of this change.

One provocative idea is that we need sleep less as we age. Rather than lamenting the loss of, for example, SWS with increasing age some researchers argue that SWS declines simply because it is a remnant of maturational processes from earlier in life (Feinberg, 2000). Or, if degree of daytime learning dictates amount of SWS (rather than vice versa; see synaptic downscaling theory, Table 1), and if learning tendency or ability decreases with aging, then the need for SWS would decrease as a natural consequence (Cirelli, 2012). The "sleep need" view is provocative, but has been difficult to test (e.g., Bliwise, 2000).

Assuming similarity in "sleep need" with increasing age, a fourth possibility draws upon the compensation theory of neurocognitive aging (e.g., Park & Reuter-Lorenz, 2009). By this view, specific cognitive functions (e.g., procedural memory) that were once supported by specific aspects of sleep (e.g., REM) might receive additional support (or become dedifferentiated) from another aspect of sleep (e.g., SWS; cf. Peters et al., 2008). Consider also that in *young* adults sleep preferentially supports memory consolidation, but consolidation can still occur in the wake state (e.g., Carr, Jadhav, & Frank, 2011; Dewar et al., 2012). Thus, it is possible that in response to age-related changes in sleep physiology, older adults' brains compensate by increasing the frequency of wake-based memory consolidation (e.g., Nemeth et al., 2013; Pace-Schott & Spencer, 2013; Salas et al., 2014).

A fifth framework is that the sleep—cognition link grows less resilient as we age because the aging brain can no longer efficiently support sleep-specific cognitive processes. Several researchers have noted this "functional weakening" possibility (Edinger et al., 2000; Kronholm, 2012; McCrae et al., 2012; Pace-Schott & Spencer, 2011; Schmidt, Peigneux, & Cajochen, 2012; Scullin, 2013; Spiegel et al., 1986), and some supportive evidence was observed in most of the reviewed literatures. Though functional weakening remains relatively unexplored, this view uniquely predicts that increasing the quantity of sleep in older adults is unlikely to restore cognitive abilities because age-related neurobiological changes (e.g., neural atrophy, decreased plasticity, nocturnal hypoxia, neuroendocrine changes, altered neuromodulation) that are presumably necessary to support sleep-specific cognitive processes will still be impaired. In the context of episodic memory consolidation, the widespread age-related neurobiological changes may cause SWS to no longer be "memory promoting" even when SWS density and amplitude are relatively preserved. Consider functional weakening within the context of the systems consolidation view (Table 1) that memories are reactivated in the hippocampus and transferred to the neocortex during SWS: If the hippocampus, neocortex, or hippocampal—neocortical connections are greatly impaired (Grady, 2012), then hippocampal-neocortical consolidation will not occur regardless of the quantity of SWS.

A particularly intriguing possibility is that sleep disturbances per se cause changes in sleep's cognitive functions across the lifespan (e.g., prompting compensation attempts and/or weakening sleep—cognition links). Acute sleep deprivation and chronic sleep restriction have diverse effects on allostatic load including increases in blood pressure, evening cortisol levels, insulin, proinflammatory cytokines, and sympathetic tone (McEwen, 2006; Vgontzas et al., 2004), all which are hypothesized to accelerate cognitive aging (McEwen & Sapolsky, 1995). Furthermore, sleep deprivation/restriction in young animals can cause protein misfolding (Naidoo, Ferber, Master, Zhu, & Pack, 2008), decreased tau phosphorylation (Di Meco, Joshi, & Pratico, 2014; Rothman, Herdener, Frankola, Mughal, & Mattson, 2013), and increased amyloid deposition (Kang et al., 2009; Xie et al., 2013), which impair memory consolidation (e.g., Borlikova et al., 2013; Freir et al., 2011) and underpin Alzheimer's disease (Hardy & Selkoe, 2002). If these effects accrue "for years in a silent but irreversible manner" (Hita-Yanez et al., 2012, p. 293), then sleep disturbances in young and middle-age could be at the root of subsequent cognitive decline, even when no sleep—cognition associations are observed in old age.

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Appendix

Sample List of Cognitive Tests and Experimental Paradigms Implicated in Sleep and Consolidation Studies.

Cognitive Test	Reference	Cognitive Test	Reference
Procedural/Per	ceptual Memory	<u>Episodic</u>	Memory
Visual discrimination	Karni et al., 1994	Nonsense syllables	Jenkins & Dallenbach, 1924
Mirror-tracing task	Plihal & Born, 1997	Word associates	Ekstrand, 1967
Semantic priming	Stickgold et al. 1999	Emotional and neutral texts	Wagner et al., 2001
Finger tapping	Walker et al., 2002a	Virtual maze	Peigneux et al., 2004
Opposition task	Fischer et al., 2002	Face-name pairs	Clemens et al., 2005
Visuomotor adaptation	Huber et al., 2004	Remember/know judgment	Hu et al., 2006
Implicit tone structure	Durrant et al., 2011	Object locations	Rasch et al., 2007
Melody production	Antony et al., 2012	Face locations	Talamini et al., 2008
		Emotional scenes	Payne et al., 2008
Creativity	and Insight	DRM lists	Fenn et al., 2009
Anagrams	Walker et al., 2002b	Prospective memory	Scullin & McDaniel, 2010
Number reduction	Wagner et al., 2004	Retrieval induced forgetting	Racsmány et al., 2010
Transitive inference	Ellenbogen et al., 2007	Dream content	Wamsley et al., 2010
Remote associates task	Cai et al., 2009	Microeconomics lecture	Scullin et al., 2011
Unusual uses task	Ritter et al., 2012	Directed forgetting	Rauchs et al., 2011
		IAPS pictures	Baran et al., 2012
Working Memo	bry and Updating	Cartoons	Chambers et al., 2013
N-back	Kuriyama et al., 2008	Testing effect	Bäuml et al., 2014
Digit span	Scullin et al., 2012		
		Language	Acquisition
Animal	Learning	French class	De Koninck et al., 1989
Inhibitory avoidance	Fishbein, 1971	Phonemes	Fenn et al., 2003
Vocal learning	Dave et al., 2000	Abstraction	Gómez et al., 2006
Courtship conditioning	Donlea et al., 2011	Vocabulary	Gais et al., 2006
Location of food reward	Martin-Ordas et al., 2011	Lexical competition	Dumay et al., 2007
Auditory classification	Brawn et al., 2013	Storybooks	Williams et al., 2014

References are sorted chronologically within cognitive domains.

Abbreviations. DRM: Deese-Roediger-McDermott; IAPS: International Affective Picture System

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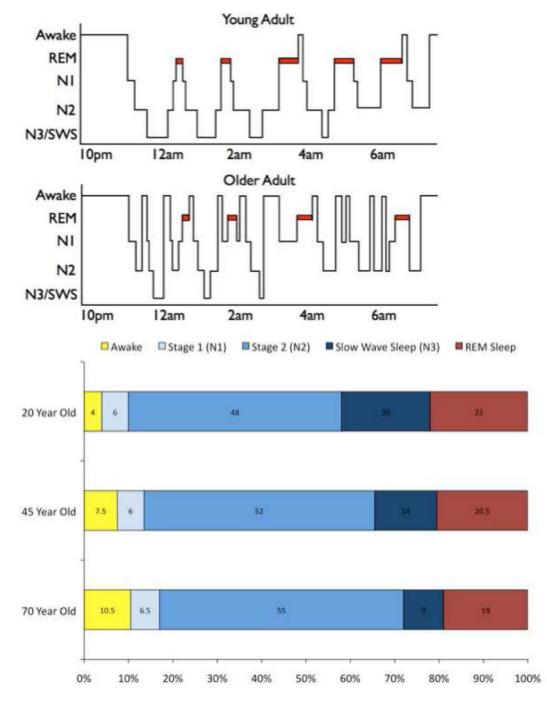


Figure 1.

Table 1

Influential Theories of the Relation between Sleep and Memory.

Theory Name	Description	References
Interference	Sleep passively protects memories against daytime interference	Jenkins & Dallenbach (1924)
System Consolidation	The hippocampus reactivates memories and transfers them to neocortical regions, primarily during sleep	Marr (1971); McClelland et al. (1995)
Synaptic Consolidation	Hippocampal long-term potentiation, primarily induced during REM, strengthens synaptic representations of memories	Bramham & Srebro (1989)
Dual Stage Consolidation	SWS promotes episodic memory consolidation and REM sleep promotes procedural memory consolidation	Plihal & Born (1997)
Multiple Trace	Each memory reactivation results in a new, but altered and distributed, memory trace rendering retrieval increasingly easier	Nadel & Moscovitch (1997); Nadel et al. (2012)
Synaptic Homeostasis	Sleep promotes global downscaling of synaptic weights, resulting in an improved signal-to-noise ratio for memories	Tononi & Cirelli (2003)
Permissive/Opportunistic Consolidation	Sleep affords an environment conducive to, but not necessary for, consolidation to occur	Wixted (2004); Mednick et al. (2011)
Recovery and Stabilization	Sleep stabilizes memories and recovers performance following daytime interference	Brawn et al. (2010)
Selective Consolidation	Only memories tagged as "relevant" during encoding are reactivated during sleep and consolidated	Stickgold & Walker (2013)

Theories are listed chronologically. For further critical review of these theories, see Ellenbogen, Payne, and Stickgold (2006) and Frankland and Bontempi (2005).

Abbreviations. SWS: slow wave sleep; REM: rapid eye movement sleep

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Table 2

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Literature	# of Studies	Typical Sample	Comments on Young Age	Comments on Middle Age	Comments on Older Adults
Self-Reported Sleep Correlational Studies	Many	Large-to-Very Large Samples	Cross-sectional and longitudinal correlations	Cross-sectional and longitudinal correlations	Fewer correlations
Motor Activity (Actigraphy) and Neuropsychology Correlational Studies	Few-Medium	Medium-to-Large Samples	N/A (too few studies)	Activity and cognition often correlate	Activity and cognition often correlate
Sleep Brain Wave (PSG) and Neuropsychology Correlational Studies	Medium	Small-to-Medium Samples	Some sleep— cognition correlations	Some sleep— cognition correlations	Some sleep— cognition correlations
Sleep Deprivation Experiments	Medium	Small Samples	Many adverse cognitive consequences	Some adverse cognitive consequences	Minimal or no cognitive consequences
Napping Experiments	Few	Small Samples	Naps benefit cognitive functioning	Naps may benefit cognitive functioning	Naps have few or no benefits to cognition
Sleep-Dependent Memory Consolidation Experiments	Medium-Many	Small Samples	Sleep promotes memory consolidation	Consolidation may be reduced	Consolidation is often absent
Nocturnal Sleep Intervention Experiments	Medium	Small Samples	Better/more sleep benefits cognition	Some cognitive benefits observed	Few cognitive benefits observed

This table provides an introduction to each literature and is not intended to capture the nuances, exceptions, and moderating variables existent in each domain. Number of studies that used healthy middle-aged or healthy older adults are estimated as few (e.g., 10), medium (e.g., 20–30), and many (e.g., >50). Typical group sample size is approximated as small (e.g., n = 20), medium (e.g., n = 100), large (e.g., n = 1,000) and very large (e.g., n = 10,000).

Abbreviations. PSG: Polysomnography

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Reference	Sample	Age	Cognitive Measure	Short Sleep	Long Sleep	IOS	Early Waking	Night Waking	Daily Naps	EDS	PSQI/ SMHS
Roth 1999	1,000	218	Self-report				Ι				
Sternberg 2013^d	127,048	218	Battery	Ι	Ι						
Stenfors $2013^{d,c}$	8,362	\mathfrak{D}_{0}	Self-report				I				
Spiegelhalder 2008	60	24	Stroop								ns
Jennum 1994 ^{d,c}	1,504	30	Self-report			I	I	-		I	
Kronholm $2009^{d,c}$	5,171	20	Battery	-	-						
Regestein 2004 ^c	75	≱5	Battery								I
Xu 2011 <i>d,c</i>	28,670	2 0	MMSE, VerM	-	-						
Gildner 2014d	32,142	250	Battery	I	Ι						
Parsey 2012d	48	20	EPT	u	ns		I				ns
Ramos 2013 d,c	927	20	MMSE	su	Ι						
Miller 2014 d,c	8,789	250	Battery	Ι	Ι		+				
Lovato 2013	49	٤1	Double Span								ns
Foley 2004 <i>d.c</i>	1,506	25	Self-report	su		I	su	I		ns	
Dealberto 1996 d,c	1,389	¥0	Battery							su	
Faubel 2009 d,c	3,212	7 00	MMSE	su	Ι						
Ohayon 2002,2005 d,c	1,026	7 00	Self-report	Ι	su	ns			I	I	
Amer 2013	100	¥0	MMSE								I
Miyata 2013 ^d	78	¥0	N-Back, CPT								ns
Wan 2013 <i>d</i>	88	W 0	Battery		Ι	I					ns
Cross 2013	43	¥0	MMSE								su
Hoch 1994	50	±14	MMSE								su
Maggi 1998 d,c	2,398	¥65	MMSE				+	ns			

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Reference	Sample	Age	Cognitive Measure	Short Sleep	Long Sleep	SOL	Early Waking	Night Waking	Daily Naps	EDS	PSQI/ SMHS
Adam 2014 ^{d,c}	2,287	¥65	MMSE	u	ns		su				su
Habte-Gabr 1991 ^d	3097	2 65	VerM	<i>I</i> +		su					
Whitney 1998 ^{d,c}	4,578	202	MMSE							su	
Foley 1995	9,282	¥65	SPMSQ				+				
Auyeung 2013 d,c	2,947	¥65	MMSE	su	I	I			su		
Blackwell 2011a ^{d,c}	3,132	¥65	MMSE,TMT,DV	I	I					su	su
Cricco $2001^{d,c}$	6,444	202	SPMSQ				su				
Saint Martin 2012 ^d ,c	272	2 65	Battery	u	su	su				su	su
Mary 2013	16	¥65	VerM	u	ns			I			
Nebes 2009 ^c	157	¥65	Battery	su			I				I
Gamaldo 2008 d,c	174	¥65	Battery			Ι					
Newman 1997 ^{d,c}	5,201	¥65	MMSE			su	su	su		su	
Gooneratue $2003^{d,c}$	76	Z 65	FOSQ-V							I	
***Ward 2013 <i>d</i>	84	99 7	Battery							su	
Tworoger $2006^{d,c}$	1,844	≥70	Battery	I	su		I				
Hayward 1992	124	≥70	Battery				ns				
Foley 1999 ^d	2,905	271	CASI							I	
Schmutte $2007^{d,c}$	375	<i>2</i> 75	Battery	su	-	I		ns			
Chang-Quan 2012dc	660	067	MMSE	u	su		I				I

Studies are sorted by age (lower limit). Significant effects after adjustment for demographic $(^{d})$ and comorbidity $(^{c})$ variables are indicated when more sleep complaints correlate with poorer (-) or better (+) cognitive scores. Merged cells indicate combined measures, blank cells indicate not collected/reported measures, and ns indicates p > .05.

 $^{\prime}$ Might also or instead indicate that long sleep is associated with poorer memory

Sleep Abbreviations. EDS: excessive daytime sleepiness; PSQI: Pittsburgh Sleep Quality Index (total score); SMHS: St. Mary's Hospital Sleep Questionnaire; SOL: sleep onset latency (difficulty falling asleep)

FOSQ-V: functional outcomes of sleep questionnaire - vigilance subscale; MMSE: mini mental state examination; SPMSQ: short portable mental status questionnaire; TMT: trail making test; VerM: verbal Cognitive Test Abbreviations. CASI: Cognitive Abilities Screening Instrument; CPT: continuous performance test; DWRT: delayed word recall test; DV: Digit Vigilance; EPT: Everyday Problems Test; memory

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Table 4

)											
Reference	Sample	Age	Cognitive Measure	F/U (yrs)	Short Sleep	Long Sleep	SOL	Early Waking	Night Waking	Daily Naps	EDS
Osorio 2011 ^c	346	24	Diagnosis	7.7				I			
Stenfors $2013^{d,c}$	3,264	20	Self-report	2				I			
Loerbroks $2010^{d,c}$	689	≱0	TICS	8.5	ns	I					
Kulmala 2013 d,c	2,994	244	IADL	28				I			
Ferrie 2011 ^d	5,431	≥45	Battery	5.4	I	I					
Jelicic $2002^{d,c}$	838	≥46	MMSE	3			su	su			
Virta 2013 <i>d.c</i>	2,336	549	TICS, TELE	22.1	I	I					
Xu 2012 d,c	11,196	≥0	MMSE, VerM	3.8	I	su		su		su	
Sterniczuk 2013d	28,697	250	Diagnosis	4				su			su
Devore $2014^{d,c}$	15,385	26	Battery	6	I	I					
Quesnot 1999 d,c	1,389	259	MMSE	4							ns
Keage 2012 ^d	2012	¥65	MMSE	10	I	su	su		su	+	Ι
Potvin 2012 ^{d,c}	1,664	¥65	MMSE	1	I	I	I				
Benito-León 2009d	3,286	¥65	MMSE	3	ns	I					
Benito-León 2013 d,c	2,715	¥65	MMSE	3	ns	I					
Cricco $2001^{d,c}$	6,444	¥65	SPMSQ	3				-			
Jaussent 2012 d,c	4,894	¥65	MMSE, VisM	8			ns	ns	+		Ι
Blackwell 2014 d,c	2,822	¥65	MMSE, TMT	3.4	ns						ns
Tworoger $2006^{d,c}$	1,844	≥70	Battery	2	ns	ns	ns				
Foley $2001^{d,c}$	2,242	<i>2</i> 71	CASI	3				ns			-
Pedraza 2012 d,c	1085	<i>2</i> 75	MMSE	3			ns	ns	+		
Hahn $2013^{d,c}$	214	<i>2</i> 75	Diagnosis	6	ns						

functioning. F/U refers to follow-up time (in years), ns indicates p > .05, merged cells indicate combined sleep measures, and blank cells indicate that the measure was not collected or reported. Studies are Significant effects following adjustment for demographic (^d) and comorbidity (^c) variables (if reported) are indicated when more sleep complaints are associated with poorer (–) or better (+) cognitive listed by chronological age (lower limit).

Sleep Abbreviations. EDS: excessive daytime sleepiness; F/U: follow-up (years); PSQI: Pittsburgh Sleep Quality Index; SOL: sleep onset latency (difficulty falling asleep)

Cognitive Test Abbreviations. CASI: Cognitive Abilities Screening Instrument; Diagnosis: Patient received dementia diagnosis (including Alzheimer's disease); IADL: instrumental activities of daily living; MMSE: mini mental state examination; TICS: telephone interview for cognitive status; TMT-B: Trail making task Version B; SPMSQ: short portable mental status questionnaire; VerM: verbal memory; VisM: visual memory

Table 5

Perspect Psychol Sci. Author manuscript; available in PMC 2016 January 01.

Polysomnography and Neuropsychological Te	nd Neui	ropsyc	hological	Testing Studies.					
Reference	N	Age	TST	Wake	N1/N2	N3/SWS	REM	Spindle	(NS) Measures
"First Wave" of Studies									
Berry 1985	119	58	us	– AA7,RPM	+ AA7, $RPM^{(N1)}$	su	su		VIQ, PIQ, WMS
Spiegel 1981	57	64			4/- VIQ	+/- VIQ, RPM	– VIQ, RPM		PIQ
Spiegel 1986	43	69				su			VIQ, PIQ, RPM
Guazzelli 1986	48	72						su	VerM, VisM, VIQ, PIQ,TMT,VF,speed
Hoch 1994 d,c	50	75		– MMSE					
Feinberg 1967d	15	77	+ RPM	– RPM	su su	– RPM	+ PIQ,WMS	su	VIQ
Spiegel 1999	30	77		+ MMSE, ERFC	su	su	+/- MMSE, Vocab, ERFC		
Kahn 1969	16	80					+ Digit		WMS, VIQ, PIQ
Prinz 1977	12	82			su su	su	+ PIQ, WMS		διν
"Second Wave" of Studies	2								
Edinger 2008	84	49		– SRT, SAT					CPT
Lafortune 2014^d	58	63	su	su	su	+ VF	+ VerM	+VerM,VF CPT, Bells	N-Back
Bastien 2003	20	63	su	– VerM, WCST,PB	+ $VerM^{(N2)}$	su	su		VisM, TMT-A/B, WRT, DS (F/B)
Anderson 2003d	24	67				+WCST, VF CFI, ToL			PVT
Kim 2011 <i>d,c</i>	30	67		– VerM, VF, CP		+ BNT	MsiV +		
Hita-Yañez 2012/2013 d	25	67		su		su	su		WMS VerM
Seeck-Hirschner 2012 ^d	19	68	ns	su	ns	su	su	su	MMSE, TMT-A
Mander 2013a ^d	14	72						+ VisM/ VerM	

VerM, DS, VF, MMSE, TMT-B

+ TMT-B, DV

ns

-TMTB,DV MMSE^(N1)

- MMSE ns

- MMSE ns

81 76

2,909

Blackwell 2011b^{d,c}

Cole 2009

82

298 90

Yaffe 2011*d*,*c*

additional (ns) cognitive measures are listed in the rightmost column. Missing cells indicate that those data were not collected or reported. Studies are sorted by timing as in the main text (e.g., "first wave"), Statistically significant positive (+) or negative (-) correlations following adjustment for demographic (^d) and comorbidity (^c) variables (if reported). The cognitive correlate is listed in each cell, and and chronological age (mean age rounded). Steep Abbreviations. N1: Stage 1 sleep; N2: Stage 2 sleep; N3/SWS: slow wave sleep duration, slow wave density/slope, or delta spectral power; REM: rapid eye movement sleep; SOL: sleep onset latency; TST: total sleep time; Wake indicates number of nighttime awakenings, sleep efficiency, arousal index, Non-REM shifts, or total time awake.

reaction time; TMT: Trail Making Task (part A and/or B); VerM: verbal memory; VF: verbal fluency; VisM: visual memory; VIQ: Wechsler Adult Intelligence Scale - Verbal Intelligence Quotient; Vocab: Intelligence Scale - digit symbol; DS: Digit Span (Forward and Backward); DV: Digit Vigilance; ERFC: Évaluation rapide des fonctions cognitives; MMSE: mini mental state examination (including modified [3MS] versions); PB: Purdue Board; PIQ: Wechsler Adult Intelligence Scale - Performance Intelligence Quotient; PVT: psychomotor vigilance task; SAT: switching attention; SRT: simple Cognitive Abbreviations. AA7: Army Alpha Test 7; BNT: Boston Naming Test; CP: Constructional Praxis; CPT: continuous performance test; CFI: Cattell Fluid Intelligence; Digit: Wechsler Adult Wechsler Adult Intelligence Scale - vocabulary subtest; WCST: Wisconsin Card Sorting Task; WMS: Wechsler Memory Scale; WRT: Wilkinson reaction time **NIH-PA Author Manuscript**

Table 6

Experimental Sleep Deprivation/Restriction Studies That Assessed Whether Cognitive Impairment Varied By Age.

Reprivation Procedures log N=5 (M=22) N=5 (M=40) N=6 (18-22) N=10 (40-49) N=34 SaVb N=14 (M=27) N=12 (50-60) N=12 (50-60) SaVb N=14 (M=27) N=13 (M=51) N=12 (50-60) SaVb N=12 (19-39) N=10 (M N=10 (M N N=12 (18-28) N=10 (M N=10 (M N N=10 (M=23) N=10 (M N=10 (M N N=10 (M=23) N=10 (M N=10 (M N N=10 (18-24) N=10 (M N=10 (M N N=10 (18-24) N=10 (M N=10 (M N N=10 (M=20) N=10 (M N=10 (M N N=12 (M=21) N=10 (M N=10 (M N N=12 (M=25) N=10 (M N N=10 (M N N=16 (M=25) N=12 (M=23) N=10 (M N N N N=14 (M=23) N=10 (M N N N N N N=14 (M=23) N=10 (M N N N N N N N N		TIOIPprind	Measure	Interpretation
22) N=5 (M=40) 22) N=10 (40 49) 25) N=12 (50-60) $=27$ N=13 (M=51) $=23$ N=10 (M $=21$ N=10 (S $=23$ N=10 (S $=23$ N=10 (M $=23$ N=10 (M $=23$ N=10 (M $=23$ N=10 (M				
22) N=10 (40-49) 25) N=12 (50-60) =27) N=13 (M=51) (M=34 (19-39) N=12 (55 -28) N=13 (M=51) -28) N=10 (M -21) N=10 (M =21) N=10 (M =22) M=10 (M =23) N=10 (M =23) N=10 (M	64	64 hours	EEG	Young impaired <i>more</i> than older
25 N=12 (50-60) $=27$ N=13 (M=51) $=34$ (19-39) N=12 (55 -28 N=12 (55 $=23$ N=10 (55 $=20$ N=10 (55 $=21$ N=10 (55 $=20$ N=10 (55 $=21$ N=10 (55 $=22$ N=10 (55 $=23$ N=10 (55 $=23$ N=10 (56 $=23$ N=10 (M $=23$ N=10 (M		41 hours	Cognitive Battery	Young impaired less than older
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		2 nights	Cognitive Battery	Age effect depended on task
i=34 (19-39) i=32 (55) 28) N=12 (55) 23) N=10 (M) -24) N=10 (55) -21) =21) =21) =21) =21) =21) =21) =21) =21) =21) =23) =23) =23) Itation Procedures itation Procedures italion (M) =23) N=10 (M)		34 hours	Cognitive battery	Young impaired more than older
28) N=12 (55 24) N=10 (M 24) N=10 (55 20) N=10 (55 21) N=10 (55 21) N=10 (55 22) N=10 (55 22) N=10 (55 23) N=10 (55 100 N=10 (55 23) N=10 (M 23) N=10 (M	49	49.5 hours	IGT	Young impaired less than older
-23) N=10 (M -24) N=10 (55 -20) =0 (52 =21) =21 =25) =21 =25) =22 =25) =23 =23) n=10 (M =23) n=10 (M =23) N=10 (M	-	64 hours	Memory, RT	Young impaired <i>more</i> than older
24) N=10 (55 =20) ==21) ==21) ==25 =25 ==25 =========================		1 night	RT	Young impaired <i>more</i> than older
20) =20) =21) =21) =25) =25) =25) =22) =22) =22) =22) =22		4 AM testing	EEG	Young impaired more than older
=21) =21) =25) =25) =22) =23) =23) =23) =23) =23) N=10 (M)	N=10 (M=80) 1 1	1 night	Vigilance	Young impaired more than older
-21) -25) -25) -25) -22) -23) -23) -23) -23) -23) -23) -23	N=12 (M=67) 28	28 hours	Multiple RT tasks	Young impaired more than older
25) 22) 22) 22) 22) 22) 22) 22) 22] 22] 22	N=14 (M=67) 1 1	1 night	Cognitive battery	Young impaired more than older (in morning)
-25)	N=11 (M=66) 40	40 hours	PVT	Young impaired more than older
22) 23) 23) 265 (M=38) 23) 233 N=10 (M	N=11 (<i>M</i> =65) 40	40 hours	PVT	Young impaired more than older
=23) [N=11 (M=68) 26	26 hours	PVT	Young impaired more than older
tation Procedure N=65 (M=38) =23)	N=11 (M =68) 40	40 hours	Go/No-Go, RT	Young impaired more than older (some tests)
N=65 (M=38) N=11 (M=23)				
N=11 (M=23)	3,	5, 7, or 9 hours for 7 days	PVT	Young impaired slightly more than older
		4 hours for 3 nights	PVT, MWT	Young impaired more than older
Stenuit 2008 $N=10 (M=23)$ $N=10 (M=50)$	N=10 (M=60) 41	4 hours for 3 nights	Cognitive battery	Young impaired same as older
Bonnet 1989 N=12 (<i>M</i> =22) N=12 (<i>M</i> =63)		14 arousals/hour for 2 nights	Addition Task	Young impaired more than older
Filtness 2012 N=20 (M=23)	N=19 (M=67) 51	5 hours for 1 night	Driving simulator	Young impaired more than older

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Sample sizes and mean age (rounded) or range are separated by age groups. Papers are sorted by age comparison group and split by total sleep deprivation versus sleep restriction and fragmentation procedures.

Abbreviations. IGT: lowa Gambling Task; MWT=Maintenance of Wakefulness Test; PVT: Psychomotor Vigilance Task; RN=recovery night; RT=reaction time task

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Table 7

Procedural Memory Consolidation Studies in Healthy Middle-Aged and Older Adults.

Reference	Samples (Age)	Procedural Memory Tests	Retention Interval	Sleep- Related Benefit?	PSG-Memory Improvement Correlations
Studies that Primarily	~	ncluded Middle-Aged Adults (Mean Age <60)			
Djonlagic 2014	N=20 (M=35.3)	PVT, MST	~10 hrs (sleep-only)	Yes (MST)	Arousals $(-)^{(Age)}$
Backhaus 2006	N=13 (M=40.1)	MT	𝔅 hrs (sleep only)	Yes	
Genzel 2014	N=16 (M=41.8)	MST fast or paced (w/in-sub)	⊎ hrs (sleep only)	Yes	Spindle trend(+)
Manoach 2010	N=15 (M=42)	MST	9 hrs w/in-sub wake vs. sleep	Yes (late)	Null effect ^(Age) , I
Manoach 2004	N=14 (M=44)	MST	24 hrs (wake + sleep)	Yes	N/A
Deak 2011	N=9 (M=44.7)	MST	12 hrs w/in-sub wake vs. sleep	Yes (late)	
Nissen 2006	N=7 (M=44.9)	MT	10 hrs (sleep-only)	Yes	Null effects
Nissen 2011	N=53 (M=46.6)	MT	12 hrs b/n-sub wake vs. sleep	Yes	REM density (+)
Kloepfer 2009	N=20 (M=47.4)	MT	10.5 hrs (sleep-only)	Yes	Null effects
Nemeth 2013	N=17 (M=57.8)	Implicit ASRT	24 hrs (wake + sleep)	Yes	N/A
Oudiette 2011	N=18 (M=57.9)	Modified SRRT	13 hrs (sleep only)	Yes	
Studies that Primarily		ncluded Older-Aged Adults (Mean Age >60)			
Siengsukon 2009a/b	N=40 (M=62.3)	Explicit or implicit CTT (b/n-sub)	12 hrs b/n-sub wake vs. sleep	No	N/A
Siengsukon 2008	N=18 (M=65.6)	Implicit CTT	12 hrs b/n-sub wake vs. sleep	No	N/A
Terpening 2013	N=20 (M=66.1)	MST	~10 hrs (sleep-only)	Yes (late)	$SWS(+Late)^{(Age)}$
Hornung 2007	N=107 (M=66.1)	MT	10 hrs AChE-I, rem-reb, rem-/nrem-depr, sleep	Yes	Null effects ^(Exp)
Studies that Compared	l Multiple Age Groups	<u>.</u>			
Wilson 2012	-N=24 (<i>M</i> =25.9) -N=32 (<i>M</i> =44.0) -N=31 (<i>M</i> =63.1)	10-item SRTT (explicit)	12 hrs w/in-sub wake vs. sleep	-Yes -Reduced -No	N/A
Dresler 2010	-N=12 (<i>M</i> =25.3) -N=38 (<i>M</i> =47.0)	MST	24 hrs (wake + sleep)	-Yes -Reduced	N/A
Brown 2009	-N=14 (<i>M</i> =20.4) -N=12 (<i>M</i> =58.3)	SRTT	24 hrs (wake + sleep)	-Yes -No	N/A
Spencer 2007	-N=38 (<i>M</i> =20.8) -N=32 (<i>M</i> =59.0)	10-item SRTT Explicit, Implicit	12 hrs w/in-sub wake vs. sleep	-Yes -No	N/A

Reference	Samples (Age)	Procedural Memory Tests	Retention Interval	Sleep- Related Benefit?	PSG-Memory Improvement Correlations
Pace-Schott 2013	-N=62 (<i>M</i> =20.1) -N=50 (<i>M</i> =62.0)	Goal- vs. Muscle-based (b/n-sub)	12 hrs b/n-sub wake vs. sleep	-Yes (goal) -No	V/N
Fogel 2014	-N=28 (<i>M</i> =24.0) -N=29 (<i>M</i> =62.6)	TSM	90-min b/n-sub nap vs no-nap	-Yes -No	
Tucker 2011	-N=15 (<i>M</i> =20.1) -N=16 (<i>M</i> =68.0)	TSM	12/24 hr w/in-s, wake vs. sleep	-Yes -Yes (late)	-N/A -Null effects
Nemeth 2010	-N=25 (<i>M</i> =21) -N=24 (<i>M</i> =69.8)	Implicit ASRT	12 hrs b/n-sub wake vs. sleep	-No -No	N/A
Peters 2008	-N=14 (<i>M</i> =20.1) -N=14 (<i>M</i> =69.8)	Pursuit rotor	Up to 1 week (wake + sleep)	-Yes -Yes	Non-significant trends

Sample refers only to the healthy (control) group. PSG correlations (if reported) with overnight memory improvement are listed after adjusting for performance baseline, chronological age (Age), & experimental group (Exp). "Late" indicates that plateau, not immediate, improvement was observed. Papers are sorted by those with a single versus multiple age groups and then sorted by mean age.

 I The authors reported this correlation following removing an outlier.

Retention Interval Abbreviations. Depr., deprivation; Reb: rebound; AChE-I: Acetylcholinesterase Inhibitor Donepezil.

Memory Task Abbreviations. ASRT: alternating serial reaction time; CTT: Continuous Tracking Task; MST: Finger Tapping Motor Sequence Test; MT: Mirror Tracing; PVT: Psychomotor Vigilance Task; SRTT: Serial Reaction Time Task

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Table 8

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Reference	Samples (Age)	Declarative Memory Tests	Retention Interval	Sleep-Related Effect?	PSG-retention Correlations
Studies that Primarily In	Studies that Primarily Included Middle-Aged Adults (Mean Age <60)	ults (Mean Age <60)			
Backhaus 2006	N=13 (M=40.1)	PAL (40 pairs to 60%)	& hrs (sleep only)	(no wake control)	SWS (+) ^(Age)
Mawdsley 2014	N=40 (M=40.3)	Item and source memory	12 hrs b/n-sub wake vs. sleep	Marginal age reduction	N/A
Deak 2011	N=9 (M=44.7)	Selective Reminding task	12 hrs w/in-sub wake vs. sleep	No	SWS (+ trend)
Nissen 2011	N=53 (M=46.6)	MVV	12 hrs b/n-sub wake vs. sleep	Yes	Null effects
Kloepfer 2009	N=20 (M=47.4)	MVV	10.5 hrs (sleep-only)	(no wake control)	Null effects
Studies that Primarily In	Studies that Primarily Included Older-Aged Adults (Mean Age >60)	lts (Mean Age >60)			
Mazzoni 1999	N=30 (M=68)	PAL: 20 pairs (no immediate test)	Sleep only	(no wake control)	Sleep cycles (+) SWS (- trend)
Hornung 2007	N=107 (M=66.1)	PAL (34 pairs studied 2×)	10 hrs b/n-sub sleep, rem-depr, rem-reb, nrem-depr, AChE-I	No group effects	Null effects ^(Exp)
Schredl 2001	N=8 (M=66.5)	40 words (read, recall 8x)	11 hrs baseline sleep vs AChE-I	(no wake control)	REM% (+) on AChE-I night
Lo 2014	N=14 (<i>M</i> =66.6)	DRM lists (lures, studied words)	8.3 hrs w/in-sub wake vs. sleep	No (study item) Yes (lure item)	Studied: Null Lures: SWS (–)
Seeck-Hirschner 2012	N=19 (<i>M</i> =68)	Rey-Osterrieth Complex Figure	≥10 hrs (sleep only)	(no wake control)	SWS(-),wake(+), spindles(+) ^(Age)
Conte 2012	N=16 (M=72.5)	PAL (study 168 pairs 3x)	>9 hrs (sleep only)	(no wake control)	arousals $(-)$, transitions $(-)$
Westerberg 2012	N=16 (M=72.7)	PAL (study 44 pairs 2x); face-fact pairs	Sleep only (two nights)	(no wake control)	PAL: delta, theta (+), Face: Null
Hot 2011	N=14 (M=76.7)	15 words (studied 5×)	Sleep only	Ceiling effects	N/A (ceiling effects)
Studies that Compared Multiple Age Groups	Multiple Age Groups				
Wilson 2012	-N=24 (<i>M</i> =25.9) -N=32 (<i>M</i> =44.0) -N=31 (<i>M</i> =63.1)	PAL (32 pairs to 62.5%)	12 hrs w/in-sub wake vs. sleep	-Yes -Yes -Yes	N/A
Backhaus 2007	-N=16 (<i>M</i> =20.4) -N=12 (<i>M</i> =50.0)	PAL (40 pairs to 60%)	3.5 hrs w/in-sub early vs late sleep	Early > Late sleep (both)	$SWS (+)^{(Age)}$
Giambra 1993 Exp 1	-N=24 (18–21) -N=24 (55–64)	48 Sentences (Studied 2×)	Up to 24 hours	Similar forgetting rates	N/A
Giambra 1993 Exp 2	-N=24 (17–21) -N=24 (65–74)	48 Sentences (Studied 3×)	Up to 24 hours	Forgetting rate was faster in OA	N/A
Cherdieu 2014	-N=20 (<i>M</i> =22.1) -N=20 (<i>M</i> =68.9)	Object location task	12 hrs b/n-sub wake vs. sleep	-Yes -No	Cycle time/Sleep time

Reference	Samples (Age)	Declarative Memory Tests	Retention Interval	Sleep-Related Effect?	PSG-retention Correlations
Mary 2013	-N=16 (<i>M</i> =21.0) -N=16 (<i>M</i> =69.7)	PAL (Study 28 pairs 5× or 100%)	7 days	Forgetting rate was faster in OA	N/A
Scullin 2013	-N=57 (M=19.7) -N=41 (M=70.7)	PAL (20 pairs to 80% criterion)	12/24 hr, b/n-sub wake vs. sleep	-Yes -No	-SWS (young) -Null (older)
Mander 2013b	-N=32 YA (<i>M</i> =20.7) -N=26 OA (<i>M</i> =73.4)	PAL (120 pairs to 100%)	10 hrs b/n-sub wake vs. sleep	-Yes -No	Relative delta (+)
Rauchs 2008	-N=14 (<i>M</i> =23.4) -N=14 (<i>M</i> =75.1)	Study 15 words 3x or 5x); Stories	(sleep only)	Age reduction trend (ceiling)	Null effects
Aly 2010	-N=10 (<i>M</i> =22.8) -N=12 (<i>M</i> =75.2)	WMS stories; Personal memory	12 hrs w/in-sub wake vs. sleep	-Yes (both tests) -Yes; Reduced	N/A
					ţ

Sample refers only to the healthy (control) group. PSG correlations with overnight retention are listed after adjusting for baseline, chronological age (Age), & experimental group (ExP). Sleep-related benefits are reported relative to wake-control conditions. Papers are sorted by those with a single group versus multiple age groups.

Sample Abbreviations. MA: middle-aged (30-60); OA: older-aged (>60); YA: younger-aged (18-30).

Retention Interval Abbreviations. Depr., deprivation; Reb: rebound. AChE-I: Acetylcholinesterase Inhibitor Donepezil.

Memory Task Abbreviations. DRM: Dese-Roediger-McDermott lists; PAL: paired associate word learning; VVM: visual and verbal memory task; WMS: Wechsler Memory Scale