THE ROLE OF SLEEP AND PHYSICAL ACTIVITY IN COGNITIVE DECLINE: DIRECT AND MEDIATING EFFECTS ON EXECUTIVE CONTROL

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Adults often exhibit a marked decline in cognitive function with aging. However, some adults show remarkable abilities to maintain cognitive function into older adulthood. There is increasing evidence that healthy lifestyle factors, such as **sleep quality** and physical activity, may benefit cognition in older adults. However, the pathway through which physical activity benefits cognition is unknown. Given that physical activity improves sleep (Lopez, 2008), and sleep often benefits cognition (Goel, Rao, Durmer, & Dinges, 2009), sleep may mediate the relationship between physical activity and cognition (Vitiello, 2008). The present study examined individual differences in sleep quality and executive function in young and older adults. Subjects wore an accelerometer armband for one week, which estimated minutes of physical activity and sleep. These estimates were used to calculate objective sleep quality operationalized as sleep efficiency (total time asleep/total time lying down) and physical activity, operationalized as average metabolic equivalents (METs) while awake ("awake METs"). Using a task-switching paradigm, which manipulated time to prepare, Study 1 showed that subjects with high sleep efficiency maximized time to prepare more so than subjects with low sleep efficiency. In Study 2, after controlling for age, gender, and education, sleep efficiency was a significant mediator of the relationship between awake METs and cognitive performance in terms of

switching, inhibition, working memory, and memory retrieval: all executive functions that show age-related decline. Thus, the relationship between physical activity and cognition may be driven by sleep quality. In Study 3, time of day was shown to influence whether older adults exhibited impaired performance relative to young adults. Additionally, this effect applied specifically to older adults with low sleep efficiency. This finding suggests that sleep quality combined with time of day are important factors in whether or not older adults exhibit cognitive impairments.

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PREFACE

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1.0 INTRODUCTION

Age-related cognitive impairments often include decline in **executive control** (Buckner, 2004; Cepeda, Kramer, & Gonzalez de Sather, 2001; Cohn, Emrich, & Moscovitch, 2008; Hasher & Zacks, 1988; Kramer, Hahn, & Gopher, 1999). Volumetric studies have suggested that atrophy of the prefrontal cortex (PFC) mediates this age-related decline (Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998; Weinstein et al., 2011). Impairments in executive control include difficulties selecting relevant and inhibiting irrelevant information and actions, and difficulties monitoring and updating information (Funahashi, 2001; Jones & Harrison, 2001). Further, white matter in older adults is particularly compromised in anterior brain regions. This has been shown with white matter lesions (De Groot et al., 2002) as well as white matter integrity assessed using diffusion tensor imaging (DTI) (Head et al., 2004; Pfefferbaum, Adalsteinsson, & Sullivan, 2005; Salat et al., 2005). Such white matter breakdown disrupts the connectivity between frontal and other cortical regions, ultimately affecting executive control. These PFC changes tend to manifest themselves in a range of cognitive tasks including task-switching, inhibition, and controlled memory retrieval (Buckner, 2003, 2004; Bucur et al., 2008). Given that decline in memory can be particularly debilitating in older adults, determining factors that contribute to PFC decline is of utmost importance. The prevalence of sleep disruption in older adults (Bliwise, 2011; Carskadon & Dement, 2011; Ohayon, Carskadon, Guilleminault, & Vitiello, 2004) and its negative impact on cognition (Durmer & Dinges, 2005; Goel, et al., 2009) suggest that sleep may play an important role in the extent to which older adults exhibit decline in PFC function and in turn, executive control. One compelling implication of this model is that ameliorating sleep deficits in healthy older adults could lead to improvements in PFC function and in turn, cognition.

1.1 EXECUTIVE CONTROL AND AGING

Older adults tend to show decline in cognitive processes that depend on the PFC and in turn impairments on tasks that engage executive control. For instance, older adults show impaired inhibition (Colcombe, Kramer, Erickson, & Scalf, 2005; Gazzaley & D'Esposito, 2007; Monsell, 2003; West & Bell, 1997), working memory (Craik, Morris, & Gick, 1990) as well as controlled **episodic memory retrieval** (i.e. free recall) (Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006; Kensinger & Schacter, 1999; Macht & Buschke, 1983; Velanova, Lustig, Jacoby, & Buckner, 2007). This is perhaps not surprising because frontal lobe integrity is often affected in aging.

One theory of cognitive aging posits that while young adults are more likely to rely on an “early selection” strategy, older adults rely more on a “late correction” cognitive strategy (Braver & West, 2008; Jacoby, 1999; Paxton, Barch, Racine, & Braver, 2008; Velanova, et al., 2007). An early selection strategy is more proactive and involves filtering of irrelevant information and selecting relevant information. In contrast, a late correction strategy takes place late within the processing stream and compensates for less efficient early filtering involving a more reactive strategy (Paxton, et al., 2008; Velanova, et al., 2007). These age-related differences in proactive versus reactive strategies may influence executive functions such as preparation and task-switching.

In a study comparing retrieval preparation between younger and older adults (Wilckens, Wolk, & Wheeler, 2010), I examined whether preparation during memory retrieval was diminished with aging. I found that retrieval preparation was absent in older adults, as indicated by event-related potentials (ERP) correlates of “task-set adoption”. This may reflect a more “diffuse” memory search strategy among older adults. However, additional processing post-retrieval was robust in older adults. These results suggest that retrieval strategies may become altered and less efficient with advanced age. This finding extended the results of an earlier study, Wolk et al. (2009), which also found ERP evidence to support the late correction model of cognitive aging for memory retrieval. Wolk et al. (2009) found that early ERP **retrieval success** effects were diminished in older adults, but that retrieval success effects late within the retrieval phase were larger in older adults. In addition, late retrieval success effects were largest in older subjects with poor performance suggesting that it is older adults who exhibit decline that tend to adopt this “late correction” strategy. This finding points to the possibility that some older adults may be able to maintain cognitive abilities and use the same strategies as young adults.

The “late selection” model of aging is consistent with other theories of cognitive decline posited outside the realm of memory retrieval (Gazzaley & D'Esposito, 2007; Hasher & Zacks, 1988; Paxton, et al., 2008). In a review of age-related differences in neural activity associated with top-down modulation of attention, Gazzaley and D’Esposito (2007) proposed that normal working memory decline is associated with a selective impairment in older adults’ ability to inhibit or suppress irrelevant processing, a view originally proposed by Hasher and Zacks (1988). Testing selection and inhibition, they further suggested that older adults’ ability to enhance processing related to relevant information is left intact. Gazzaley and colleagues found evidence to support this claim using a variety of neuroimaging techniques. In an fMRI (functional magnetic resonance imaging) study, Gazzaley et al. (2005) investigated enhancement and suppression of neural activity selective for information that was cued as relevant or irrelevant, respectively. Using a working memory task in which young adults were instructed to either remember or ignore faces versus scenes, or passively view either stimulus, Gazzaley and colleagues found that instructions to remember scenes were associated with enhancement of neural activity related to scene processing above baseline in a scene-selective region (left parahippocampal/lingual gyrus), whereas instructions to ignore scenes were associated with reduced scene-selective activity below baseline. In contrast, an older group displayed enhancement of scene-selective neural activity with instructions to remember scenes, but were less likely to show significant suppression activity below baseline with instructions to ignore scenes. This finding suggests that inhibitory processes were impaired in older adults. Relating these findings to behavior, they found that suppression deficits were exhibited only by older adults who were impaired at remembering target stimuli following a working memory delay, and those who were more likely to later remember stimuli they were instructed to ignore. These results revealed that older adults with poor performance were less likely to inhibit task-irrelevant processing and reflect age-related deficits in inhibitory control particularly for poor performing older adults.

1.2 AGE-RELATED CHANGES IN SLEEP CONTRIBUTE TO COGNITIVE DECLINE

Having established that age-related changes involve deficits in early selection processes including preparation and inhibition for episodic and working memory tasks, we can ask which factors result in this specific pattern of impairments. Several factors including sleep have been shown to influence PFC function and executive control in both young and older adults (Blackwell et al., 2006; Harrison, Horne, & Rothwell, 2000; Jones & Harrison, 2001; Nebes, Buysse, Halligan, Houck, & Monk, 2009; Pace-Schott & Spencer, 2011). Although sleep behaviors change dramatically with aging (Table 1), sleep has been relatively ignored in studies of normal cognitive decline. Research examining the relationship between cognition and age-related changes in sleep is important however, given the negative impact of sleep deprivation and disruption on cognition (Durmer & Dinges, 2005; Goel, et al., 2009).

Table 1. Consistent sleep changes reported from young to older adulthood

Total sleep time (decrease) (Bliwise, 2011; Ohayon, et al., 2004; Pace-Schott & Spencer, 2011; Vitiello, 2006)

Sleep efficiency (decrease) (Bliwise, 2011; Kupfer, Reynolds, Ulrich, Shaw, & Coble, 1982; Ohayon, et al., 2004)

Wake after sleep onset (WASO) (increase) (Bliwise, 2011; Ohayon, et al., 2004; Vitiello, 2006)

Slow-wave sleep (decrease) (Cajochen, Munch, Knoblauch, Blatter, & Wirz-Justice, 2006; Carrier, Land, Buysse, Kupfer, & Monk, 2001; Carskadon & Dement, 2011; Espiritu, 2008; Kupfer, et al., 1982; Landolt, Dijk, Achermann, & Borbely, 1996; Ohayon, et al., 2004; Van Cauter, Leproult, & Plat, 2000; Vitiello, 2006)

In addition to being more sleep-deprived than younger adults, older adults also show a decline in **sleep efficiency**, sleep continuity, and **slow-wave sleep**, (Bliwise, 2011; Cajochen, et al., 2006; Carskadon & Dement, 2011; Duffy, Willson, Wang, & Czeisler, 2009; Feinberg, 1974; Kupfer, et al., 1982; Landolt, et al., 1996; Ohayon, et al., 2004; Prinz, 1977). Slow-wave sleep refers to stages 3 and 4 of non-REM (rapid eye movement) sleep measured with polysomnography, an electrophysiological technique to characterize sleep. Slow-wave sleep is characterized by high amplitude, low-frequency delta waves measured with EEG (electroencephalogram) (Muzur, Pace-Schott, & Hobson, 2002). Slow-wave sleep is thought to restore PFC function (Harrison, et al., 2000; Muzur, et al., 2002), given that from wake to slow-wave sleep, there is significant deactivation in the PFC. Results from PET (positron emission tomography), fMRI, and EEG support this theory (Kajimura et al., 1999; Kaufmann et al., 2006; Maquet et al., 1997; Muzur, et al., 2002; Werth, Achermann, & Borbely, 1997). Muzur et al. (2002) hypothesized that a PFC respite is critical to restore frontal lobe function for wakefulness, which in turn may benefit executive control. Another possibility, suggested more recently by Dang-Vu et al. (2008) is that slow-wave sleep actively supports frontal lobe function, based on increased activity found during slow-wave sleep in frontal regions relative to baseline non-REM activity. In contrast to prior studies, Dang-Vu et al. (2008) compared discrete slow-wave sleep waves with baseline non-REM activity as opposed to wake EEG activity. This lead to the conclusion that slow-wave sleep is not a quiescent state, but rather actively restores brain function. The decrease in slow-wave sleep that is found in late adulthood may contribute to a decline in PFC restoration. This may in turn affect waking PFC function and performance on executive control tasks in older adults.

In the next sections, I will review studies involving sleep and sleep deprivation and how they relate to deficits in executive control processes (i.e. inhibition). I propose that age-related decreases in slow-wave sleep may drive age-related changes in PFC function and in turn executive control.

1.3 IMPACT OF SLEEP DEPRVIATION ON EXECUTIVE CONTROL AND THE PFC

Sleep deprivation influences performance on a variety of cognitive tasks (Durmer & Dinges, 2005; Goel, et al., 2009; Jones & Harrison, 2001). This outcome does not appear, however, to be explained simply by fatigue or boredom, but by direct effects of sleep deprivation on frontal lobe function, and in turn, cognitive processes that depend on the frontal lobes (Gosselin, De Koninck, & Campbell, 2005; Harrison & Horne, 2000a; Harrison, et al., 2000; Horne, 1993; Jones & Harrison, 2001; Muzur, et al., 2002). It is principally the loss of slow-wave sleep that occurs with sleep deprivation that is thought to affect the frontal lobes and underlie the impact of sleep deprivation on executive control (Harrison & Horne, 2000a; Muzur, et al., 2002).

Significant decreases in frontal lobe metabolism have been demonstrated in studies of sleep deprivation (Muzur, et al., 2002; Thomas et al., 2000; J. C. Wu et al., 2006). This may be driven particularly by the lack of slow-wave sleep (J. C. Wu, et al., 2006). Moreover, this decrease in metabolism is not fully restored with a full night of recovery sleep (J. C. Wu, et al., 2006), suggesting that while a recovery sleep may increase alertness (Tietzel & Lack, 2001) underlying effects on the frontal lobes may persist.

It is hypothesized that sleep-deprived young adults may serve as an experimental model for age-related cognitive decline (Harrison, et al., 2000). Similarities in patterns of cognitive performance and brain activity between older adults and sleep-deprived young adults support this view (Chee & Choo, 2004; Drummond, Meloy, Yanagi, Orff, & Brown, 2005). Older adults often paradoxically over-recruit the PFC during tasks that depend on executive control such as inhibition and controlled retrieval (Colcombe, et al., 2005; Grady, 2008; Reuter-Lorenz, 2002;

Velanova, et al., 2007). Similarly, young adults over-recruit PFC during executive tasks following sleep deprivation (Chee & Choo, 2004; Drummond, et al., 2005) but see (Drummond et al., 1999; Mograss, Guillem, Brazzini-Poisson, & Godbout, 2009; Mograss, Guillem, & Godbout, 2008). In one of these studies, Drummond et al. (2005) had subjects take part in a verbal learning task. Subjects that were sleep-deprived for 36 hours showed increased activation of several "control" regions including the dorsolateral PFC relative to control subjects. As noted by the authors, this pattern of activation was similar to the pattern found in older adults. Similarly, Chee and Choo (2004) found with a working memory paradigm that young subjects sleep-deprived for 24 hours showed a pattern of activation and deactivation in parts of frontal and parietal cortex that closely resembled the pattern typically observed in healthy older subjects. They found that while anterior medial frontal and posterior cingulate cortex showed significant deactivation, the left dorsolateral PFC showed an increase with sleep deprivation. These similarities in PFC over-recruitment among healthy older adults and sleep-deprived young adults suggest a common mechanism between sleep disruption and cognitive decline (Harrison, et al., 2000). This common mechanism may be decline in executive control, or broadly PFC function.

Cognitive impairments that arise from sleep deprivation are often found for executive control tasks (Breimhorst, Falkenstein, Marks, & Griefahn, 2008; Drummond, et al., 1999; Drummond, et al., 2005; Jennings, Monk, & van der Molen, 2003; Jones & Harrison, 2001; Mograss, et al., 2009; Pilcher & Huffcutt, 1996; Qi, Shao, Miao, Guo-Hua Bi, & Yang, 2010). Neuroimaging studies have also provided evidence to suggest that sleep deprivation affects executive control dependent on the frontal lobes (Breimhorst, et al., 2008; Chee & Choo, 2004; Chuah, Venkatraman, Dinges, & Chee, 2006; Drummond, et al., 1999; Drummond, et al., 2005; Durmer & Dinges, 2005; Goel, et al., 2009; Mograss, et al., 2009; Mu et al., 2005; Schapkin, Falkenstein, Marks, & Griefahn, 2006; Thomas, et al., 2000). In contrast to some studies that have failed to demonstrate significant effects of sleep deprivation on cognition using non-executive tasks (A. M. Morris, So, Lee, Lash, & Becker, 1992), studies using “executive tasks” have demonstrated a specific influence of sleep on PFC function. Some of these studies have investigated executive processes that are important for controlled memory retrieval, such as inhibition. For example, Breimhorst et al. (2008) and Schapkin et al. (2006) used a Go-NoGo paradigm to test the hypothesis that inhibitory processing is impaired with sleep disruption. This task requires inhibition on NoGo trials when subjects are instructed to inhibit their response to distracters. Using noise to disrupt sleep in young individuals, Schapkin et al. (2006) examined ERPs associated with Go and NoGo trials. They showed that the fronto-central P3 amplitude (a positive wave with a 300 ms peak latency) elicited by NoGo trials was reduced in the sleep disruption condition. However, the P3 elicited by Go trials was not affected by sleep disruption. The authors concluded based on these results that the decision process associated with Go trials was not influenced by sleep disruption. However, inhibitory processing associated with NoGo trials was negatively affected. This finding suggests that inhibitory control is impaired with sleep disruption.

Also testing a Go-NoGo paradigm in young adults, Breimhorst et al. (2008) examined Go-NoGo ERP effects in good and poor sleepers based on an objective sleep disturbance index using polysomnography. Breimhorst et al. (2008) also found that the NoGo P3 latency was longer in poor sleepers relative to good sleepers, reflecting deficient inhibitory processing. However, in contrast to the Schapkin et al. (2006) study, Breimhorst et al. (2008) also found decreased Go P3 amplitude in poor sleepers. This suggests that poor sleep also affected task-relevant processing, not just inhibition. Despite these differences, these studies collectively suggest that inhibitory processes are negatively impacted by sleep disruption.

Sleep deprivation also appears to influence task-switching processes. Task-switching involves cognitive flexibility and inhibition of irrelevant task-sets, and is often considered a model paradigm of executive control (Logan, 2004; Monsell, 2003). Couyoumdjian et al. (2010) found a significant increase in switch-costs with sleep deprivation in young adults. Importantly, this effect was driven by an increase in response time (RT) on switch trials. There was no change in RT on repeat trials, suggesting that sleep deprivation did not globally influence response time. Instead it specifically affected subjects' ability to switch between task-sets. Also using a task-switching paradigm, Heuer et al. (2004) found deficits with task-switching following sleep deprivation. In this study, the task-switching costs were influenced by sleep deprivation only when subjects switched between two tasks as opposed to two stimulus-response mappings. This dissociation may support the view that sleep-deprivation influences inhibition of competing task-sets.

Harrison & Horne (1998) revealed marked impairments on a short and entertaining test of inhibition shown to have a PFC-focus (The Haylings Test (Burgess & Shallice, 1996)) following 36 hours of sleep deprivation. This study demonstrated that it was not the tedium of the task that brought about sleep-related deficits, but rather the putative impairments in PFC-mediated inhibition.

Although multiple aspects of sleep deprivation, including a lack of all sleep stages, and increased stress and fatigue on the part of the subject, may contribute to these impairments, the lack of slow-wave sleep affecting PFC restoration is a possible mechanism by which sleep deprivation affects executive control (J. C. Wu, et al., 2006). Together, these behavioral and neuroimaging investigations suggest that sleep deprivation has a considerable impact on executive control.

In terms of episodic memory, there are very few studies that have investigated how different retrieval processes are influenced by sleep. Nonetheless, these studies have demonstrated specific impairments in retrieval processes that depend on the PFC (Table 2). Harrison & Horne (2000b) examined both recognition memory and temporal order memory judgments. Following a period of sleep or sleep deprivation, subjects were asked to identify whether faces were presented at study or not (recognition) and to make a recency judgment by identifying on which of two study lists the face appeared (temporal order). This temporal order task was posited to depend on the PFC. They found that while recognition memory was left intact, temporal order memory was significantly impaired following sleep deprivation. Using a verbal learning task, Drummond et al. (2005) found that recall, but not recognition performance decreased with sleep deprivation. FMRI data collected in this study found increased PFC recruitment during encoding following sleep deprivation. However, the retrieval phase was not scanned in this particular paradigm. So it is unclear whether PFC over-recruitment occurred during retrieval as well following sleep deprivation. These findings suggest that sleep affects controlled retrieval tasks like recall, but leaves more automatic retrieval processes intact.

Table 2. Controlled memory processes influenced by advanced aging, PFC damage, and sleep deprivation.

Cued Recall

Aging (Cabeza et al., 1997; McIntyre & Craik, 1987)

Frontal Lobe Damage (Baldo, Delis, Kramer, & Shimamura, 2002)

Sleep Deprivation (Drake et al., 2001; Nilsson, Backman, & Karlsson, 1989)

False Recognition (False alarming to related lures)

Aging (Buchler, Faunce, Light, Gottfredson, & Reder, 2011; Kensinger & Schacter, 1999; Schacter, Koutstaal, & Norman, 1997)

Frontal Lobe Damage (Baldo, et al., 2002; Baldo & Shimamura, 2002; Schacter, Curran, Galluccio, Milberg, & Bates, 1996; Verfaellie, Rapcsak, Keane, & Alexander, 2004)

Sleep deprivation (Diekelmann, Landolt, Lahl, Born, & Wagner, 2008)

Free Recall

Aging (Kensinger & Schacter, 1999; Macht & Buschke, 1983)

Frontal Lobe Damage (Baldo & Shimamura, 2002; Gershberg & Shimamura, 1995; Incisa della Rocchetta & Milner, 1993)

Sleep Deprivation (Drummond et al., 2000; Drummond, et al., 2005)

Table 2 Continued

Temporal Order Memory

Aging (Cabeza, Anderson, Houle, Mangels, & Nyberg, 2000; Trott, Friedman, Ritter, & Fabiani, 1997; Trott, Friedman, Ritter, Fabiani, & Snodgrass, 1999)[1]

Frontal Lobe Damage (Mangels, 1997; McAndrews & Milner, 1991)

Sleep deprivation (Harrison & Horne, 2000b)

Supporting the notion that cognitive deficits in older adults and sleep-deprived young adults are similar, Nilsson et al. (1989) found similarities in memory performance between older, young alcohol intoxicated, and young sleep-deprived subjects. In a recall test using weakly and strongly related word pairs, they found that all experimental groups (older, intoxicated, and sleep-deprived) demonstrated the same pattern of deficits in which recall of weakly related word pairs was significantly lower than that of the control young adult group. Recall of strongly related word pairs, however was not affected. In this study, recall of weakly related word pairs should require greater reliance on executive control than recall of strongly related word pairs. The authors attributed this finding to both deficient encoding and retrieval and suggested a functional similarity between sleep deprivation, intoxication, and normal aging in terms of controlled memory processes.

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[1] Note that in table 2 some effects of aging, PFC, and sleep deprivation on these memory processes are attributable to impairments in both encoding and retrieval strategies.

Recognition memory is primarily uninfluenced by sleep deprivation, however similar to frontal lobe patients (Baldo, et al., 2002; Baldo & Shimamura, 2002; Schacter, et al., 1996; Verfaellie, et al., 2004) and older adults (Kensinger & Schacter, 1999; Schacter, et al., 1997), false recognition to semantically related lures has been shown to increase with sleep deprivation (Table 2). Diekelmann et al. (2008) used a false memory paradigm (Roediger & McDermott, 1995) to test false recognition in young subjects sleep deprived during memory retrieval. Subjects sleep deprived during memory retrieval were more likely to incorrectly judge new words semantically related to studied words as “old”. This suggests that forms of recognition memory that depend on the PFC (distinguishing semantically-related lures from studied items) are influenced by sleep deprivation. To further support the view that this effect was not a result of less consistent memory consolidation, this study found that manipulations in sleep within the study-test interval did not influence false recognition. It was specifically the effect of sleep deprivation on retrieval that brought about an increase in false recognition.

Overall these sleep-deprivation studies of memory retrieval suggest that more controlled retrieval processes are impaired with sleep deprivation compared with more automatic ones and this dissociation may be driven by a breakdown in PFC function.

These results point to the possibility that age-related decreases in sleep contribute to executive control deficits. Conversely, because there is more to age-related sleep changes than a mere overall decrease in sleep, the impact of age-related sleep changes on cognition may not be completely comparable to sleep deprivation in young adults. Further, while many older adults exhibit marked impairments in cognitive performance and changes in brain activity, some older adults show little cognitive decline (Stern, 2009). These individual differences in cognitive decline may be explained, at least partially, by individual differences in sleep. Determining the way in which sleep plays a role in age-related cognitive decline may shed light on why some older adults but not others exhibit impairments.

1.4 INDIVIDUAL DIFFERENCES IN SLEEP AND EXECUTIVE CONTROL IN OLDER ADULTS

Inadequate sleep is very common among the adult population (Kapiro, Partinen, & Koskenvuo, 2001). According to Mander et al. (2008) only 26 percent of adults report getting the recommended eight or more hours of sleep per night. In addition, total sleep deprivation (when subjects are deprived for a full night) is not necessary to reveal significant cognitive impairments. More ecologically valid studies of chronic sleep restriction involving less than 7 hours of sleep per night for multiple nights have revealed a range of cognitive deficits including deficits on tasks of attention and working memory (Durmer & Dinges, 2005; Goel, et al., 2009; Van Dongen, Maislin, Mullington, & Dinges, 2003). Moreover, chronic sleep restriction for two weeks has been shown to result in cognitive deficits equivalent to that found with total sleep deprivation (Van Dongen, et al., 2003). This type of chronic inadequate sleep, which is similar to sleep behavior of older adults, could potentially result in cognitive impairments that may be difficult to reverse with a few good nights of sleep. Although the data are somewhat inconsistent, older adults with greater sleep quantity and quality tend to perform better on cognitive tasks (Blackwell, et al., 2006; Nebes, et al., 2009; Pace-Schott & Spencer, 2011).

Given the importance of slow-wave sleep in PFC restoration, decline in slow-wave sleep is a critical age-related sleep change that may contribute to impairments in executive control. Both human and animal studies have shown a decrease in slow-wave sleep with age (Buechel et al., 2011; Cajochen, et al., 2006; Carrier, et al., 2001; Carskadon & Dement, 2011; Espiritu, 2008; Feinberg, 1974; Kupfer, et al., 1982; Ohayon, et al., 2004; Pace-Schott & Spencer, 2011; 2000). This decline in slow-wave sleep gradually manifests itself during the middle years of life (Cajochen, et al., 2006; Carrier, et al., 2001; Van Cauter, et al., 2000). It is possible that the decrease in slow-wave sleep that occurs with aging could negatively impact PFC function by diminishing the restoration process. In addition, older adults that exhibit reduced slow-wave sleep may be more likely to exhibit cognitive decline. This relationship leading to decline in executive control is illustrated in Figure 1: Increasing age leads to decline in slow-wave sleep, and in turn, decreased prefrontal restoration, which leads to impaired executive control.

Alternatively, the proposed pathways illustrated in Figure 1 may be neither unidirectional nor an exhaustive model of moderators and possible mediators involved in age-related deficits. For example, amyloid deposition has been shown to disrupt slow-wave sleep (Hermann et al., 2009). Accordingly, cognitive abilities may be related to slow-wave sleep as a result of age-related neuropathological changes negatively impacting slow-wave sleep.

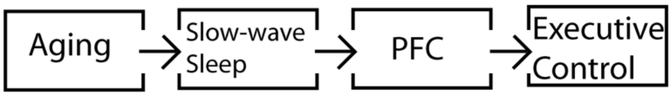


Figure 1. Sleep-mediated relationship between aging and executive control

It should be noted that several reports suggest that older adults are more resilient to sleep deprivation than young adults (Duffy, et al., 2009; Philip et al., 2004), suggesting that sleep need declines with age. However, other studies suggest that young and older adults require the same amount of sleep, and time spent in slow-wave sleep to perform well on executive control tasks (Killgore, Balkin, & Wesensten, 2006). Moreover, older adults may be less likely to restore frontal lobe function following sleep deprivation compared with young adults (Munch et al., 2004). Despite these age differences in responses to sleep deprivation, it is unclear from these studies whether sleep normally exhibited by older adults negatively impacts cognitive performance. Although there is a dearth of research on the topic, examining whether individual differences in sleep among older adults explain variation in memory and cognitive function is essential given the preponderance of sleep and cognition-related problems among older adults.

A few studies have suggested that individual differences in slow-wave sleep are related to executive control abilities in older adults. Anderson & Horne (2003) examined low-frequency delta EEG activity during non-REM sleep, which is highest during slow-wave sleep, in a group of healthy older adults. They found a positive correlation between low-frequency delta activity in frontal EEG sites and performance on cognitive tasks thought to be relatively "PFC-specific", including the Wisconsin Card-Sorting Task, and the Tower of London task (a non-verbal planning task). According to the authors, the non-verbal planning task required flexibility in planning and in changing of strategies. The Wisconsin card sorting task is thought to depend on inhibitory control (and other processing) in that it tests for perseveration of strategies. Though this study was purely behavioral, this result points to the relationship between slow-wave sleep and PFC function among older adults.

In an earlier study, Crenshaw and Edinger (1999) investigated whether slow-wave sleep was related to performance on “simple reaction time” and vigilance tasks among older adults with normal sleep and those with insomnia. Older adults who were normal sleepers showed no relationship between cognitive performance and slow-wave sleep. In contrast to the Anderson & Horne (2003) study mentioned above, the cognitive measures of this study were not “executive tasks”. Based on the view that slow-wave sleep specifically affects PFC function responsible for executive control, slow-wave sleep would not be related to behavior on these tasks in healthy older adults. Accordingly, the Anderson & Horne (2003) study measured simple response time as well and found no relationship between this cognitive measure and slow-wave sleep.

To corroborate these findings, a more recent study, Nebes et al. (2009) showed that subjective poor sleep (sleep latency and sleep efficiency) in older adults was associated with poor performance on a range of executive control tasks, including those that tested working memory and attentional set shifting. There was however, no relationship between sleep quality and a processing speed task. Though, in this study there was not a clear distinction between executive and non-executive tasks: no relationship was found between sleep and inhibitory processing as assessed by the Stroop task and Haylings task, or episodic memory, as assessed by the logical memory test (Wechsler, 1987). Regardless of the lack of a clear distinction, these studies examining individual differences in sleep suggest that poor sleep, particularly slow-wave sleep, in older adults may lead to poor performance on some tasks of executive control. It should also be noted that subjective sleep quality, as measured by the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) in the Nebes et al. study, primarily measures sleep quality based on time spent in bed, as opposed to objective amount of time spent sleeping, sleep efficiency, or time spent in specific sleep stages. Consequently, relationships between sleep and these cognitive tasks may have differed if objective sleep measures, such as amount of time spent in slow-wave sleep, were investigated.

Based on the studies reviewed above, there is clearly some support for the hypothesis that age-related changes in sleep quality contribute to decline in PFC and executive control and this may affect controlled memory abilities. Should future research support this model of cognitive aging, treatments aimed at improving slow-wave sleep in healthy older adults could improve executive control, potentially leading to improvements in memory.

1.5 SLEEP AS A MEDIATING VARIABLE FOR EFFECTS OF EXERCISE ON COGNITION

Having concluded that age-related changes in sleep may contribute to the pattern of cognitive deficits displayed by older adults, we can next ask whether sleep acts as a mediating factor for other variables that influence cognition. For example, physical activity interventions have been shown to improve executive control in both young and older adults (Erickson, Miller, Weinstein, Akl, & Banducci, 2012; Kramer, Erickson, & Colcombe, 2006). There are consistent benefits of physical activity and exercise interventions on executive control that appear to be mediated by biological markers of brain function (Erickson, et al., 2012; Kramer, et al., 2006; Weinstein, et al., 2011). The pathway through which exercise benefits executive control however, is not well understood (Vitiello, 2008). One possibility is that exercise improves cerebral vasculature, thereby influencing cognitive function (Brown et al., 2010). Another possible mechanism is that exercise improves sleep, which in turn benefits cognition. Figure 2 illustrates the possible mediating relationship between sleep, physical activity and executive control. This mediation model taken from (Wilckens, Erickson, & Wheeler, 2012) illustrates slow-wave sleep as mediating the relationship between physical activity and PFC function: With an increase in physical activity, there is an increase in slow-wave sleep, leading to improved PFC function and in turn improved executive control function.

Reviews of the literature on the relationship between sleep and physical activity suggest that exercise improves both subjective and objective sleep measures, especially in older adults with poor sleep (Driver & Taylor, 2000; Lopez, 2008; 2008). Older adults who are more physically fit tend to have shorter sleep latencies (time it takes to fall asleep) and more slow-wave sleep than sedentary older adults (Vitiello, 2008). Subjective sleep quality has also been shown to improve with chronic exercise (Benloucif et al., 2004; King, Oman, Brassington, Bliwise, & Haskell, 1997; Reid et al., 2010). King, Oman, Brassington, Bliwise, and Haskell (1997) found that subjective sleep quality in older adults, as measured by the Pittsburgh Sleep Quality Index, improved with 16 weeks of aerobic exercise. Though few studies have used objective sleep measures, particularly polysomnography, to test the effects of chronic exercise on sleep (Lopez, 2008), chronic aerobic exercise in sedentary older adults has been shown to selectively improve slow-wave sleep with a 6-month exercise intervention (Vitiello, Prinz, & Schwartz, 1994). Although not directly addressing cognition, these findings are noteworthy in that they suggest that exercise might improve PFC function and executive control by improving slow-wave sleep.

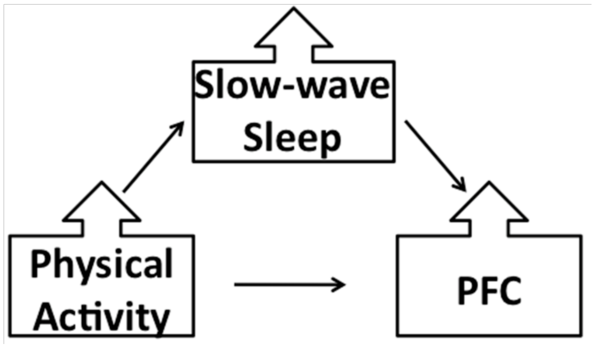


Figure 2. Model illustrating slow-wave sleep as mediating the relationship between physical activity and PFC function

1.6 CONCLUSIONS

Given that aging is (a) associated with changes in sleep, and (b) that sleep deprivation and aging reveal similar patterns of deficient cognition and brain activity, it is conceivable that sleep-deprived young adults may serve as a model for cognitive deficits found in older adults (Harrison, et al., 2000). Although sleep deprivation consistently reveals significant impairments in executive control, the sleep deprivation literature has also revealed a wide range of cognitive impairments, some consistent and others inconsistent with the pattern of results typically found in older adults. Additionally, some aging studies have used sleep deprivation to examine how poor sleep affects cognition in older adults. This literature points to both increased and decreased cognitive impairments in older adults relative to young (Duffy, et al., 2009; Killgore, et al., 2006). These inconsistencies could be explained by there being different mechanisms underlying cognitive deficits with aging and sleep deprivation. One drawback to using sleep deprivation as a model for cognitive decline is that slow-wave sleep is the sleep stage that most reliably shows age-related changes (Pace-Schott & Spencer, 2011) and appears to restore PFC function (Muzur, et al., 2002). Total sleep deprivation studies however, deprive subjects of both REM and non-REM sleep. Further, sleep deprivation is known to influence not only the PFC and “control regions”, but other brain regions including the thalamus, and in turn alertness (J. C. Wu, et al., 2006). Thus, sleep deprivation’s influence on cognition may not be specific to executive control. The way in which age-related decreases in slow-wave sleep affect the PFC may shed light on whether similar mechanisms underlie cognitive deficits resulting from aging and sleep deprivation. For instance, age-related changes in slow-wave sleep may have an immediate or gradual cumulative impact on PFC structure and function. It may be that chronic diminished slow-wave sleep over time brings about changes in the PFC seen with advanced age. Alternatively age-related reductions in slow-wave sleep could have an immediate effect, similar to experimentally induced sleep deprivation. Examination of individual differences in slow-wave sleep among healthy older adults may prove effective in revealing the specific processes influenced by age-related changes in sleep and more directly address whether age-related changes in sleep robustly affect cognitive decline. The present study examined individual differences in objective sleep, measured with accelerometry, in young and older adults to identify how sleep normally exhibited by older adults relates to executive control abilities.

1.7 PRESENT STUDY

The present study elaborated upon this literature in several ways. The first question, which is based on my prior research in memory retrieval, that retrieval preparation is impaired with aging

(Wilckens, et al., 2010), was whether this age-related change in preparation reflects a general preparation deficit. The first section describes a task-switching paradigm that manipulated preparation time to test whether age-related impairments include diminished engagement of preparation strategies to improve performance compared with young adults.

Because some older adults exhibit marked impairments in cognition and show altered brain activations compared with young adults, while others show remarkable abilities to maintain cognition, Study 1 also sought to identify whether individual differences sleep behavior had an influence on whether older adults showed impairments or not. Because both sleep and cognition tend to decline with aging, and sleep is thought to restore the PFC (Muzur, et al., 2002), I posited that older adults who exhibited poor sleep would be more likely to exhibit impairments in executive control. To test this, in Study 1, I examined how individual differences in subjects' sleep quality and quantity were related to improvement in performance with preparation.

In addition, given that physical activity and cardiovascular fitness in older adults is associated with higher cognitive performance (Colcombe et al., 2004; Erickson, et al., 2012; Weinstein, et al., 2011), I proposed that sleep behavior mediates the relationship between physical activity and executive control. In Study 2, I tested the mediating effect of sleep on the relationship between physical activity and cognition. I hypothesized that the mediating effect of sleep would be significant, but that this effect would be specific to tasks that tax executive control; not those that measure processing speed. Given that prior research has shown that sleep efficiency is related to cognition more so than sleep time (Blackwell, et al., 2006; Nebes, et al., 2009), I expected that sleep efficiency would relate to cognition more consistently than sleep time. In addition, I posited that sleep efficiency would more consistently be a significant mediator of the relationship between physical activity and cognition. This is the first study, to my knowledge, that has specifically tested the mediating effect of sleep on the relationship between physical activity and cognitive performance.

Finally, there is evidence that time of day influences the degree to which older adults show impairments in cognitive performance relative to young adults (Winocur & Hasher, 1999). Arousal often peaks in the morning in older adults, resulting in higher cognitive performance in the morning. In Study 3, I examined whether older adults who participated in the experiment in the morning were more likely to perform similarly to young adults and perform better. I also tested whether time of day had an influence on the extent to which sleep was related to cognitive performance in older adults. I expected that older adults with high sleep efficiency who participated in the morning would exhibit the highest cognitive performance, similar to young adults.

1.7.1 General methods

Each of the three studies derived from the same data set ("Frontal Lobe" collected in the Wheeler lab). Analytic methods specific to each of the studies are described in the individual sections below.

Subjects

Subjects were paid at a rate of $10 per hour for participation in the experiment and $50 for wearing an accelerometer armband for one week. Subjects provided informed consent as required by the University of Pittsburgh Institutional Review Board. 125 subjects participated in the experiment. Exclusion criteria included having depression or currently taking psychiatric medication, dependence on drugs or alcohol, or a diagnosis with a neurodegenerative disease. All subjects had normal or corrected vision. Subjects were excluded from further analysis if their accelerometer collected less than 4 days of data, the subject did not complete both experimental sessions, or scored below 27 on the mini mental state exam (MMSE) (n = 15). One subject that was an outlier in Trails B analyses was excluded from all analyses due to an extreme Trails B time and a low sleep efficiency to avoid biasing the data to favor a relationship between performance and sleep efficiency (Appendix C). Additional exclusion of subjects was determined on a task-by-task basis depending upon whether the subject achieved above chance accuracy.

1.7.2 General results

Neuropsychological Assessments

Results from the neuropsychological assessments, sleep, and physical activity metrics for young and older adults are displayed in Table 3.

Table 3. Demographic data, means and standard deviations (SD) for neuropsychological assessment scores, sleep, and physical activity measures

	Younger		**Older**	
N	59		50	
Females	39		34	
	Mean	**SD**	**Mean**	**SD**
Age	23.03	2.44	62.80	6.17
Education	16.05	1.65	15.33	3.09
MMSW	29.58	0.67	29.02	0.91
Forward Digit Span	7.57	1.17	7.26	1.26
Backward Digit Span	5.28	1.42	5.02	1.38
Recall 1	5.12	1.23	4.40	1.50
Recall 2	7.95	1.09	7.34	1.39
Recall 3	9.12	0.91	8.24	1.49
Delayed Recall	7.17	1.66	5.70	1.99
Trails A (sec)	21.57	7.27	30.14	11.36
Trails B (sec)	46.84	20.60	75.90	27.25
Digit Symbol	45.61	7.02	34.30	7.48
Nighttime Sleep Efficiency	0.83	0.07	0.83	0.09
Overall Sleep Efficiency	0.80	0.08	0.81	0.10
Overall Sleep Time	6.95	1.01	6.42	1.15
Awake METs	1.86	0.33	1.51	0.31

Age and Sleep

Figure 3 shows age differences in sleep efficiency and sleep time. There was no difference in sleep efficiency overall t(107) = 0.533, p = 0.595, or nighttime, t(107) = 0.246, p = 0.806, between age groups. The mean overall sleep efficiency was M (mean) = 0.805, SD (standard deviation) = 0.079 for the younger group and M = 0.814, SD = 0.0955 for the older group. The mean nighttime sleep efficiency was M = 0.829, SD = 0.072 in the younger group, and M = 0.825, SD = 0.093 in the older group. Sleep time overall, t(107) = 2.553, p = 0.012, and nighttime, t(107) = 2.044, p = 0.043, were significantly greater in the young group. The mean number of sleep hours overall was M = 6.95, SD = 1.01 in the younger group, and M = 6.42, SD = 1.15 in the older group. The mean number of nighttime sleep hours in the young group was M = 6.33, SD = 1.00. The mean number of nighttime sleep hours in the older group was M = 5.91, SD = 1.15.

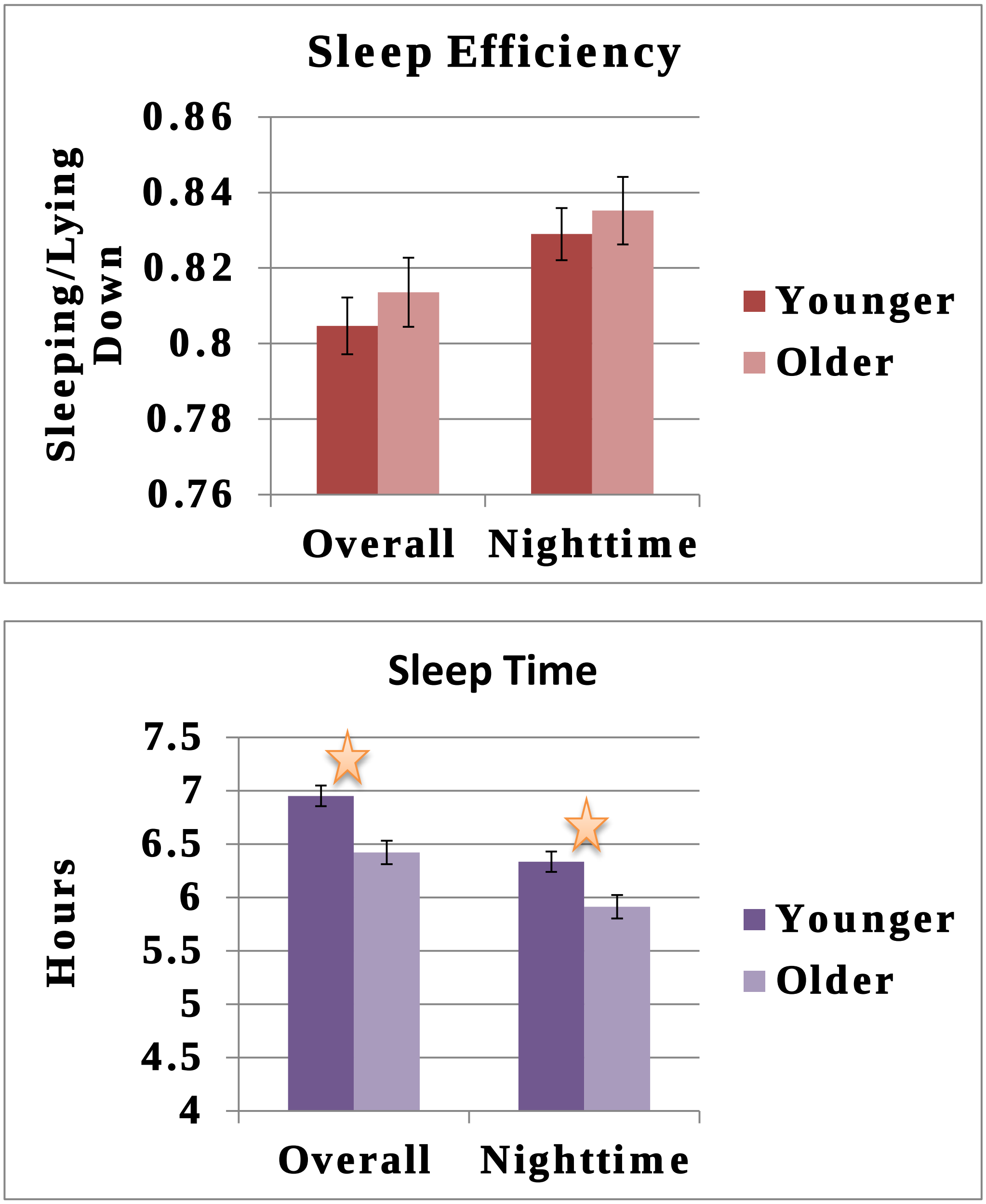


Figure 3. Nighttime and overall sleep efficiency (upper) and sleep time (lower) for young and older adults

2.0 STUDY 1: AGING AND SLEEP INFLUENCE PREPARATION ABILITIES

2.1 INTRODUCTION

Among the “executive tasks” in which older adults tend to show decline, is task-switching (DiGirolamo et al., 2001; Monsell, 2003). In particular, “switch costs”, in which performance is poorer on switch trials compared to repeat trials, are often smaller in older adults (Kramer et al. 1999, Kray et al., 2006); but see (Cepeda, et al., 2001). This is due to difficulties adopting a task-set. In contrast, young adults exert executive control to adopt a task-set which is maintained on repeat trials to improve performance. However, this sometimes leads to a decrement in performance on switch trials (Kramer et al. 1999, Kray et al., 2006). Time to prepare often leads to improved performance and a reduction in switch costs (differences in performance between switch and repeat trials) in young adults (Monsell, 2003). This is referred to as the “preparation effect”.

One factor that may contribute to individual differences in decline executive functions, like switching and preparation, is sleep. Given that sleep declines with age and sleep is thought to restore the prefrontal cortex (Muzur, et al., 2002), age-related sleep changes may play a role in the extent to which older adults exhibit decline in executive control and in turn impaired switching and preparation abilities.

One ERP study (Wilckens, et al., 2010), used a memory task-switching paradigm to compare memory retrieval preparation effects between younger and older adults. This study found that retrieval preparation was absent in older adults, as indicated by ERP correlates of “memory task-set adoption”. However, there is conflicting behavioral evidence to suggest that preparation in general is impaired in older adults; and practice may play a role (Cepeda, et al., 2001; Kramer, et al., 1999).

The goals of Study 1 were three-fold. First, I investigated whether older adults showed deficits in preparatory processing compared with young adults. In other words, whether older adults demonstrated a “preparation effect” in which preparation time, operationalized as longer cue to target intervals (CTIs), would reduce switch costs to the same degree as young adults. Second, using several metrics of sleep, I examined whether subjects with poor sleep were less likely to capitalize on preparation time. The third goal was to determine whether switching and preparation abilities differed in young and older adults with good versus poor sleep quality and quantity, and whether older adults with good sleep would exhibit a preparation effect similar to young adults.

I expected that preparation effects would be diminished in older adults, but that older adults with good sleep would demonstrate preparation effects similar to young adults.

2.2 METHODS

2.2.1 Subjects

After excluding subjects with less than 4 days of accelerometer data, MMSE scores below 27, and switching block accuracy below 55% accuracy at either session (n = 29), analyses included a total of 100 subjects (57 younger, 21- 30 years of age, 43 older, 55 – 76 years of age). A conservative cut off for accuracy (55%) was set to ensure that all subjects included in the analysis had paid attention to the task cues during the switching block. A median split on the remaining subjects separated subjects into high and low overall sleep efficiency groups (+/- 0.825) and nighttime sleep efficiency groups (+/- 0.847). Subjects were separated into overall and nighttime sleep time groups based on the median for their age group: overall sleep time groups (+/- 428.74 minutes for young adults, +/- 387.03 minutes for older adults) , and nighttime sleep time groups (+/- 393.29 minutes for young adults, +/- 357.5 minutes for older adults).

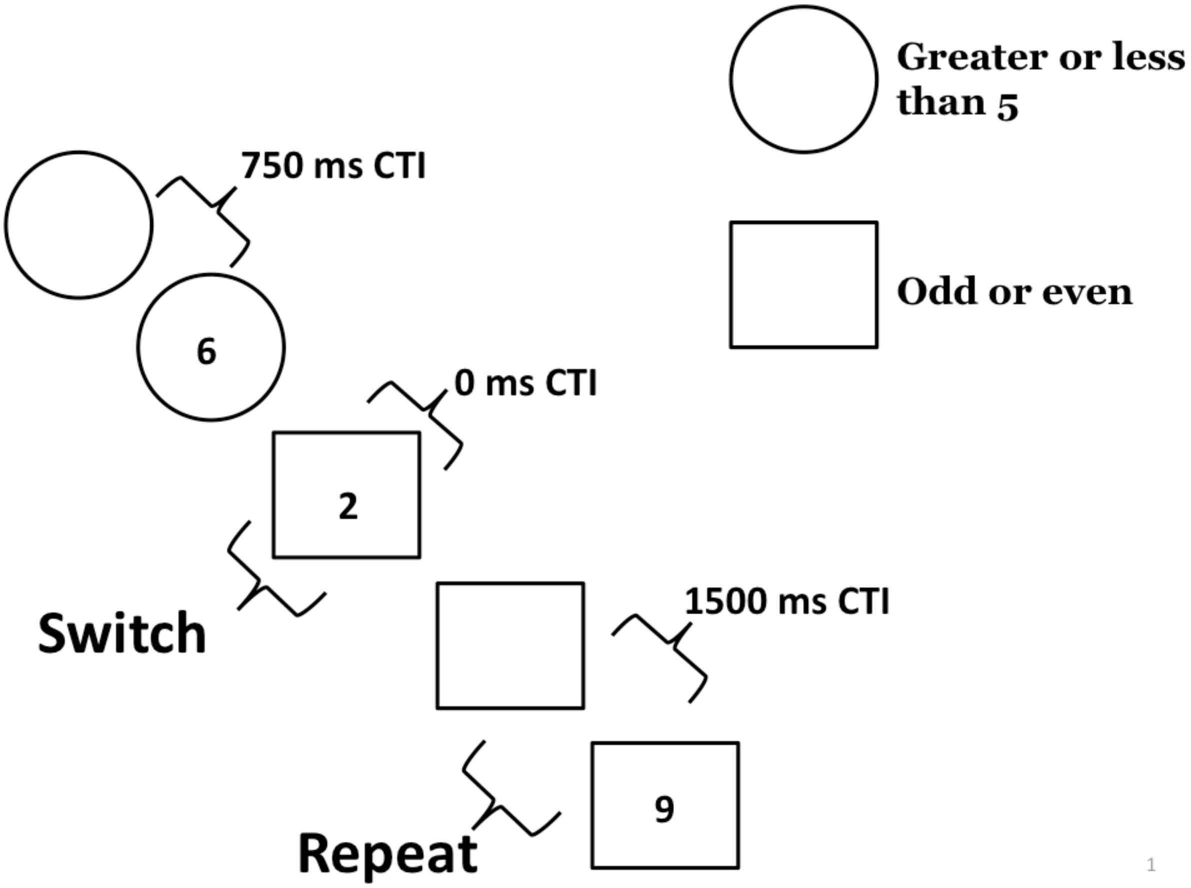


Figure 4. Example sequence of trials in the Task-switch procedure

2.2.2 Experimental procedure

Subjects participated in the Task-switch procedure (Figure 4) twice (once at session 1 and again at session 2) spaced one week apart. In the Task-switch procedure the CTI varied on a trial-by-trial basis. Subjects were cued on each trial to perform one of two tasks that required judgments about a single-digit number presented on the screen. For one task they judged whether the number was greater than or less than 5 (GL task). In the other task, they judged whether the number was odd or even (OE task). A circle preceding or accompanying the target number cued subjects to perform the GL task. A square preceding or accompanying the target number cued subjects to perform the OE task. The CTI was either 0 ms (simultaneous cue and target), 750 ms, or 1500 ms. A practice session comprised of 48 trials (24 of each task) and one experimental block session of each task (GL and OE), comprised of 32 trials of each task, preceded the task-switching block. The switching block was comprised of a total of 96 trials: 16 trials of each cue type (GL and OE) for each of the 3 CTI conditions were presented randomly in the switching block with 8 of each correct response type (greater than, less than, odd, even). This Task-switch paradigm allowed us to assess switch costs with no preparation time (0 CTI) and with preparation time (750 and 1500 CTIs). Figure 4 illustrates an example sequence of trials in the Task-switch procedure: The subject is cued with the circle instructing them to say whether the number is greater than or less than 5. Following a 750 ms CTI, the number appears on the screen (6) and the subject responds “greater”. The next trial, the square and number are presented simultaneously (0 ms CTI) and the subject responds “even”. The last trial, the square cues the subject to prepare to indicate whether the number is odd or even. The number appears following a 1500 ms CTI (9) and the subject responds “odd”. The second trial is a switch trial (switch from circle to square).The third trial is a repeat trial (square to square).

2.3 RESULTS

2.3.1 Preparation and switching

For clarity's sake, in the present section, effects involving sleep efficiency are graphed in red, effects involving sleep time are graphed in purple, and effects involving neither of these factors are graphed in gray.

Task-switch data were separated by CTI or "preparation time" (0, 750, and 1500 ms) and transition condition (switch and repeat).

Response Times

Initial analyses involved a preparation × transition × age group × sleep efficiency group mixed effects ANOVA on RTs collapsed across session to investigate how preparation effects were influenced by sleep efficiency in young and older adults.

Main effects

There were significant main effects of preparation, $F(2,192) = 573.21$, $p < 0.001$ and transition, $F(1,192) = 52.123$, $p < 0.001$, reflecting that subjects were faster with longer preparation times (750 and 1500 ms CTIs) and on repeat trials. There were also significant main effects of age group, $F(1,96) = 49.088$, $p < 0.001$, and sleep efficiency group, $F(1,96) = 5.850$, $p = 0.017$. The main effect of age group reflected that young adults were faster to respond than older adults. The main effect of sleep efficiency group reflected that subjects with higher sleep efficiency were faster to respond.

Interactions with preparation

There was a significant preparation × transition interaction, $F(2,192) = 6.494$, $p = 0.002$, reflecting a "preparation effect" in which switch costs in RT were reduced with time to prepare.

Interactions with Age Group

There were no significant interactions with age group for RT collapsed across session.

Interactions with Overall Sleep Efficiency

There were no significant interactions with overall sleep efficiency group for RT collapsed across session.

Interactions with Overall Sleep Time

A preparation × transition × age group × overall sleep time group ANOVA revealed a significant preparation × overall sleep time group interaction, F(2,192) = 4.566, p = 0.012, reflecting that subjects with longer sleep times were faster to respond, especially on trials with no time to prepare (0 ms CTI). There was also a significant preparation × age group × sleep time group interaction, F(2,192) = 5.207, p = 0.006, reflecting that age differences in RT were largest in the 0 ms preparation time condition, for subjects with short sleep times, but that 1500 ms preparation times eliminated sleep group differences. This suggests that older adults with shorter sleep times show impairments when they have less time to prepare. Figure 5 illustrates this pattern of age differences (Older – Younger) in RT based on overall sleep time group. Age differences were largest in subjects with shorter sleep times in the 0 ms preparation condition. Error bars reflect age differences in standard error.

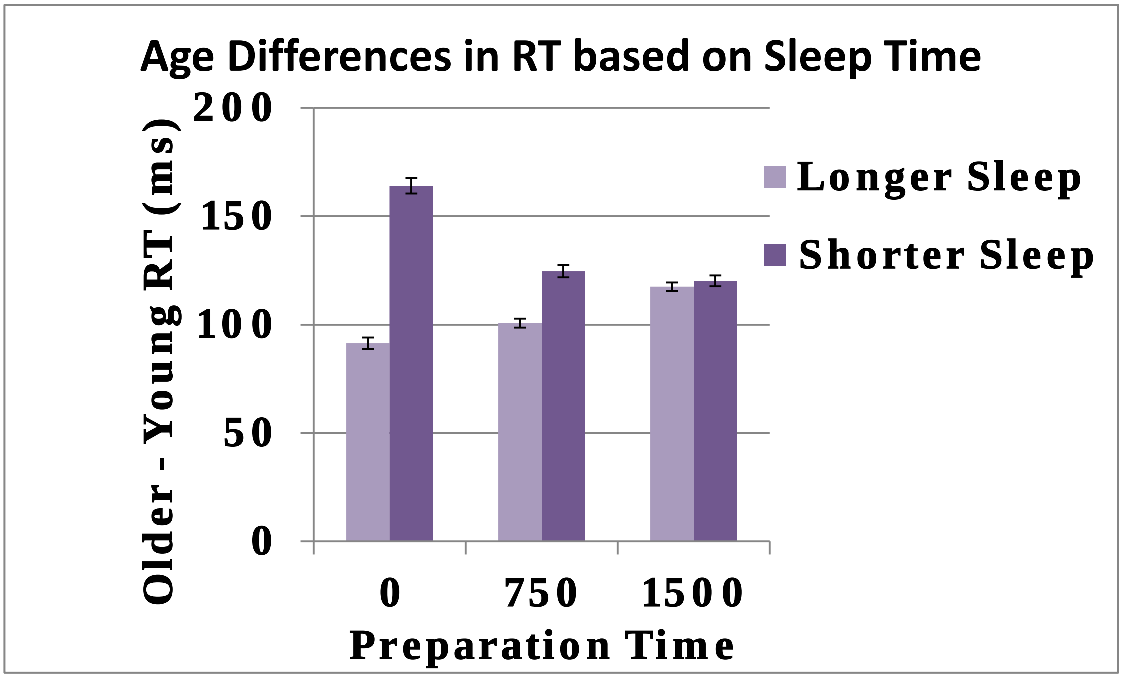


Figure 5. Age differences in RT based on overall sleep time group

Nighttime Sleep

There were no differences in significant effects on RT between overall sleep efficiency and nighttime sleep efficiency, including the main effect, p = 0.031. However, the interactions with preparation, age group, and sleep time were not significant for nighttime sleep time, p's > 0.30. This finding may suggest that time spent sleeping during the day is important for cognition in older adults.

Accuracy

Initial analyses with accuracy involved a preparation × transition × age group × sleep efficiency group mixed effects ANOVA collapsed across session.

Main Effects

There were significant main effects of preparation, F(2,192) = 191.921, p < 0.001 and transition, F(1,104) = 113.28, p < 0.001, reflecting higher accuracy with time to prepare and higher accuracy on repeat trials. There was also a main effect of age group, F(1,96) = 12.123, p = 0.001, reflecting higher accuracy in the younger group.

Preparation

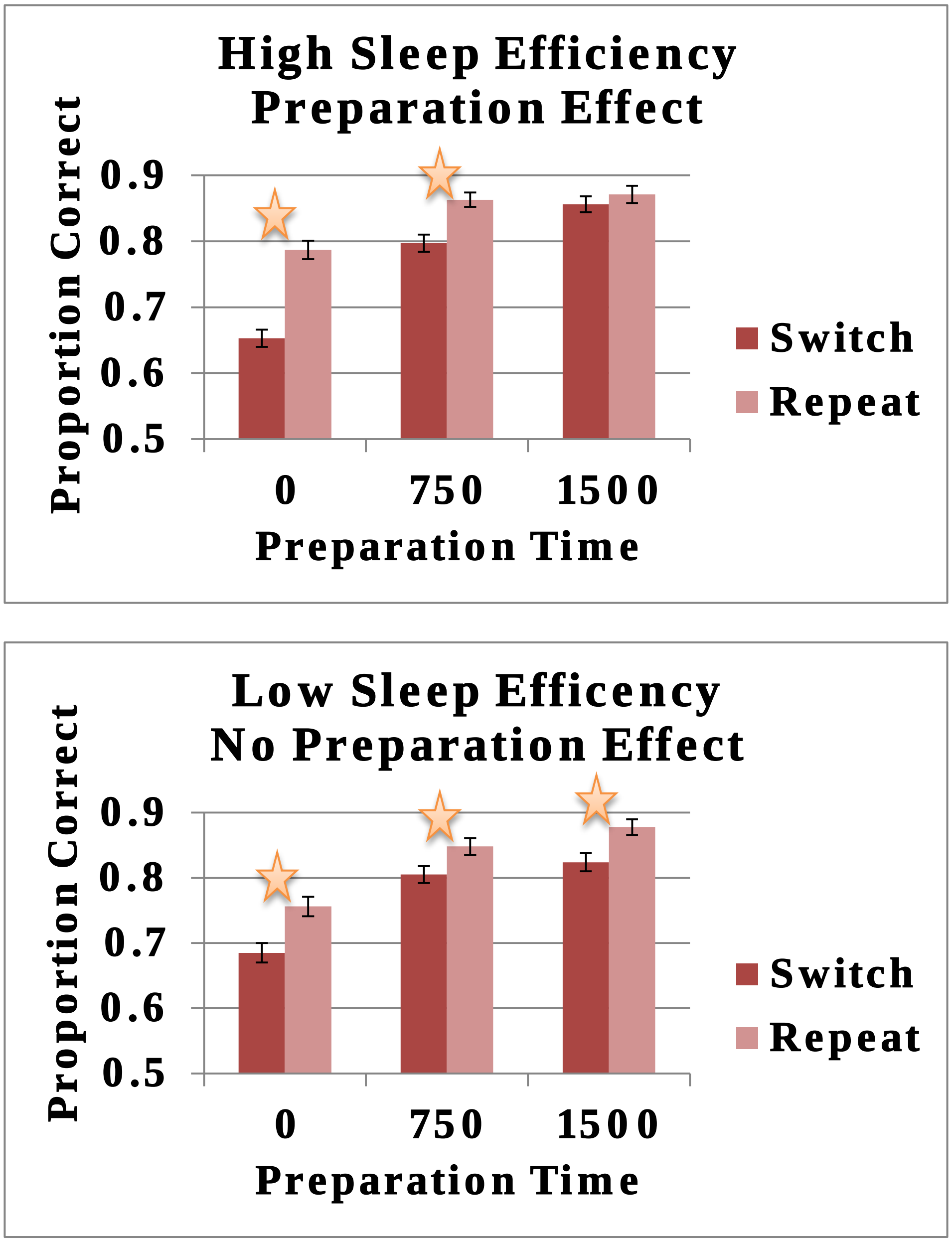
There was a significant preparation × transition interaction, F(2,192) = 13.103, p < 0.001, reflecting a preparation effect in which switch costs in accuracy were reduced with longer preparation times.

Interactions with Age Group

There was a marginally significant transition × age group interaction, F(1,96) = 3.314, p = 0.072, reflecting greater switch costs in the younger group due to a greater benefit from repeat trials compared with older adults. This finding is consistent with the view that younger adults are more likely to adopt a task set. There was no interaction involving preparation and age group, p = 0.360 collapsed across session.

Interactions with Overall Sleep Efficiency

Of primary interest was the significant preparation × transition × overall sleep efficiency interaction, F(2,192) = 7.105, p = 0.001. This finding reflects that subjects with high sleep efficiency were more likely to exhibit a “preparation effect” than subjects with low sleep efficiency. In other words, subjects with high sleep efficiency were more likely to display a reduction in switch costs with time to prepare. Figure 6 shows this “preparation effect” in subjects with high (upper graph) and low (lower graph) sleep efficiency collapsed across younger and older subjects. A reduction in switch costs with longer preparation times (preparation effect) was only evident in the high sleep efficiency group.



High Sleep Efficiency
Preparation Effect

Low Sleep Efficiency
No Preparation Effect

Figure 6. Preparation effect in subjects high (upper) and low (lower) sleep efficiency

Interactions with Overall Sleep Time

There were no significant effects of overall sleep time on accuracy. However, there was a marginally significant transition × overall sleep time interaction, reflecting larger switch costs in subjects with longer sleep times due to higher accuracy on repeat trials and lower accuracy on switch trials, consistent with the view that subjects with longer sleep times are more likely to adopt a task-set.

Nighttime Sleep

There were no differences in significant effects on accuracy between overall sleep efficiency and nighttime sleep efficiency, though there was a marginally significant main effect of nighttime sleep efficiency, $p = 0.081$. There were no differences in significant effects on accuracy between overall sleep time and nighttime sleep time.

2.3.2 Influence of practice on effects of age and sleep on preparation

Prior task-switching studies in older adults have demonstrated that practice can significantly influence age-related impairments in performance (Kramer, et al., 1999). To investigate how practice effects may have influenced effects of age group on preparation, I performed the mixed effects ANOVA reported above again with session as a within subjects factor.

Response Times

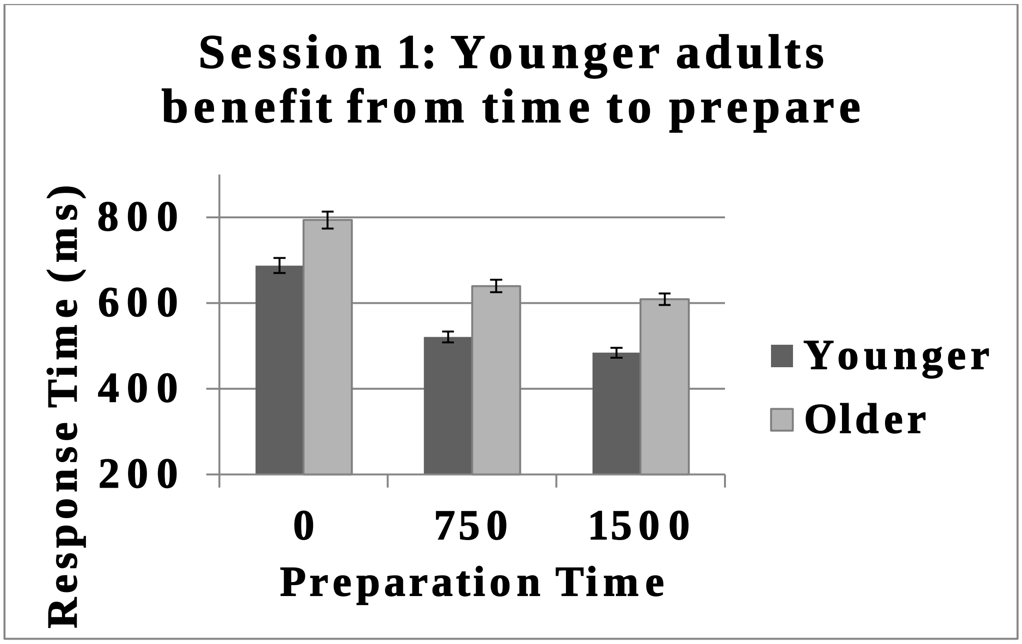
In addition to the effects reported above, there were significant interactions between session, preparation time, and age group, as well as significant interactions between session, preparation time, and sleep group.

Interactions with Session, Preparation, and Transition

There was a significant main effect of session, F(1,96) = 45.381, $p < 0.001$, reflecting that subjects were significantly faster at session 2. There was also a significant session × preparation time interaction, F(2,192) = 5.506, $p = 0.004$, reflecting that the 0 ms CTI benefitted most with practice from session 1 to session 2.

Interactions with Age Group

There was a significant session × preparation time × age group interaction, F(2,192) = 8.574, $p < 0.001$. As shown in Figure 7 below, this interaction reflected the finding that at session 1, young adults showed a disproportionate decrease in RT with time to prepare *(750 and 1500 ms CTIs)* compared with older adults. However, at session 2, *older adults* showed a disproportionate decrease in RT with time to prepare. There was no preparation time × transition × age group interaction, $F < 1$. Thus, contrary to what I expected, a reduction in switch costs with time to prepare was not diminished in the older group. However, without practice (session 1), older adults were less likely to maximize time to prepare in terms of overall RT in the switching block. It can be seen in Figure 8, that at session 1, age differences increased from 0 to 750 to 1500 ms preparation time. However, at session 2, age differences *decreased* from 0 to 750 to 1500 ms preparation time, reflecting that at session 2, older adults began to maximize time to prepare and decrease RT. (Error bars reflect age differences in standard errors).



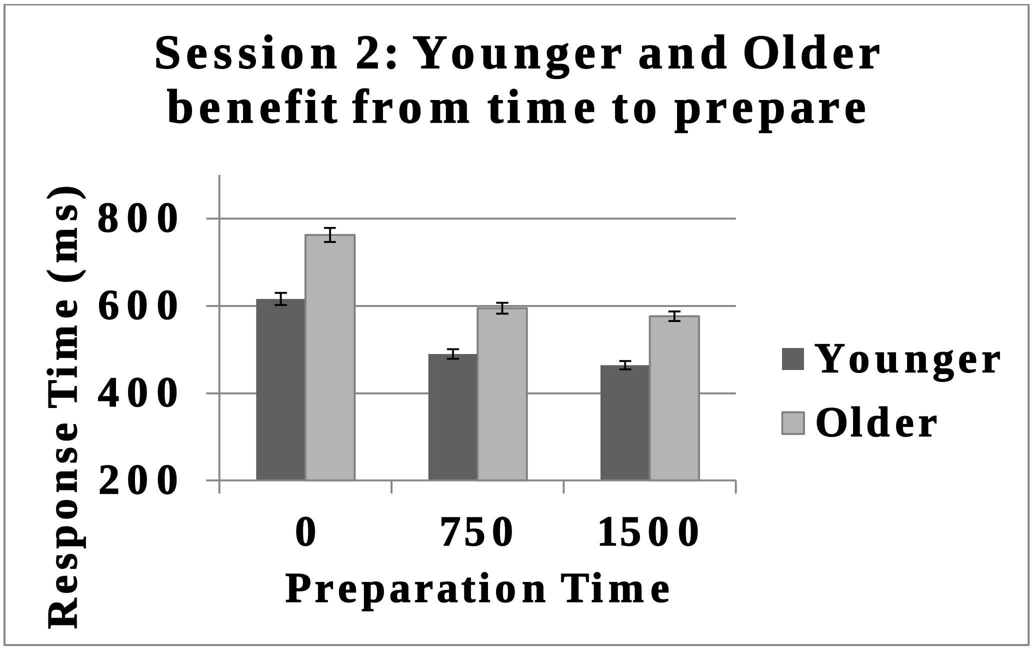


Figure 7. Session 1 (upper) and session 2 (lower) RT as a function of preparation time in young and older adults

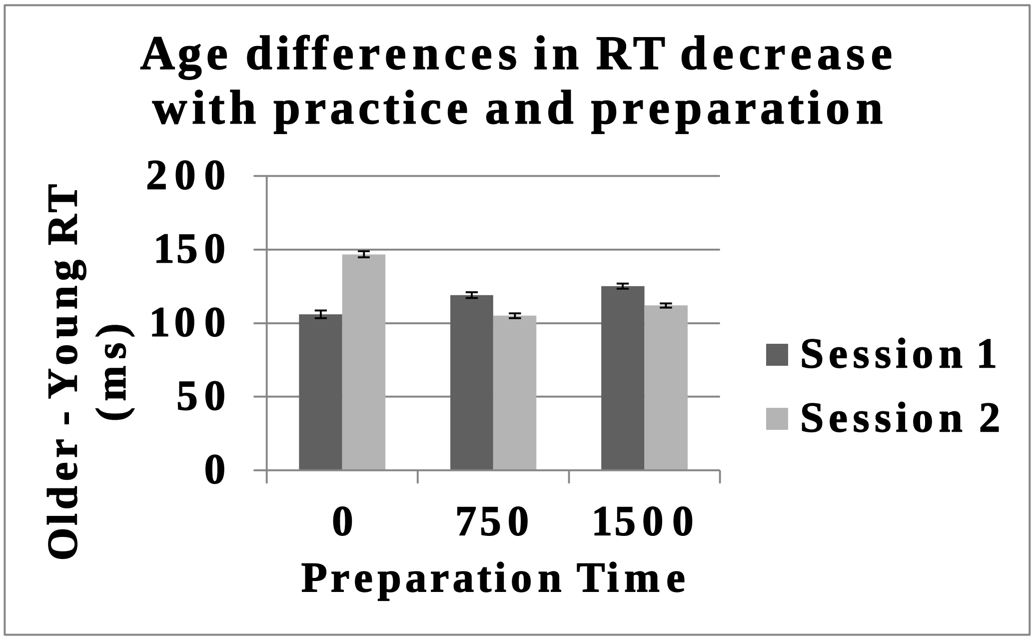


Figure 8. Age differences in RT as a function of preparation time and session

Interactions with Overall Sleep Efficiency Group

There was a marginally significant session × preparation time × sleep efficiency group interaction, F(2,192) = 2.384, p = 0.095, reflecting that at session 1, subjects with high sleep efficiency had disproportionately faster RT with time to prepare compared with subjects with low sleep efficiency. In contrast, at session 2, subjects with low sleep efficiency made use of time to prepare. This pattern in which preparation was influenced by session differently between groups is a similar pattern to what was found with age group as a between subjects factor (Figure 7 above). These parallel findings with age group and sleep efficiency group suggest that older adults and subjects with low sleep efficiency can maximize time to prepare with practice. However, given that this effect of sleep efficiency group was only marginally significant, this interpretation is tentative.

Sleep Time

There were no significant interactions involving session and sleep time group for RT.

Accuracy

In addition to the significant effects on accuracy reported above, there were significant interactions involving session, preparation time, age group, and sleep time group.

There was a significant main effect of session, F(1,96) = 19.254, $p < 0.001$, reflecting improved accuracy at session 2.

Interactions with Age Group

Similar to what was found with RT, there was also a significant session × preparation time × age group interaction with accuracy, F(2,192) = 3.825, $p = 0.024$, reflecting that at session 1, young adults displayed a disproportionate benefit in accuracy with time to prepare compared with older adults (Figure 9, upper panel). However at session 2, older adults improved with time to prepare similarly to young adults (Figure 9, lower panel), and the advantage went away in the young group. This result again suggests that older adults may, with practice, engage preparation strategies similar to young adults. Similar to the effect found with RT, this effect can be seen as an increase in age differences with time to prepare at session 1, but smaller age differences with time to prepare at session 2 (Figure 10). Figure 10 below shows how age differences increased with preparation time at session 1, but to a lesser degree at session 2. Age differences were largest with 1500 ms preparation times at session 1, but these age differences were diminished at session 2 when older adults also benefitted from preparation time. (Error bars reflect age differences in standard errors).

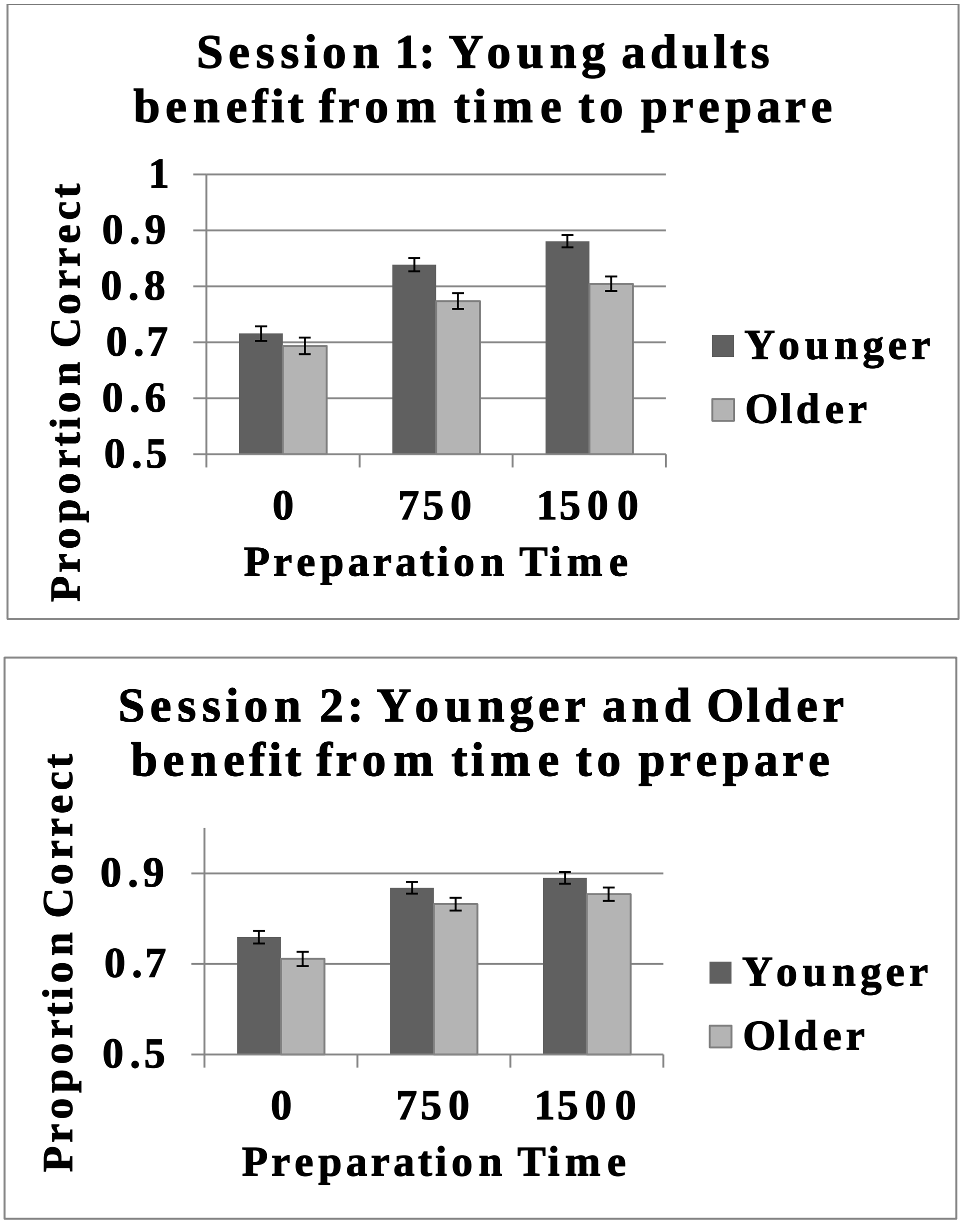


Figure 9. Session 1 (upper) and 2 (lower) accuracy as a function of preparation time in young and older adults

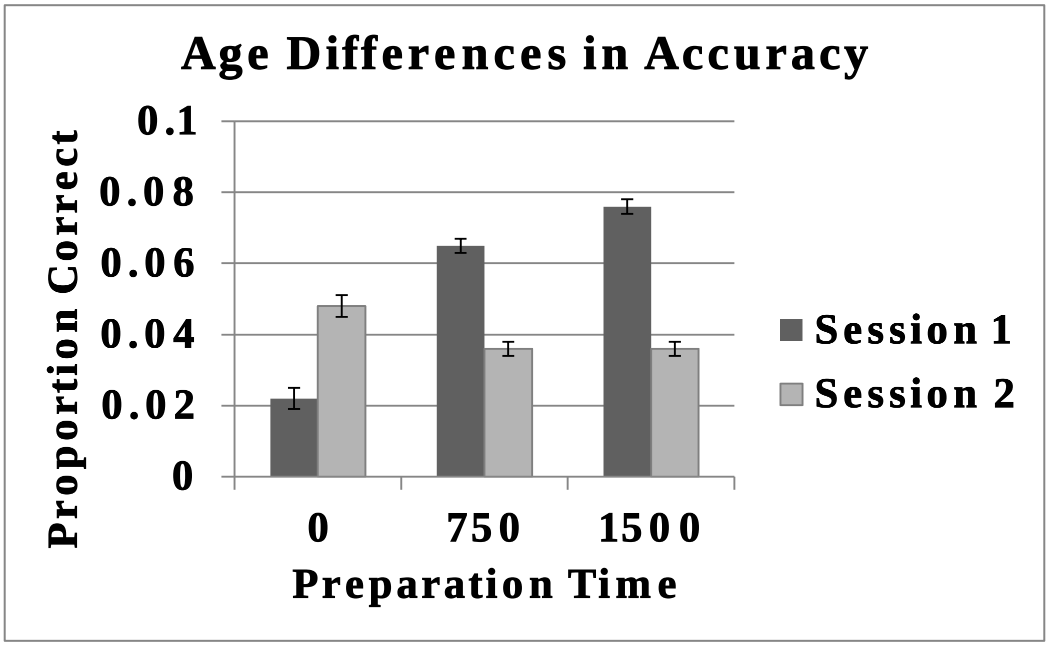


Figure 10. Age differences in accuracy as a function of preparation time and session

Sleep Time

There was a significant session × transition × age group × overall sleep time group interaction, F(1,96) = 4.265, p = 0.042, reflecting that young adults with longer sleep times showed a greater benefit from task repeats at session 2. This may suggest that they were able to adopt a task set more readily than young adults with less sleep time, particularly when the task was well learned at session 2. This effect was also significant for nighttime sleep time group, F(1,96) = 7.367, p = 0.008. Though, this interaction is difficult to interpret because it is driven by a reduction in switch costs from session 1 to session 2 for young adults with shorter sleep times (Figure 11, upper panel) and older adults with longer sleep times (Figure 11, lower panel). Figure 11 shows switch costs in accuracy from session 1 to session 2 in young and older adults. Young adults with longer sleep times benefitted more from repeat trials reflecting larger switch costs at session 2.

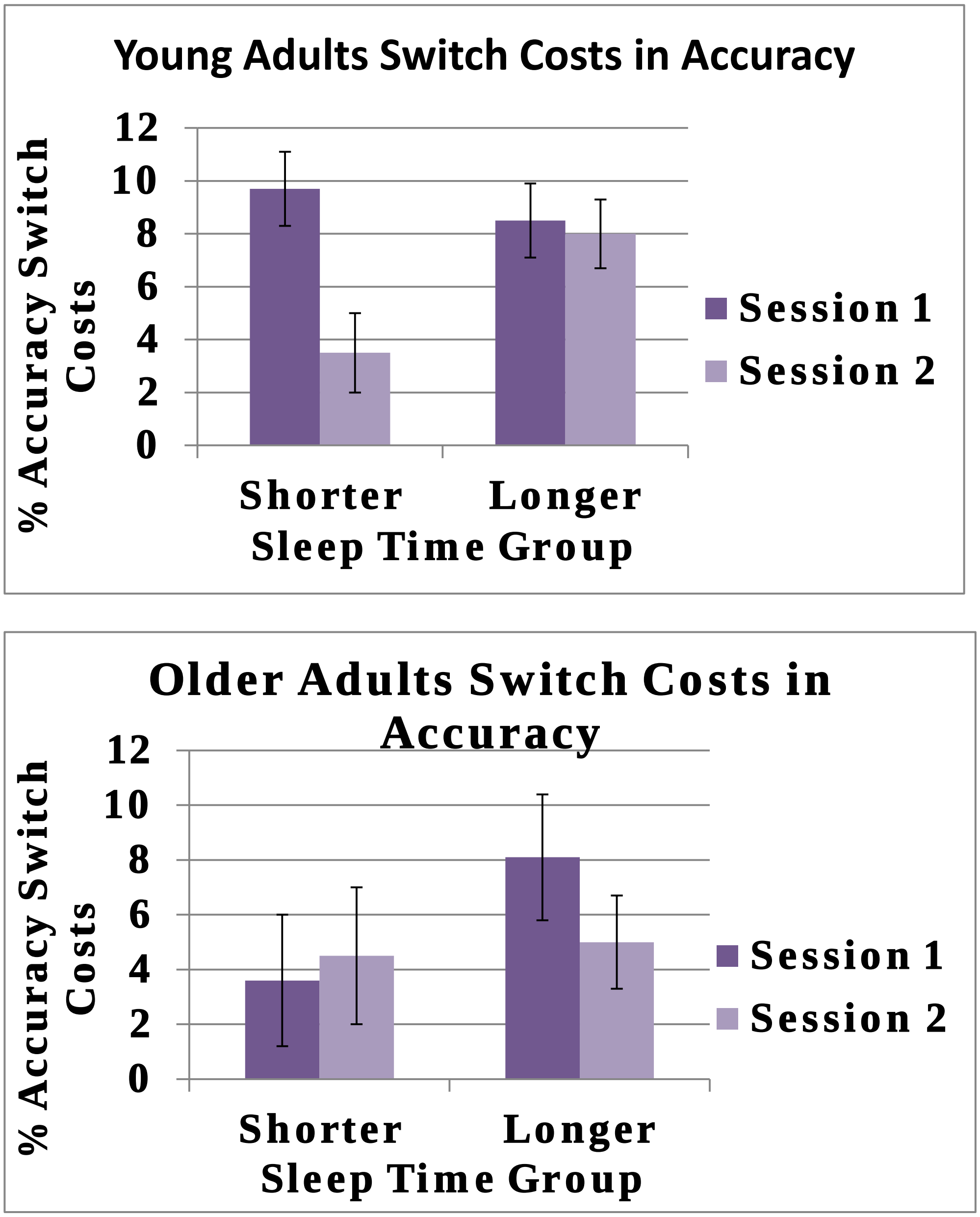


Figure 11. Switch costs in accuracy by session as a function of sleep time

2.3.3 Switching versus single task block performance

To examine how age and sleep influenced task “mixing” compared with single task block performance, I performed a mixed effects ANOVA with switch and repeat trials types in the switching block and GL and OE single task blocks. Performance on repeat trials in the switching block reflects costs from “mixing” tasks compared with performance in either single task block.

Only effects of age group and sleep efficiency group are reported here.

Response Times

A block (switch, repeat, GL, OE) × age group sleep × efficiency group mixed effects ANOVA revealed a significant main effect of age group, $F(1,96) = 56.621$, $p < 0.001$, a main effect of sleep efficiency group, $F(1,96) = 5.598$, $p = 0.020$, a significant block × age group interaction, $F(3,288) = 14.048$, $p < 0.001$, and a significant block × sleep efficiency group interaction, $F(3,288) = 4.183$, $p = 0.006$ reflecting that the greatest effects of sleep efficiency group were on RTs in switch trials, $t(98) = 2.011$, $p = 0.047$, especially compared with the GL task block, $p = 0.239$, reflecting an effect of sleep efficiency on switching (Figure 12). Figure 12 shows RTs for switch and single task blocks as a function of sleep efficiency group: Subjects with high sleep efficiency were faster on switch trials compared with subjects with low sleep efficiency. These differences in sleep efficiency were not significant for the other trial types (repeats, GL block, or OE block).

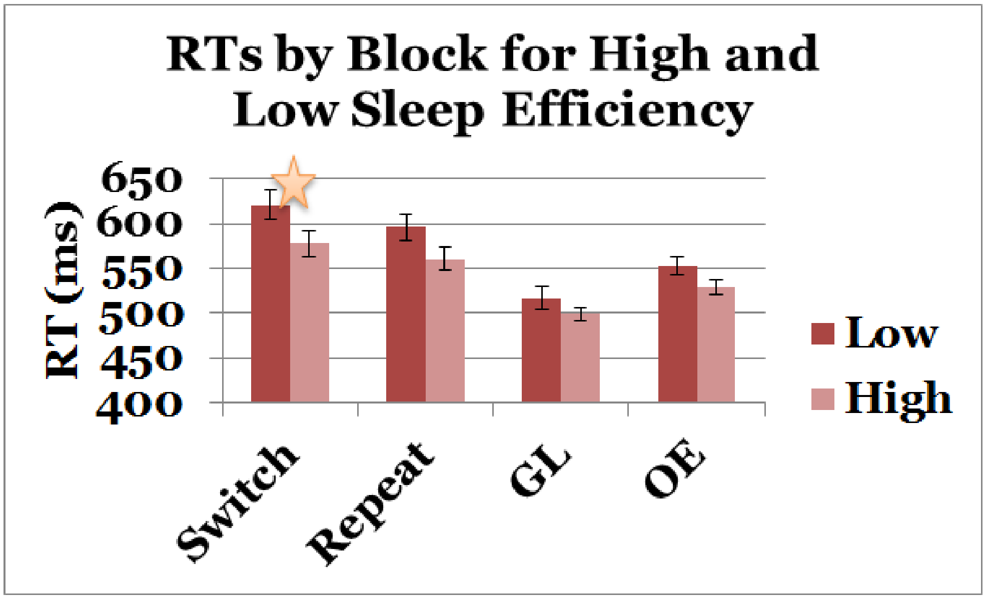


Figure 12. RTs by block as a function of sleep efficiency

Accuracy

A block (switch, repeat, GL, OE) × age group × overall sleep efficiency group ANOVA revealed a main effect of age group, F(1,96) = 10.148, p = 0.002. There was also a significant block × age group interaction, F(3,288) = 5.748, p = 0.001, reflecting that age differences were larger in the switching block and GL block compared with the OE block.

These findings with block as a within subjects factor reveal that effects of overall sleep efficiency did not differentially influence switching versus single task block accuracy. However, they did differentially influence RT in switching versus single task blocks.

Nighttime Sleep Efficiency

Nighttime sleep efficiency group as a between subjects factor revealed the same effects on RT and accuracy as well as a main effect of nighttime sleep efficiency group on overall accuracy, F(1,96) = 5.504, p = 0.021.

Sleep Time

Response Times

In terms of RT, there was a significant block × age group × overall sleep time group interaction, F(3,288) = 2.793, p = 0.041, reflecting that age differences in the switching block were exacerbated in subjects with shorter sleep times. In other words, older adults performed worse in the switching block if they were in the shorter sleep time group (Figure 13). Figure 13 shows that age differences in RT were largest on switch trials for subjects with shorter sleep times: Older adults with shorter sleep times showed the largest impairments compared with young adults on switch trials.

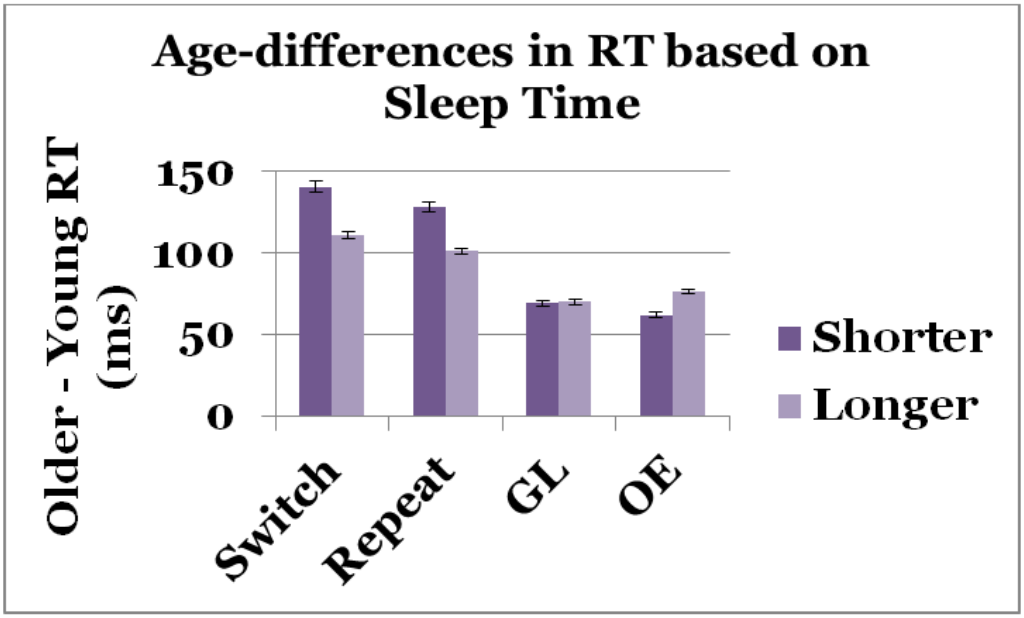


Figure 13. Age differences in RT based on sleep time

There was however, no block × nighttime sleep time interaction, $p > 0.25$, again reflecting that sleep outside of the nighttime sleep bout may influence performance in older adults.

Accuracy

There were no significant interactions between block and overall sleep time for accuracy.

2.3.4 Inhibition and Working Memory

Preparation in this task may have been dependent on inhibitory control. This would be consistent with the view that preparation involves inhibition of irrelevant task-sets. To test this, I assessed whether preparation effects were eliminated after controlling for inhibitory control abilities. Inhibition was operationalized as Stroop inhibition (incongruent/congruent) response time and accuracy. I reasoned that if the effect of sleep was eliminated when controlling for inhibition, this would suggest that preparation in the Task-switch paradigm depends on inhibitory control. Using Stroop inhibition RT and accuracy as a covariate, both age group and sleep efficiency group interactions with preparation remained robust, p’s < 0.03.

Likewise, preparation in this task may have been dependent on working memory, suggesting that preparation involves the maintenance of a relevant task-set during the cue-target interval. I assessed whether preparation effects were eliminated after controlling for working memory abilities operationalized as Sternberg 5-letter and 2-back RT and accuracy. Accordingly, if the effect of sleep on preparation was eliminated when controlling for working memory abilities, this would suggest that preparation in the Task-switch paradigm depends on working memory. Indeed, accuracy in the 2-back task altered the session × preparation × age group interaction with accuracy (Figure 14, upper panel). This effect was no longer significant, F(2,188) < 1 after controlling for 2-back accuracy (Figure 14, lower panel). This finding suggests that age differences in preparation abilities may be driven by individual differences in working memory abilities during the cue-target interval. Controlling for working memory abilities (2-back accuracy) reduced age differences, particularly at session 1. However, the effect was not eliminated, suggesting that there is something above and beyond working memory that contributes to age differences in preparation. Figure 14 shows age differences in accuracy before (upper) and after (lower) controlling for 2-back accuracy. Age differences are diminished such that the session × preparation time × age group interaction (upper) is no longer significant (lower).

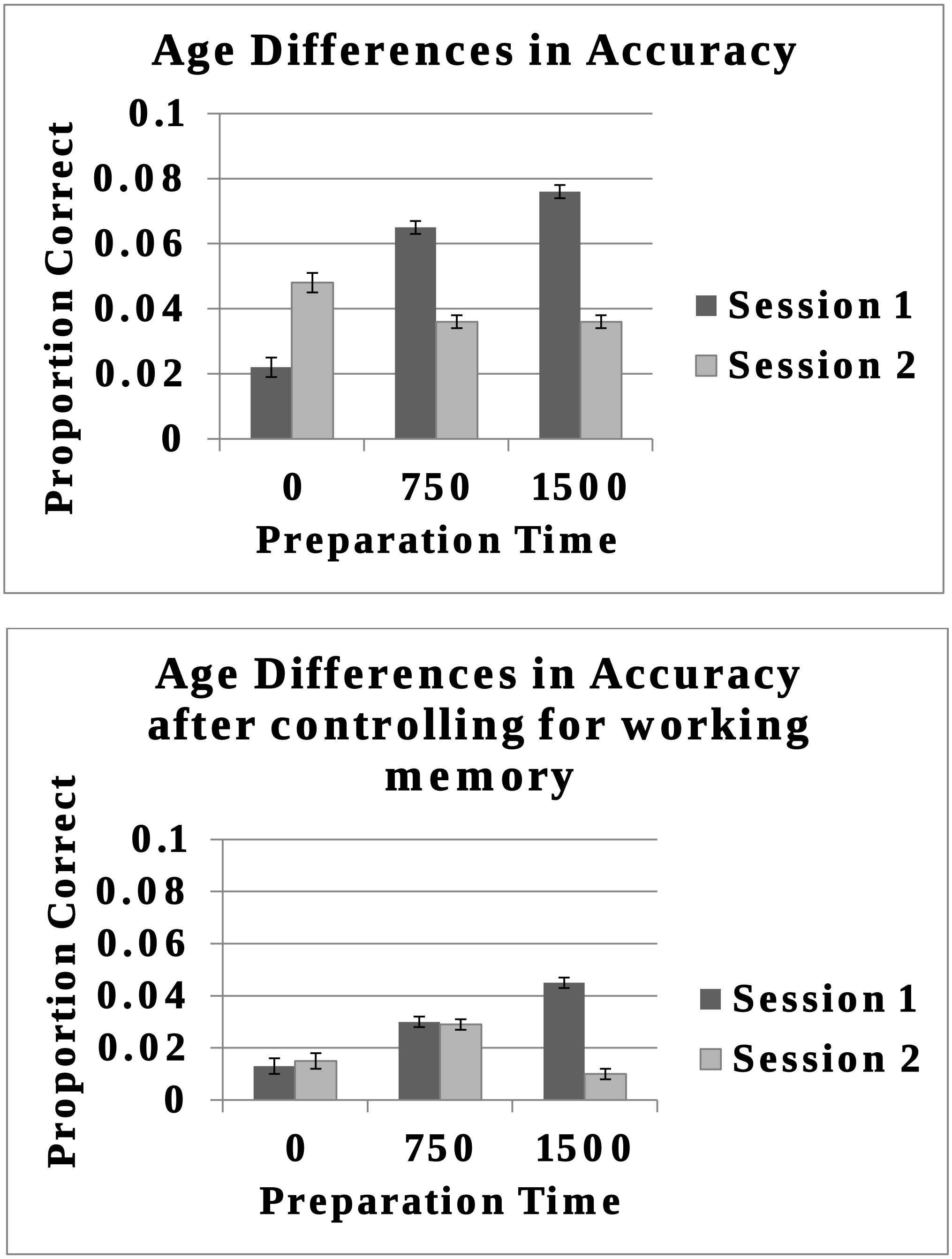


Figure 14. Influence of working memory on age differences in preparation

2.4 DISCUSSION

2.4.1 Preparation

Consistent with prior studies, young and older adults exhibited a robust preparation effect in which RTs were faster, accuracy was higher, and switch costs in terms of response time and accuracy are reduced with time to prepare.

2.4.2 Age and preparation

In terms of effects of age group on preparation, the novel finding here was that young adults were more likely to maximize time to prepare during session 1. Young adults demonstrated disproportionately faster RT and higher accuracy with time to prepare. However, during session 2, older adults also maximized time to prepare by demonstrating disproportionately faster RT and higher accuracy with time to prepare compared with their session 1 performance. This result suggests that with sufficient practice, older adults also engage preparatory strategies. This may also suggest that for tasks that are more difficult, older adults may be less likely to engage preparatory strategies compared with tasks that are either easier or better learned.

These results are reminiscent of the results of Kramer et al. (1999) who showed that older adults exhibited large age differences in switch costs early on, however with a modest amount of practice, switch costs were similar between young and older adults, reflecting that when a task is well learned, switch costs are smaller in older adults. Similarly, in the present study, age differences in response time and accuracy for longer preparation times were reduced at session 2, reflecting that age-related decrements in preparation are reduced with practice. Similar to the present study, Cepeda et al. (2001) examined how CTI influenced switch costs in young and older adults. They expected that without practice older adults would benefit less from preparation time (longer CTIs), but that with practice, older adults would be able to benefit from preparation. Instead they found that older adults were able to benefit from preparation time just as much as young adults in terms of switch costs. The critical difference with their findings compared to the present interaction between session, age group, and preparation is that Cepeda et al. (2001) specifically examined switch costs, whereas the present interaction applied to RT and accuracy collapsed across switch and repeat trials, suggesting that age decrements in preparation more broadly, decrease with practice. Future analyses will examine how age differences in preparation change *within* each session. It may be that age differences in preparation are eliminated by the end of session 2.

It is possible that the diminishing of age differences with preparation at session 2 was driven by a floor effect with RT and a ceiling effect with accuracy. However, the means are below 90% correct for young adults at session 2, so a ceiling effect in the younger group may not entirely explain the reduction in age differences with longer preparation times.

2.4.3 Working memory and preparation

I tested whether the age differences in preparation were driven by higher working memory abilities in the younger group. Using 2-back accuracy as a covariate, I found that the interaction between session, age group, and preparation time on accuracy was no longer significant after accounting for working memory abilities. However, age differences were not eliminated suggesting that some advantage above and beyond working memory underlies age differences in preparation.

2.4.4 Sleep efficiency

Two novel results reported here support the view that adults with high sleep efficiency are more likely to engage preparatory strategies to enhance performance compared with adults with low sleep efficiency. The most robust of these findings was the transition × preparation time × sleep efficiency interaction found with accuracy. This interaction reflected that the preparation effect was only evident in subjects with high sleep efficiency (switch costs were reduced with time to prepare only in subjects with high sleep efficiency). Studies using sleep manipulations, such as sleep deprivation have shown significant impairments in task-switching with sleep deprivation (Couyoumdjian, et al., 2010). However, this is the first report of differences in switching *and* preparation abilities as a function of individual differences in sleep quality. This finding provides evidence that adults who have difficulties sleeping may be impaired cognitively; it is not necessary to experimentally disrupt or deprive subjects of sleep to find robust effects of sleep on executive control. In addition, this effect was not moderated by session, suggesting that practice does not eliminate sleep group differences in the benefit that preparation has on switching.

The second of these findings was the marginal session × preparation time × sleep efficiency group interaction. Particularly in the first session, subjects with high sleep efficiency were disproportionately faster to respond with time to prepare compared with subjects with low sleep efficiency. This result suggests that subjects with high sleep efficiency engage preparatory strategies to enhance response speed when they are cued in advance. The finding that this effect of preparation time disappeared at session 2, suggests that with practice, sleep efficiency has less of an influence on subjects' ability to engage preparatory strategies. This finding supports the view that sleep quality is important for more controlled tasks. When a task becomes automated, sleep quality is less critical for overall response speed. It should be noted again, that because this effect was marginally significant, this interpretation is tentative.

2.4.5 Sleep time

Sleep time was the only sleep metric to reveal significant interactions with age group. These were found for both RT and accuracy. Young and older adults were split into sleep groups based on the median for their age group, given that older adults had significantly shorter sleep times on average compared with young adults. Analyses involving sleep time revealed significant effects of preparation time in terms of RTs: In the 0 ms preparation time condition older adults with longer sleep times had faster RTs compared with those with shorter sleep times. In addition, age differences in the switching block were exacerbated for older adults with shorter sleep durations. This finding is in contrast to sleep deprivation studies that suggest that older adults are resilient to sleep deprivation (Duffy, et al., 2009; Philip, et al., 2004) or require less sleep than younger adults. It appears as though older adults with shorter sleep times are slower especially on more cognitively demanding trials (switching block compared with single task block and trials with no time to prepare). It is also noteworthy that in contrast to sleep efficiency, there were no main effects of sleep time on RTs or accuracy, again suggesting that the influence of sleep time on performance is more specific to cognitively demanding tasks. This is consistent with the view that older adults exhibit impairments in cognition with less sleep time when “executive tasks” are used (Killgore, et al., 2006). Interactions in accuracy between age group and sleep time depended on session, which makes these effects more difficult to interpret, especially since they were driven by a reduction in switch costs in young adults with shorter sleep durations and older adults with longer sleep durations. Nonetheless, these results suggest that switch costs in accuracy may be influenced by sleep duration.

3.0 STUDY 2: SLEEP EFFICIENCY MEDIATES THE RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND COGNITION IN YOUNG AND OLDER ADULTS

3.1 INTRODUCTION

Aging is often characterized by a decline in executive control. Physical activity interventions have been shown to improve executive control in both young and older adults (Erickson, et al., 2012; Kramer, et al., 2006). There are consistent benefits of physical activity and exercise interventions on executive control that appear to be mediated by biological markers of brain function (Erickson, et al., 2012; Kramer, et al., 2006; Weinstein, et al., 2011). It is not well understood, however, how exercise directly benefits cognition. One possibility is that exercise improves cerebral vasculature, thereby influencing cognitive function (Brown, et al., 2010). Another possible mechanism is that exercise improves sleep, which in turn benefits cognition. In terms of objective sleep measures, older adults who are more physically fit tend to have shorter sleep latencies (time it takes to fall asleep) and more slow-wave sleep than sedentary older adults (Vitiello, 2008). Significant improvement in subjective sleep quality has been shown in sedentary older adults with poor sleep who took part in an exercise intervention (Reid, et al., 2010). In addition, exercise in sedentary older adults has been shown to selectively improve slow-wave sleep (Vitiello, 2008; Vitiello, et al., 1994). It has yet to be determined, however, whether these improvements in sleep affect cognition in older adults.

One prior pilot study examined how sleep and performance on neuropsychological tasks improved with physical activity (Benloucif, et al., 2004). This study revealed improvement in subjective sleep assessed with the PSQI and improvement in neuropsychological performance following a physical activity intervention. However, there was no relationship between subjective sleep quality and cognitive performance. The lack of a sleep-cognition correlation in this study is likely due to the small sample size (n = 12). This sample size was also insufficient to test mediation which requires a sample size of 100 -150 subjects.

The present study used accelerometry (SenseWear®) to assess physical activity and sleep behavior in young and older adults. A battery of cognitive tasks, some thought to depend on executive control (i.e. Trails B) and others thought to be "non-executive" and depend more on processing speed (i.e. Trails A), was used to assess cognition. I used these measures to test the mediating effect of sleep on the relationship between physical activity and executive control in 109 subjects. I expected to find significant relationships between physical activity and sleep, physical activity and executive control, and sleep and executive control in young and older adults. I expected that neither physical activity nor sleep would be significantly related to performance on processing speed tasks (Trails A and digit symbol substitution). Critically, I expected that the mediating effect of sleep on the relationship between physical activity and executive control would be significant. This finding would suggest that physical activity improves executive control abilities, at least in part, through improvements in sleep (Figure 15). Figure 15 shows the theoretical mediation model illustrating the indirect pathway of sleep between physical activity and executive control. Physical activity influences executive control through its influence on sleep.

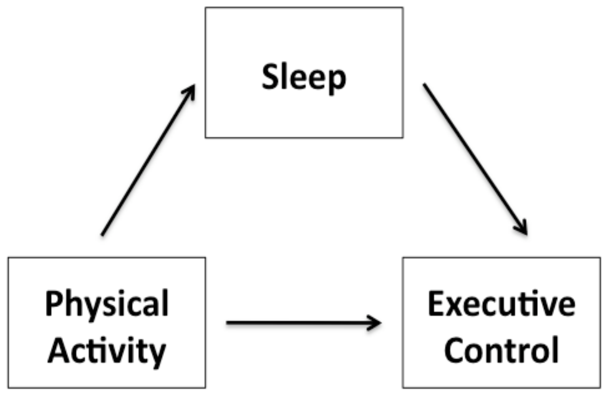


Figure 15. Mediation model of indirect pathway of sleep between physical activity and executive control

3.2 METHODS

3.2.1 Subjects

109 subjects were included in the analysis. 59 were young adults (mean age = 23.03, SD = 2.26) and 50 were older adults (mean age = 62.80, SD = 6.17).

3.2.2 Experimental Procedure

Neuropsychological Assessments

The computer-based tasks and neuropsychological assessments were used to test the mediating effect of sleep on cognition. The assessments included in this analysis were the Digit Span (forward and backward) and digit symbol substitution subsets of the Wechsler Adult Intelligence Scale III (Wechsler, 1997), Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word List Memory test (J. C. Morris et al., 1989), which includes three trials of immediate word recall and one trial of delayed word recall, and Trail making Tests A and B (Reitan, 1958). The computer-based tasks included here were the Stroop, Flanker, N-back, Sternberg Working Memory, and the Task-switch paradigm described above in Study 1.

Cognitive Tasks

Switching

Switching was assessed with the computerized Task-switch paradigm (TS) (described in detail in Study 1) and a paper-and-pencil version of Trials B. In contrast to Trails A, in which the subject is asked to draw lines connecting encircled numbers distributed throughout a sheet of paper in sequential order 1-25, for Trails B, the subject must alternate between numbers and letters distributed throughout the page (1- A- 2- B) (Tombaugh, 2004). Time to complete the Trail making tests was the dependent variable.

Inhibition

Inhibition was assessed with a computerized version of the Stroop and Flanker tasks. In the Stroop task, subjects viewed words one at a time on the screen in blue, red, or green ink colors and were asked to judge the ink color of the word. There were congruent (i.e. red), incongruent (i.e. red), and neutral (i.e. table) trials. In the Flanker task, subjects viewed 5 arrows (“flankers”) on the screen on a given trial (< < < < <) and were asked to judge the direction in which the center arrow was pointing. This task included congruent (< < < < <) and incongruent trials (< < > < <). For both tasks inhibition was assessed for RT and accuracy, which was calculated as incongruent mean/congruent mean) multiplied by 100%. Because both congruent and incongruent trials included color information in the form of the word itself and the ink color, both of these conditions impose demands on attentional control (Milham et al., 2002).

Working Memory

Working memory was assessed with a computerized version of the Sternberg working memory and N-back tasks and paper-and-pencil version of backward digit span. In the Sternberg task, subjects viewed 2 and 5-letter strings in upper case letters. After a 3000 ms delay, subjects saw a lower case letter and were asked to judge whether the lower case letter matched one of the previous upper case letters. In the N-back task, subjects viewed a series of letters appearing one at a time on the screen. Subjects were required in one condition to identify whether the letter currently on the screen was the same as the previous letter (1-back) or, in the other condition, the same as the letter two previous (2-back). The 5-letter condition in the Sternberg task and the 2-back condition in the N-back task were expected to engage working memory more than the other conditions and be more strongly related to sleep and physical activity.

Processing speed

Processing speed was assessed with Trails A (described above) and the digit symbol substitution task. In the digit symbol substitution task subjects were given a series of symbols that corresponded to the numbers 1-9. The test required subjects to write as many symbols as possible in 60 seconds within a box below each number.

3.2.3 Analytic Techniques

Sleep

Overall and nighttime sleep efficiency and sleep time were used as sleep metrics posited to relate to cognitive performance. Given that prior research has shown that sleep efficiency is more related to cognition than sleep time, I expected that sleep efficiency would be correlated with cognition more consistently than sleep time with cognition. In addition, I posited that sleep efficiency would more consistently be a significant mediator of the relationship between physical activity and cognition due to the established effect of physical activity on sleep quality (Benloucif, et al., 2004; Driver & Taylor, 2000; Lopez, 2008; Vitiello, 2008).

Physical activity

A number of physical activity metrics were calculated from the accelerometer physical activity estimates, including average METs while awake, referred to here as “awake METs”, overall average daily METs, average daily METs while physically active, average daily minutes of moderate, vigorous, and very vigorous physical activity. Awake METs was used here to avoid skewing average METs in the lower direction due to the amount of time spent sleeping.

Regression analysis

Relationships between sleep efficiency and sleep time (overall and nighttime), physical activity, and cognition were subjected to a linear regression analysis with age, gender, and education as covariates.

Outliers

Outliers were identified by visually inspecting scatterplots of all subjects in terms of sleep efficiency, cognitive performance, and physical activity. Analyses were conducted with and without potential outliers. Any such cases are reported in detail in Appendix C. Subjects were excluded if they performed at or below chance accuracy on incongruent conditions in Stroop and Flanker tasks (33% accuracy on Stroop, 50% accuracy on Flanker). 3 subjects were excluded from Sternberg task analyses because they achieved below 10% accuracy on the 2-letter condition (Appendix C).

Mediation analysis

Mediating effects of sleep on the relationship between physical activity and cognition were assessed using the bias corrected and accelerated bootstrapping method (Preacher & Hayes, 2008) in SPSS with 5000 bootstrap samples. A mediating factor is part of a causal pathway through which an independent variable (physical activity) affects a dependent variable (cognition). The main requirement for mediation is that the indirect effect of the independent variable (physical activity) through the mediator variable (sleep) on the dependent variable (cognition) be significant. There is no requirement that the direct effect of the independent variable on the dependent variable be significant (Gelfand, Mensinger, & Tenhave, 2009; Zhao, Lynch, & Chen, 2010). Covariates were age, gender, and years of education.

3.3 RESULTS

3.3.1 Objective and subjective physical activity and sleep metrics

Objective and subjective physical activity

Scores from the self-report exercise history questionnaire were significantly correlated with all physical activity metrics, awake METS, r = 0.197, p = 0.040, peak METs, r = 0.265, p = 0.005, average physical activity (METs => 3) minutes per day, r = 0.255, p = 0.007, average total

METs, r = 0.201, p = 0.036, average minutes of moderate activity (3-6 METs), r = 0.244, p = 0.010, average minutes of vigorous activity (6-9 METs), r = 0.019, and average minutes of very vigorous (9+ METs), r = 0.255, p = 0.007. These significant correlations reflect that overall, subjects were accurate in their self-report of physical activity.

Subjective physical activity and sleep

There were no significant correlations between subjective physical activity measured with the exercise history questionnaire and subjective or objective sleep quality and quantity measured with the PSQI and accelerometer, nor was subjective physical activity a significant predictor of subjective sleep quality or quantity after accounting for age, gender, and education. Though subjective physical activity was a marginally significant predictor of objective overall sleep efficiency, $\beta = 0.175$, R^2 Change = 0.029, F(1,104) = 3.231, p= 0.075.

Objective physical activity and sleep

There was no correlation between sleep efficiency or sleep time and any physical activity measures. However, a regression testing the predictive value of all of the physical activity metrics, taking age, gender, and education into account, revealed that awake METs was the only physical activity metric that was a significant predictor of sleep efficiency $\beta = 0.562$, t(109) = 2.061, p = 0.042. Therefore, awake METs was used as the physical activity metric in subsequent analyses.

A regression testing the predictive value of awake METs on sleep efficiency, taking age, gender, and education into account, revealed that awake METs was a significant predictor of overall sleep efficiency, $\beta = 0.191$, R2 Change = 0.035, F(1,104) = 5.08, p = 0.026, and a marginally significant predictor of nighttime sleep efficiency, $\beta = 0.167$, R^2 Change = 0.026, F(1,104) = 3.812, p = 0.054. Awake METs was not a significant predictor of sleep time. This suggests that if physical activity improves sleep, improvements may be specific to sleep quality. This finding is consistent with exercise interventions studies which have shown improvements in sleep quality, not quantity (Benloucif, et al., 2004; Driver & Taylor, 2000; Lopez, 2008; Vitiello, 2008; Vitiello, et al., 1994). This makes sense given that subjects may have more control over their sleep duration than sleep quality.

To further ensure that the relationship between physical activity and sleep efficiency was not driven by time spent lying down during the day, average lying down time was included with age, gender, and education in model 1 of the regression analyses to account for all of these factors. This analysis revealed that awake METs was still a significant predictor of overall sleep efficiency, R^2 change = 0.036, F(1,103) = 4.205, p = 0.043. A Pearson Correlation analysis revealed no relationship between average time spent lying down and awake METs, r = 0.00, p = 0.99.

3.3.2 Relationship between Sleep and Cognitive Performance

Correlations

Consistent with my hypotheses, sleep efficiency was significantly correlated with a number of cognitive variables (Figure 16). Significant correlations between sleep and cognition were found with nighttime sleep efficiency and **Trails B**, r = -0.20, p < 0.037, **delayed recall**, r = 0.204, p = 0.033, **NART accuracy**, r = 0.243, p = 0.011, **Stroop** performance in terms of RT and accuracy in **congruent, incongruent, and neutral** conditions, all p’s < 0.015, **Stroop inhibition accuracy**, r = 0.218, p = 0.027, **2-back accuracy**, r = 0.237, p = 0.014, and Sternberg working memory accuracy in the **5-letter** condition, r = 0.198, p < 0.041. There were no significant correlations with any other computer task conditions or neuropsychological assessments, including Trails A, r = -0.067, p = 0.490, or digit symbol substitution, r = 0.120, p = 0.214. Scatterplots of the significant relationships (in bold) between nighttime sleep efficiency and executive task performance, and digit symbol substitution (bottom right), which was not significantly correlated with nighttime sleep efficiency are illustrated in Figure 16.

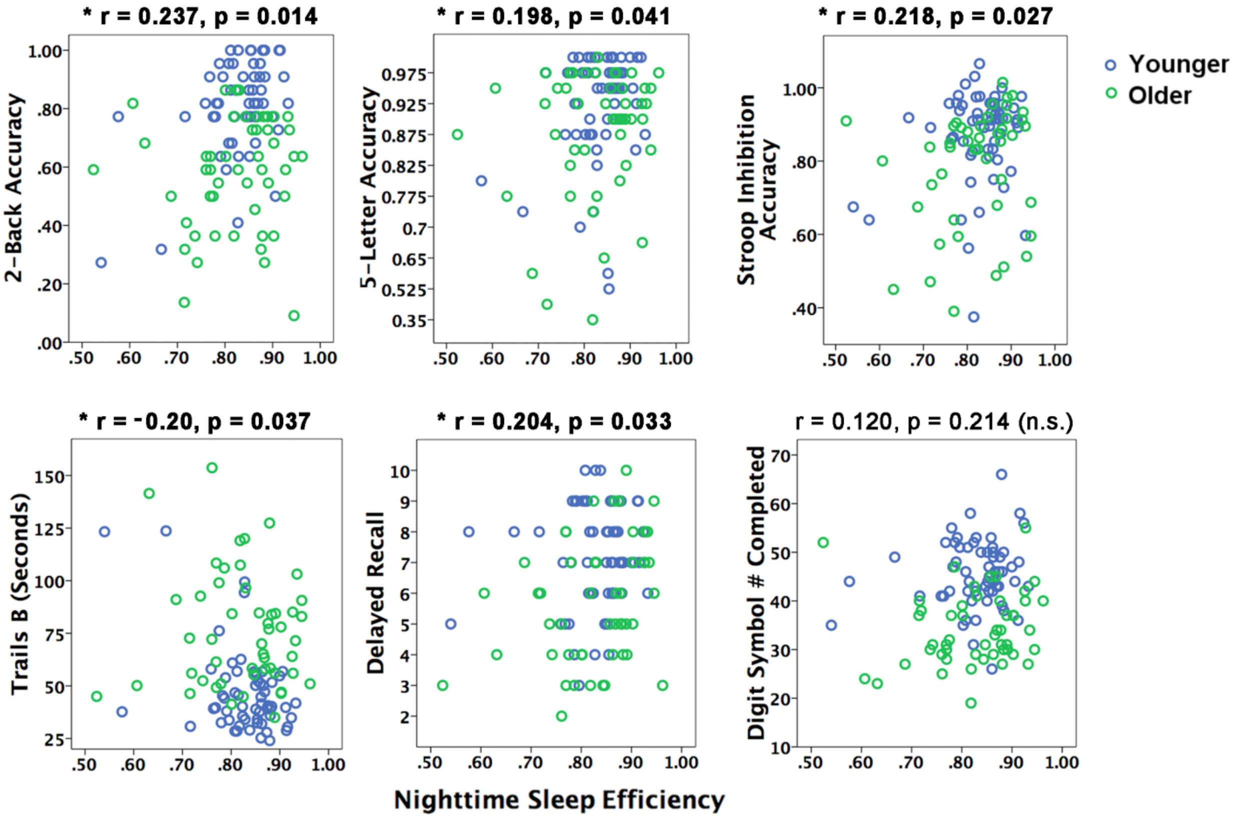


Figure 16. Scatterplots of nighttime sleep efficiency and task performance by age

Overall Sleep Efficiency Correlations

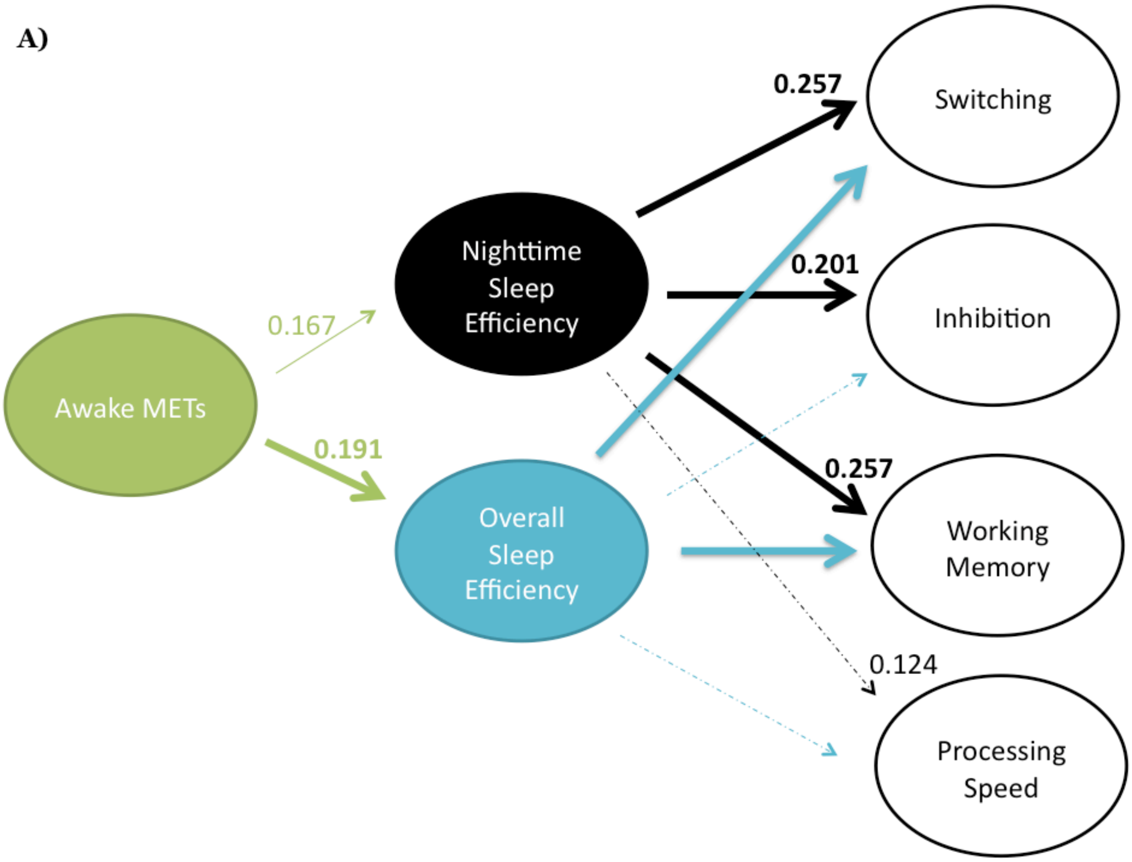
The relationship between the cognitive tasks and overall sleep efficiency was weaker compared with nighttime sleep efficiency. The correlation with Trails B, Stroop congruent RT and accuracy, incongruent accuracy, and 2-back were all marginally significant (p’s < 0.1) and the correlations between overall sleep efficiency and Stroop incongruent RT, inhibition accuracy, Sternberg working memory accuracy, and delayed recall were not significant, p’s > 0.1.

3.3.3 Sleep as a predictor for performance on cognitive tasks

Regression

Multiple linear regression analyses were performed to determine the predictive value of sleep efficiency and sleep time on each of the cognitive task conditions. Figure 17 indicates the sleep factors (sleep efficiency in the upper graph and sleep time in the lower graph) that were significant predictors for each of the cognitive domains after accounting for age, gender, and education: Switching as assessed by TS switching block accuracy, inhibition as assessed by Stroop inhibition accuracy, working memory as assessed by the 2-back, and processing speed as assessed by digit symbol substitution. Beta values in green are from the regression analyses between awake METs and each sleep variable. Beta values in black are from the regression analyses between nighttime sleep and cognitive domains. Thick arrows represent significant relationships, thin arrows represent marginal relationships, and dotted arrows represent non-significant relationships, all after taking age, gender, and education into account.

A)



Awake METs
0.167
0.191
Nighttime Sleep Efficiency
Overall Sleep Efficiency
0.257
0.201
0.257
0.124
Switching
Inhibition
Working Memory
Processing Speed

B)

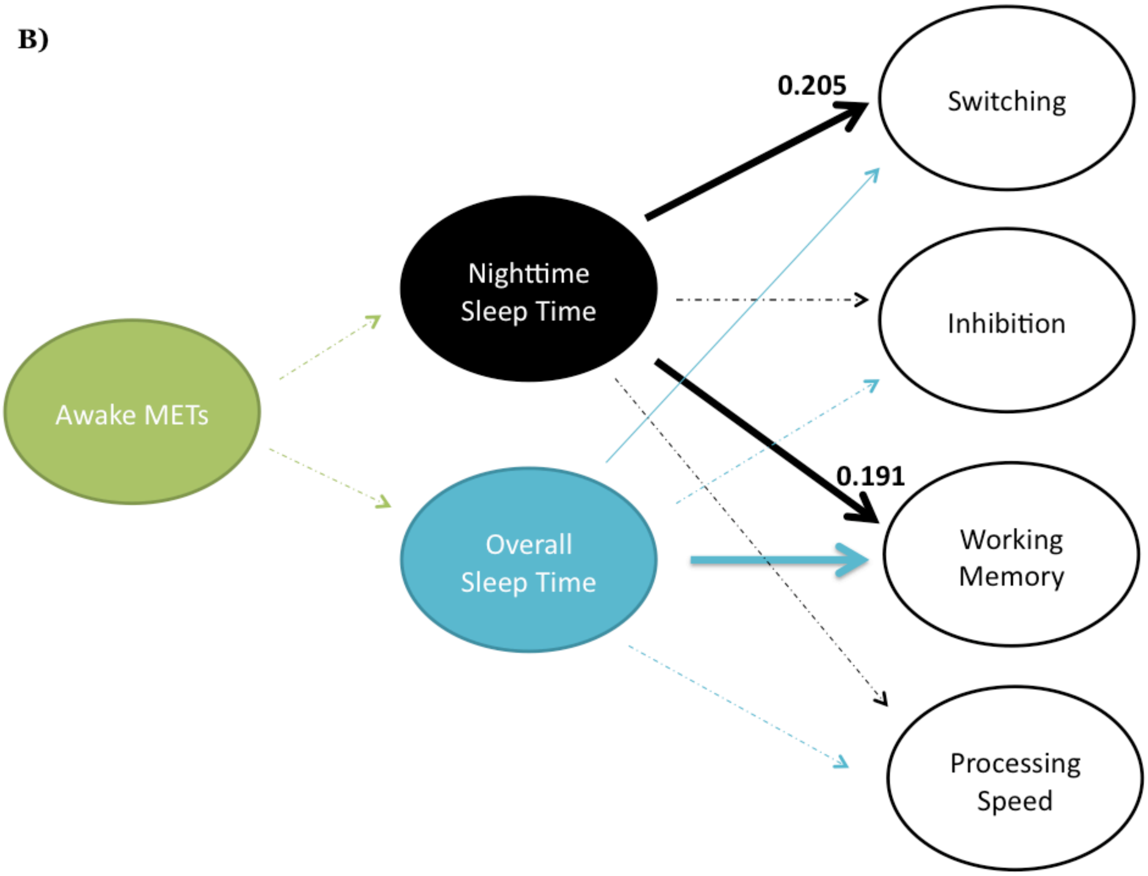


Figure 17. Diagram illustrating relationships between physical activity, sleep, and executive control

Nighttime Sleep Efficiency

After accounting for age, gender, and education, nighttime sleep efficiency was a significant predictor for **Trails B** performance, $p = 0.005$, **TS Switching Block RT**, $p = 0.033$, **and accuracy**, $p = 0.005$, **TS Single Task Block RT,** $p = 0.047$, and **accuracy**, $p = 0.021$, **Stroop Congruent RT,** $p = 0.013$, **Incongruent RT**, $p = 0.011$, **Neutral RT**, $p = 0.003$, **Congruent Accuracy**, $p = 0.012$, **Incongruent Accuracy,** $p = 0.007$, **Neutral Accuracy,** $p = 0.001$, and **Stroop Inhibition Accuracy (Incongruent/Congruent)**, $p = 0.034$, **Flanker Incongruent RT**, $p = 0.014$, **Delayed Recall**, $p = 0.019$, **2-back accuracy**, $p = 0.002$, and **5-letter Sternberg working memory accuracy**, $p = 0.014$. β, R^2 Change, and F Change values are displayed for each of these conditions in Table 4.

Because preparation time was a clear moderator of performance in the Task-switch paradigm (Study 1), I tested the predictive value of nighttime sleep efficiency on performance in each of the 3 preparation times collapsed across session and transition conditions. This analysis revealed that nighttime sleep efficiency was a marginally significant predictor of accuracy in the 0 ms CTI condition, $p = 0.053$, but was a significant predictor of performance in the 750 ms and 1500 ms CTI conditions, $p = 0.016$ and $p = 0.002$, respectively.

Table 4. Significant R2 change with sleep efficiency

Condition	**β**	**R^2 Change**	**df**	**F Change**	**p value**
Trails B	-0.231	0.5	1,104	8.195	0.005
TS Switching Block RT	-0.171	0.028	1,103	4.696	0.033
TS Switching Block Acc	0.257	0.062	1,103	8.371	0.005
TS Single Task Block RT	-0.156	0.023	1,103	4.042	0.047
TS Single Task Block Acc	0.222	0.046	1,103	5.456	0.021
Stroop Congruent RT	-0.219	0.46	1,98	6.367	0.013
Stroop Incongruent RT	-0.215	0.044	1,98	6.794	0.011
Stroop Neutral RT	-0.255	0.62	1,98	9.379	0.003
Stroop Congruent Acc	0.252	0.061	1,98	6.509	0.012
Stroop Incongruent Acc	0.256	0.063	1,98	7.556	0.007
Stroop Neutral Acc	0.33	0.104	1,98	11.523	0.001
Stroop Inhibition Accuracy	0.201	0.039	1,98	4.619	0.034
Flanker Incongruent RT	-0.17	0.027	1,98	6.199	0.014
Delayed Recall	0.208	0.41	1,104	5.697	0.019
2-back Acc	0.257	0.063	1,104	10.545	0.002
5-letter Sternberg WM	0.244	0.054	1,101	6.215	0.014

Overall Sleep Efficiency

After accounting for age, gender, and education, overall sleep efficiency was a significant predictor of the same set of task conditions for which nighttime sleep efficiency was a significant predictor, except for Stroop inhibition accuracy, $\beta = 0.140$, R^2 Change = 0.19 F(1,98) = 2.194, p = 0.142. (Neither sleep efficiency metric was a significant predictor for Stroop Inhibition RT).

Nighttime Sleep Time

After accounting for age, gender, and education, average nighttime sleep time was a significant predictor of **digits forward**, $\beta = 0.267$, R^2 Change = 0.068, F(1,103) = 7.933, p = 0.006, **2-back accuracy**, $\beta = 0.191$, R^2 Change = 0.035, F(1,102) = 5.627, p = 0.020, and **TS switching block accuracy**, $\beta = 0.205$, R^2 Change = 0.040, F(1,103) = 5.238, p = 0.024.

Overall Sleep Time

Similar to nighttime sleep time, after accounting for age, gender, and education, average overall sleep time was a significant predictor for **digits forward**, $\beta = 0.348$, R^2 Change = 0.111, F(1,103) = 13.635, $p < 0.001$, and **2-back accuracy**, $\beta = 0.243$, R^2 Change = 0.054, F(1,102) = 9.010, p = 0.003. These relationships for overall and nighttime sleep time are illustrated in Figure 17B.

Subjective Sleep: PSQI

After accounting for age, gender, and education, sleep latency and hours of sleep assessed with the PSQI did not significantly predict performance on any of the tasks.

Control Tasks

After accounting for age, gender, and education, no sleep metrics were significant predictors for the **digit symbol substitution task**, p = 0.114, **Trails A**, p = 0.163, **or immediate Recall 1,** p = 0.631, **Recall 2**, p = 0.511, or **Recall 3**, p = 0.114). These p values represent the regression analyses with nighttime sleep efficiency. β, R^2 Change, and F Change values are presented in Table 5.

Table 5. Non-significant R2 change with sleep efficiency

Condition	β	R^2 Change	df	F Change	p value
Digit Symbol	0.124	0.015	1,104	2.539	0.114
Trails A	-1.404	0.018	1,104	1.972	0.163
Recall 1	0.05	0.002	1,104	0.232	0.631
Recall 2	0.068	0.004	1,104	0.434	0.511
Recall 3	0.165	0.022	1,104	2.544	0.114

The fact that sleep efficiency remained a significant predictor of performance on a wide range of executive tasks above and beyond individual differences in age, gender, and education, suggests that sleep efficiency in itself may have an influence on cognition in young and older adults.

3.3.4 Physical activity as a predictor for cognitive performance

Physical activity operationalized as awake METs was significantly correlated with many cognitive variables. Significant correlations between awake METs and cognition were found for

Trails A, r = -0.256, p = 0.007, Trails B, r = -0.384, p < 0.001, **immediate recall 1, 2, and 3**, all p’s < 0.038, **delayed recall**, r = 0.213, p = 0.026, **digit symbol substitution**, r = 0.435, p < 0.001, **Stroop RT on congruent**, r = -0.253, p = 0.010, **neutral**, r = -0.311, p = 0.001, and **incongruent** trials, r = -0.329, p = 0.001, and **Stroop accuracy on incongruent** trials, r = 0.208, p = 0.035, and **Stroop inhibition accuracy**, r = 0.235, p = 0.017, **Flanker RT on congruent**, r = -0.378, p < 0.001, and **incongruent** trials, r = -0.409, p < 0.001, **2-back accuracy**, r = 0.404, p < 0.001 and **Sternberg working memory RT in the 5-letter** condition, r = -0.219, p = 0.023.

However, after accounting for age, gender, and education, the only conditions for which awake METs was a significant predictor was digit symbol substitution, p = 0.023, reflecting that to a large degree, the correlations reported above between awake METs and cognitive performance were driven by individual differences in age, gender, and education.

In sum, there were multiple cognitive variables that significantly correlated with both sleep efficiency and awake METs, especially nighttime sleep efficiency. The tasks which were significantly correlated with both nighttime sleep efficiency and awake METs were Trails B, delayed recall, Stroop RT in all conditions, Stroop incongruent accuracy, Stroop inhibition accuracy, and 2-back accuracy. It should be emphasized, however, that according to the Preacher and Hayes (2008) bootstrapping method, a significant bivariate correlation between the independent variable (physical activity) and the dependent variable (cognition) is not required to test the mediating effect of a potential mediator (sleep). Therefore, it is not necessary to restrict mediation analyses to the cognitive variables that were significantly related to both physical activity and sleep.

3.3.5 Mediation Analysis

To examine whether sleep mediated the relationship between physical activity and cognition, I conducted a series of mediation analyses to determine whether sleep efficiency and sleep time significantly mediated the relationship between physical activity and any of the cognitive conditions. Awake METs was used as the physical activity metric for all analyses because of its relation to sleep efficiency. In addition, this physical activity metric reflects how physically active subjects are during the day and is not biased by how much time they spend sleeping. In addition, this variable had a wider range of values compared with vigorous and very vigorous activity. Many subjects had no vigorous or very vigorous activity, (22.9% and 86.2%, respectively).

Nighttime Sleep Efficiency

Consistent with what I expected, after accounting for age, gender, and education, the mediating effect of nighttime sleep efficiency was significant for many of the task conditions (Figure 18A & B). For each of the following tasks, the 95% confidence interval (CI) did not contain zero reflecting that mediation was established. The indirect effect of awake METs through nighttime sleep efficiency on cognition was significant for **Trails B** (indirect effect = -3.58, CI = -13.56 : -0.09**), congruent and incongruent Flanker RT** (congruent indirect effect = -9.20, CI = -33.93 : - 0.52) (incongruent indirect effect = -9.65, CI = -34.56: - 0.45), **congruent and incongruent Flanker accuracy,** (congruent indirect effect = 0.35, CI = 0.03 : 2.24), incongruent indirect effect = 0.71, CI = 0.0015 : 2.73), **congruent, incongruent, and neutral Stroop RT** (congruent indirect effect = -8.98, CI = -37.01: -0.15) (incongruent indirect effect = -10.04, CI = -32.84 : -0.07) (neutral indirect effect = -10.49, CI = -0.32 : -35.78), c**ongruent, incongruent, and neutral Stroop accuracy**, (congruent indirect effect = 0.88, CI = 0.08: 2.55) (incongruent indirect effect = 2.20, CI = 0.02 : 7.01) (neutral indirect effect = 1.17, CI = 0.04 : 3.50), **2-back accuracy** (indirect effect = 2.96, CI = 0.12 : 9.50), **Sternberg working memory accuracy in the 2-letter** (indirect effect = 1.20, CI = 0.07 : 3.75), and **5 letter conditions** (indirect effect = 1.65, CI = 0.17 : 5.28), **TS switching and single task blocks accuracy** (switching block indirect effect = 1.36, CI = 0.12 : 4.00) (single task block indirect effect = 0.87, CI = 0.03 : 3.31) and **delayed recall** (indirect effect = 0.23, CI = 0.01 : 0.73). Flanker and Stroop inhibition RT & accuracy were not significant for nighttime or overall sleep efficiency. The mediating effect of nighttime sleep efficiency on performance was not significant for any other task conditions including Trails A and digit symbol substitution (Figure 18C). Figure 18 indicates cognitive measures for which sleep efficiency was a significant mediator with performance and awake METs.

Indirect mediating effects (blue square) and lower and upper confidence intervals (green and red lines) are displayed in Figure 18 for nighttime sleep efficiency for tasks in which A) the indirect mediating effect of nighttime sleep efficiency was significant for response times (RT), B) the indirect mediating effect of nighttime sleep efficiency was significant for accuracy, and C) the indirect mediating effect of nighttime sleep efficiency was not significant. None of the confidence intervals contained zero in the tasks displayed in A or B indicating that mediation was established. Note that in contrast to the other accuracy measures which are on a scale of 100%, delayed recall is on a 0-10 scale, making the effect size appear small relative to the other tasks, when it is actually much larger when on a 100% scale. Fln = Flanker task, Str = Stroop task, Cng = Congruent, Incng = Incongruent, Neut = Neutral, 2 WM and 5 WM = 2 and 5-letter Sternberg Working Memory, TS Switch = Switching Block, TS Single = Single Task Block 750 = 750 ms CTI, 1500 = 1500 ms CTI, recall = delayed recall.

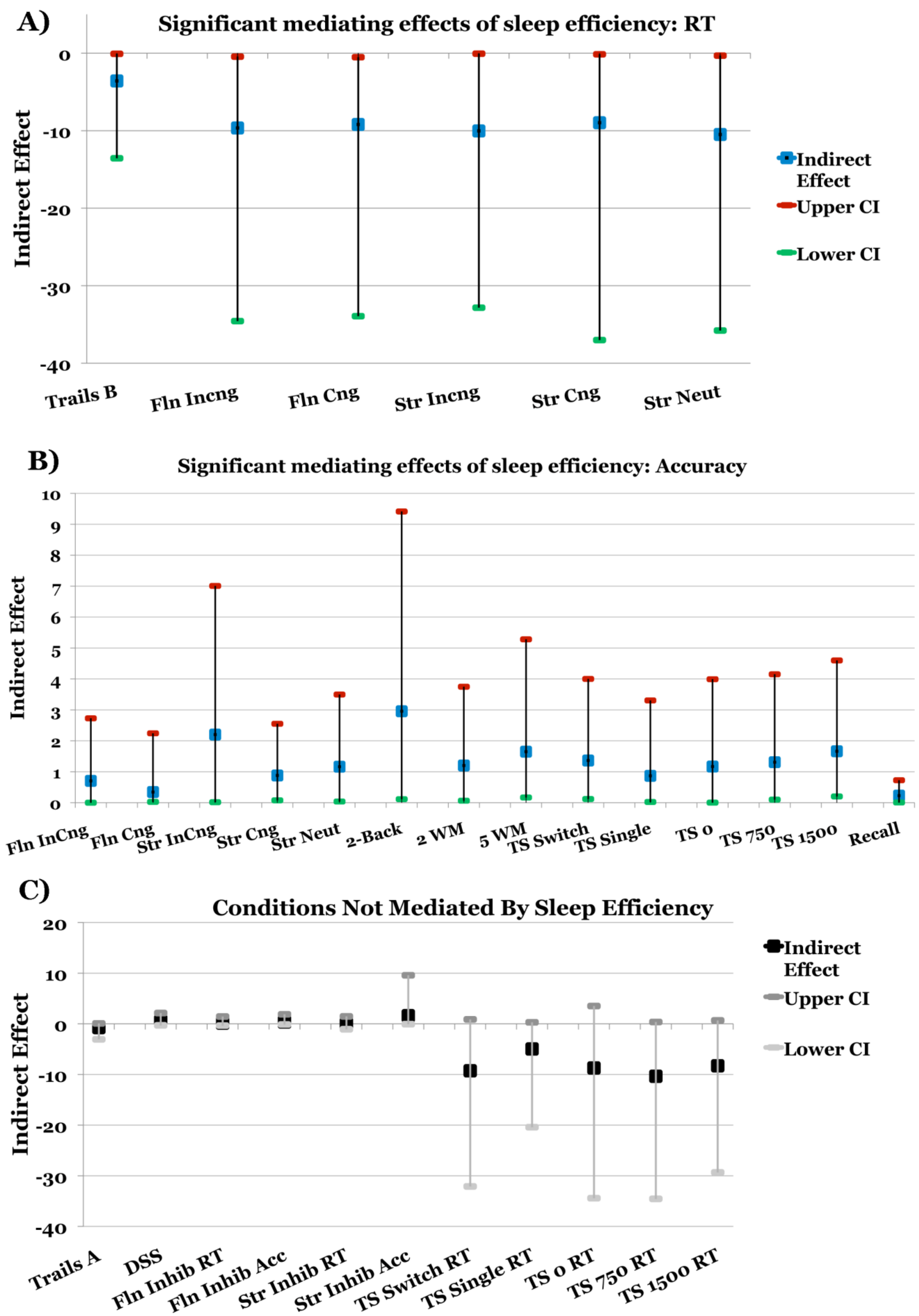


Figure 18. Mediation analysis results: Indirect effects and confidence intervals

Overall Sleep Efficiency

After accounting for age, gender, and education, the mediating effect of overall sleep efficiency was significant for Trails B (indirect effect = -4.38, CI = -14.53: -0.64), incongruent RT in the Stroop task, (indirect effect = -8.59, CI= -33.41 : -.0701), delayed recall (indirect effect = 0.22, CI = 0.01: 0.67) and 5-letter Sternberg working memory accuracy (indirect effect = 0.0159, CI = 0.0016 : 0.05).

Nighttime sleep time and Overall Sleep time

Nighttime sleep time and overall sleep time were not significant mediators for any tasks primarily because of the lack of a relationship between sleep time and physical activity.

3.3.6 Potential Confounds

Mood

When relating sleep quality to cognitive performance, one must consider depression and mood as potential confounds (Nebes, et al., 2009). Although all participants reported not having depression and were not currently taking psychiatric medication, subjects also completed a mood questionnaire, which included questions of both positive and negative affect. This questionnaire was compiled into a single score based on the number of “no” responses to positive affect questions and “yes” responses to negative affect questions. (Higher scores corresponded to less positive and more negative affect). A correlation analysis revealed no significant relationship between mood and nighttime sleep efficiency, r = -0.108, p = 0.30. A regression analysis including mood score as a control variable along with age, education, and gender between sleep efficiency and each of the significant effects again revealed that sleep efficiency was a significant predictor of **Trails B,** $\beta = -0.206$, R^2 Change = 0.039, F Change (1,92) = 5.882, p =

0.017, **delayed recall**, β = R^2 Change = 0.045, F Change(1,92) = 5.514, p = 0.021, **2-back accuracy**, β = 0.249, R^2 Change = 0.056, F Change (1,92) = 7.813, p = 0.006, **Stroop congruent RT**, β = -0.225, R^2 Change = 0.045, F Change (1,86) = 5.487, p = 0.021, **incongruent RT**, β = -0.245, R2 Change = 0.053, F Change (1,86) = 7.114, p = 0.009, **neutral RT**, β = -0.265, R2 Change = 0.062, F Change (1,86) = 8.166, p = 0.005, **congruent accuracy**, β = 0.261, R2 Change = 0.061, F Change (1,86) = 5.730, p = 0.019, **incongruent accuracy**, β = 0.297, R2 Change = 0.078, F Change (1,86) = 8.274, p = 0.005, **neutral accuracy**, β = 0.378, R2 Change = 0.127, F Change (1,86) = 12.697, p = 0.001, **inhibition accuracy**, β = 0.242, R2 Change = 0.052, F Change (1,86) = 5.392, p = 0.023, **incongruent Flanker RT**, β = -0.172, R2 Change = 0.027, F Change (1,90) = 5.375, p = 0.023. **5-letter accuracy** was marginally significant, p = 0.078. This analysis did not include subjects who did not complete the mood questionnaire (n = 11). These results suggest that the relationship between sleep efficiency and cognitive performance was not driven by individual differences in mood.

3.4 DISCUSSION

This study examined whether sleep efficiency and sleep time were related to cognitive performance and whether the mediating effect of sleep on the relationship between physical activity and cognition was significant. I predicted that these relationships would be specific to executive control. Sleep efficiency, particularly nighttime sleep efficiency, which takes into account both objective and self-report sleep measures, most reliably predicted cognitive performance and was the most reliable mediator of the relationship between physical activity and cognition. Sleep time was a significant predictor only for digits forward, 2-back accuracy, and TS switching block performance. This finding that sleep efficiency, more consistently than sleep time, influenced performance (Figure 17) is consistent with prior work (Blackwell, et al., 2006; Nebes, et al., 2009). Blackwell et al. (2006) found that sleep efficiency, but not sleep time was related to performance on Trails B and the MMSE, and that cognitive impairment was more common in subjects with poor sleep efficiency. Though, as reported in Study 1, sleep time *did* have an influence on task-switching performance, particularly on the most cognitively demanding trials. This suggests that sleep time may influence performance, but sleep efficiency may be more sensitive in identifying sleep-related cognitive impairments.

Consistent with my predictions, sleep efficiency was a significant predictor for multiple task conditions that depend on executive control (switching as assessed by Trails B and Task-switch, attentional control and inhibition as assessed with the Flanker and Stroop tasks, controlled memory retrieval as assessed with delayed recall, working memory as assessed with Sternberg working memory accuracy in the 5-letter condition and 2-back accuracy). Thus, each domain of executive control (switching, inhibition, working memory and controlled retrieval) that I tested was related to sleep efficiency after controlling for age, gender, and education. To contrast this to task conditions that measure processing speed, sleep efficiency was not a significant predictor of Trails A time or digit symbol substitution performance. No sleep metrics (sleep efficiency or sleep time) were significant predictors of performance on the digit symbol substitution task suggesting that sleep efficiency has less of an influence on overall processing speed. Rather high sleep efficiency may have a specific benefit on more goal-driven executive functions.

One interpretation of this finding that sleep efficiency was related to executive control is that disrupted sleep has an influence on more PFC-mediated cognitive processes. I speculate that this specificity to executive control may be driven by disruption of slow-wave sleep in subjects with poor sleep efficiency. Because slow-wave sleep benefits PFC function, it is plausible that with improved sleep quality, time spent in slow-wave sleep increases, restoring PFC function to in turn benefit executive control.

Alternatively, brain changes that affect cognition may precede disruptions in sleep. For instance, decline in brain volume with aging may influence an individual's ability to fall asleep and stay asleep, in which case sleep quality would not directly or indirectly influence cognition.

Nebes et al. (2009) showed significant relationships between subjective sleep quality and performance on a range of executive tasks, but not processing speed. As mentioned in the introduction, there was not a clear distinction in which all "executive tasks" were related to subjective sleep quality. This study found no relationship between inhibition as assessed by the Stroop task and sleep quality, which may be due to the use of subjective sleep measures. The current study, however, showed a robust relationship between nighttime sleep efficiency and inhibition as assessed by the Stroop task. Thus, lack of a clear distinction between executive and non-executive tasks in the Nebes study may be due to the fact that purely subjective self-report sleep measures were used. However, purely objective overall sleep efficiency was not a significant predictor of Stroop inhibition accuracy, suggesting that it may nighttime sleep efficiency in particular that relates to inhibition.

I tested the mediating effect of sleep efficiency on the relationship between physical activity (operationalized as awake METs) and executive control (operationalized as switching, inhibition, working memory, and controlled retrieval). The mediating effect of nighttime sleep efficiency on the relationship between awake METs and performance was significant for a wide range of task conditions including Trails B, Flanker RT and accuracy, Stroop RT and accuracy, 2-back accuracy, 2 and 5-letter Sternberg working memory accuracy, Task-switch accuracy, and delayed recall. I also tested the mediating effect of sleep efficiency on the relationship between awake METs and processing speed (Trails A and digit symbol substitution). The mediating effect was not significant for either of these tasks, reflecting that indirect effects of physical activity through sleep may apply less to processing speed. These findings are consistent with the view that physical activity-related benefits to executive control may be partly attributable to sleep. Young and older adults who are more physically active may have better sleep, and this improved sleep may benefit the PFC and in turn result in superior day time executive function.

Overall these results suggest that for many cognitive tasks, the association between physical activity and executive function is driven by individual differences in sleep quality.

4.0 STUDY 3: SLEEP EFFICIENCY INFLUENCES TIME-OF-DAY EFFECTS IN OLDER ADULTS

4.1 INTRODUCTION

Decades of research have shown that older humans and other animals tend perform better in the morning on cognitive tasks (May, Hasher, & Foong, 2005; Winocur & Hasher, 1999). This is due to age-related changes in circadian rhythms in which peak arousal takes place earlier in the day. As a result, older adults tend to be morning chonotypes, whereas young adults tend to be evening chronotypes (night owls). Accordingly, it is possible that time of day may have influenced whether older adults showed cognitive impairments in the present set of studies. In addition, time of day may influence whether sleep impacts older adults' performance. For instance, if an older adult has poor sleep efficiency, this may impact his/her performance in the afternoon or evening, when arousal is low, more so than it would in the morning.

In Study 3, I tested the interaction between sleep efficiency and time of day on younger and older adults' performance on the computer-based cognitive tasks described above.

4.2 METHODS

4.2.1 Analytic techniques

Responses from the morningness/eveningness questionnaire were used to identify age group differences in chronotype. Subjects were separated into two groups (AM/PM), based on when they participated in the experiment, to identify how performance differed for the two age groups in the morning and in the afternoon.

Principal components analysis (PCA) with virimax rotation was used to reduce the data from the computer-based cognitive tasks (Stroop, Flanker, N-back, and Sternberg working memory) to fewer variables given that performance on these tasks were highly correlated. This analysis resulted in 1 factor for RT and 4 factors for accuracy. Two ANOVAs were performed: One on PCA values generated from RT (Table 6) and one on PCA values generated from accuracy.

Table 6. Means, standard deviations and N's for time-of-day analyses with RT (PCA values)

Age Group	**Sleep Efficiency**	**Time of Day**	**Mean**	**SD**	**N**
Younger	**Low**	**AM**	-.4123	.8813	16
		PM	-.5214	.6701	10
		Total	-.4542	.7941	26
	High	**AM**	-.6089	.6754	20
		PM	-1.0260	.4783	10
		Total	-.7480	.6402	30
Older	**Low**	**AM**	.5838	.6230	9
		PM	1.1215	.7370	15
		Total	.9199	.7324	24
	High	**AM**	.4435	.9382	14
		PM	.5816	.6622	9
		Total	.4975	.8273	23

4.3 RESULTS

4.3.1 Age differences in morningness/eveningness

Older subjects had significantly higher scores on the morningness/eveningness questionnaires, suggesting that they were more likely to be morning chronotypes, t(105) = 5.93, $p < 0.001$.

4.3.2 Time of Day, Age and Sleep Efficiency

Response Time

To test whether time of day influenced the effect of nighttime sleep efficiency on RT, I conducted a 2 (age group) × 2 (nighttime sleep efficiency) × 2 time of day (AM/PM) ANOVA. This analysis revealed significant main effects of age group, $F(1,95) = 76.13$, $p < 0.001$, and sleep efficiency group, $F(1,95) = 5.17$, $p = 0.025$, and a marginally significant age group × AM/PM interaction, $F(1,95) = 3.92$, $p = 0.051$. These findings reflected that RT was fastest in young adults and subjects with high sleep efficiency across tasks. The marginal age group × AM/PM interaction reflected a time-of-day effect in which older adults had faster RT in the morning compared with the afternoon (Figure 19).

Figure 19 illustrates the marginally significant time-of-day effect in which RTs were fastest for young adults in the PM and fastest for older adults in the AM. Y-axis represents values generated from the principal components analysis.

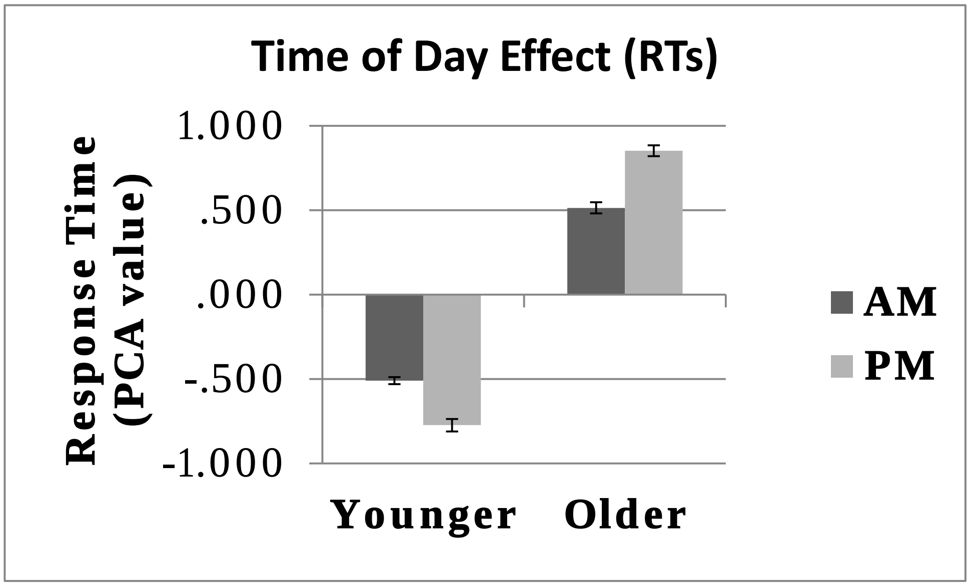


Figure 19. Marginally significant time-of-day effect on RTs

Accuracy

To test whether time of day influenced the effect of nighttime sleep efficiency on accuracy, I conducted a 4 (factor) × 2 (age group) × 2 (nighttime sleep efficiency group) × 2 (AM/PM) mixed effects ANOVA with factor as a within subjects variable. This analysis revealed a significant main effect of age group, $F(1,97) = 7.89$, $p = 0.006$, an age group × factor interaction, $F(3,291) = 7.612$, $p < 0.001$, an age group × AM/PM interaction, $F(1,97) = 4.931$, $p = 0.029$, reflecting a time-of-day effect, and a significant age group × nighttime sleep efficiency group × AM/PM interaction, $F(1,97) = 4.00$, $p = 0.048$. The latter interaction revealed that the time of day effect was particularly robust for subjects with low sleep efficiency (Figure 20A). The effect was virtually absent in young and older subjects with high sleep efficiency (Figure

20B). This result reflects that the extent to which older adults showed impairments in the afternoon depended on how low their sleep quality was. However, this interpretation is tentative because older adults with low sleep efficiency performed numerically higher than older adults with high sleep efficiency in the morning, possibly exaggerating the size of the interaction.

Figure 20 displays the time-of-day effect in subjects with A) low sleep efficiency and B) high sleep efficiency. The figure illustrates that the time-of-day effects were absent for the high sleep efficiency group, but robust in the low-sleep efficiency group.

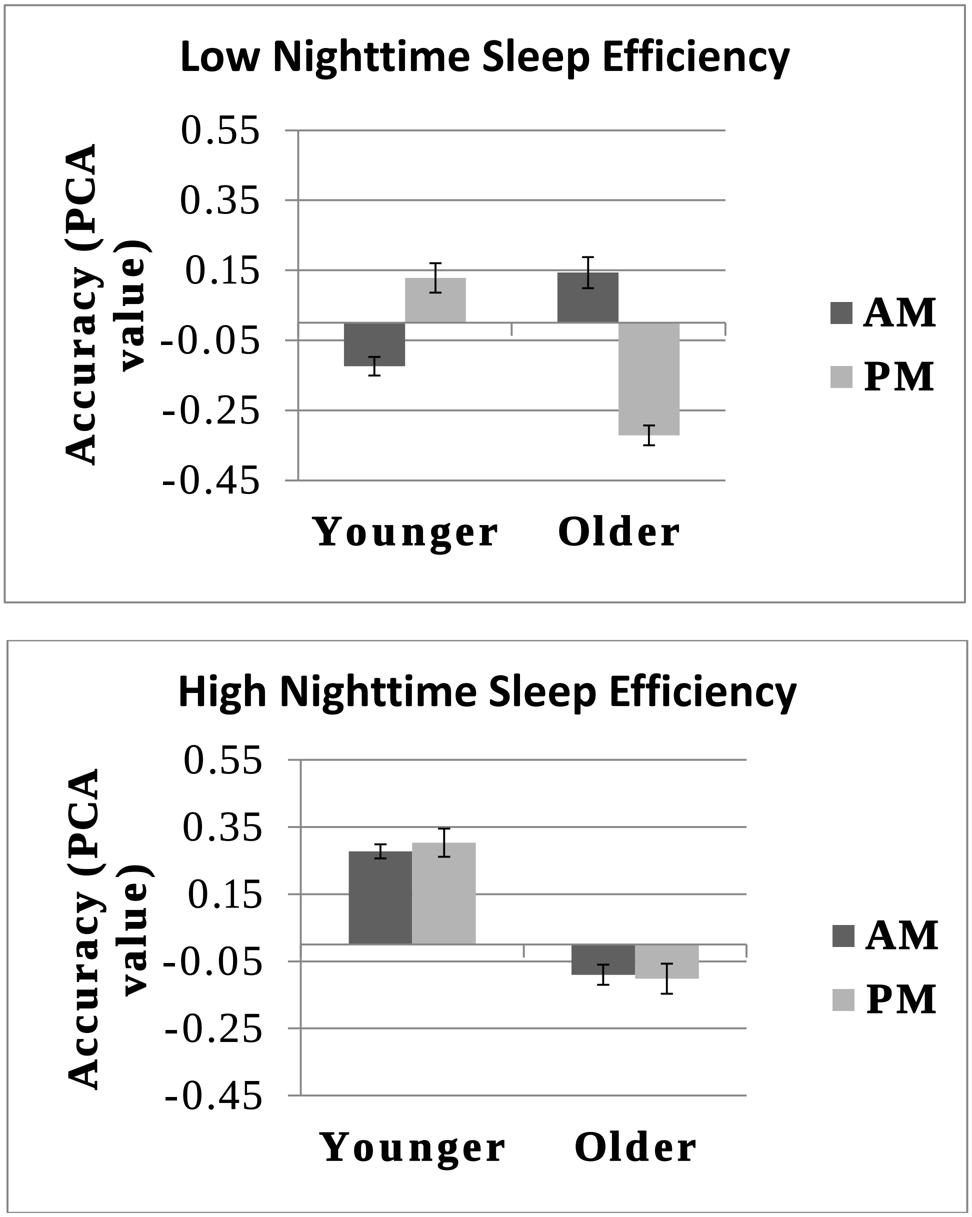


Figure 20. Time-of-day effect as a function of sleep efficiency

4.4 DISCUSSION

Consistent with prior studies, time of day influenced how large an impairment in cognition older adults exhibited relative to young adults. Older adults who participated in the morning performed better than those who participated in the afternoon. However, for accuracy, this time of day effect applied only to subjects with low sleep efficiency. These results suggest that high sleep efficiency may counteract time-of-day effects, although they do not eliminate impairments in older adults.

4.4.1 Limitations

One limitation to the present time-of-day analysis is that this study was not designed to specifically examine time-of-day effects and age groups were not counterbalanced across morning and afternoon times. As a result, there were an uneven number of groups (age, sleep efficiency, and AM/PM) as can be seen in Table 6. This discrepancy may explain why the mean for older adults with low sleep efficiency in the morning was numerically higher than those with high sleep efficiency. There were 9 older adults with low sleep efficiency who participated in the morning, and 14 with high sleep efficiency who participated in the morning. This may have exaggerated the time-of-day effect in the low sleep efficiency group, possibly exaggerating the age group × sleep efficiency group × AM/PM interaction.

Overall, these effects reflect that although time-of-day effects are influenced by sleep efficiency, they do not eliminate age differences in older adults with high sleep efficiency.

5.0 GENERAL DISCUSSION

The results presented above revealed that individual differences in sleep efficiency were robustly related to individual differences in cognitive performance in younger and older adults. This was found with a variety of analytic techniques. A simple median split was robust enough to reveal highly significant differences between sleep efficiency groups. Analyses splitting subjects into high and low sleep efficiency revealed robust between-group effects on task-switching and preparation. In particular, subjects with high sleep efficiency showed a more robust "preparation effect" which is often reported in the task switching literature and reflects engagement of preparation strategies. In addition, regression analyses with sleep efficiency as a continuous variable showed that sleep efficiency was a significant predictor of many cognitive variables that are thought to depend on executive control.

Not only are these cognitive effects reported above novel, but the finding that individual differences in sleep measured by accelerometry were significantly related to cognition is novel in itself. Accelerometer-measured sleep efficiency was overall, a better predictor of cognitive function compared with subjective sleep. While it is less accurate than polysomnography and does not measure **sleep architecture**, it is a more naturalistic, convenient, and cost-effective measure of objective sleep relative to polysomnography. Overall, these studies demonstrate the feasibility of using accelerometry to estimate sleep metrics that relate to cognitive performance.

The most noteworthy finding reported here is the significant mediating effect of sleep efficiency on the relationship between physical activity and cognitive performance on a wide range of cognitive and neuropsychological tasks. There are very few studies that have examined sleep, physical activity, and cognition together in one study (Vitiello, 2008) and those studies failed to provide strong evidence that subjects with high cognitive performance and high physical activity also have good sleep behavior. Nor were those studies large enough to specifically test whether sleep mediates the relationship between physical activity and cognition (Benloucif, et al., 2004). The present study, on the other hand, was sufficiently large to test mediation, and successfully demonstrated that the mediating effect of sleep on the association between physical activity and cognition was significant. Thus subjects who are physically active may have higher sleep efficiency, and this higher sleep efficiency may restore cognitive function during the day for both young and older adults.

Intervention studies manipulating both physical activity and sleep may be useful in identifying the mechanisms underlying this mediating effect and address whether sleep-related benefits to executive control are directly driven by sleep. Physical activity interventions will be useful in demonstrating whether improved physical activity improves sleep and whether these improvements predict changes in cognition and brain regions important in executive control. Interventions may also serve as a useful technique for improving sleep-related cognitive decline in older adults (Wilckens, Erickson, & Wheeler, 2012).

5.1 LIMITATIONS

The present study did not exclude subjects based on their sleep habits, sleep complaints, or whether subjects reported a sleep disorder. Instead, I was interested in examining cognition in relation to a wide range of sleep quality and quantity in young and older adults. From the perspective of determining whether very poor sleep is associated with very poor cognition, it is important to include subjects with a wide range of sleep habits. However, it is possible that the relationship between sleep and cognition is different in subjects with sleep disorders from those with no sleep disorders. In addition, it is possible that sleep relates to cognition differently with different sleep disorders. For example, cognitive impairments may be greater in patients with sleep-related breathing disorders and narcolepsy compared with insomnia (Fulda & Schulz, 2001).

Moreover, there are many different factors that affect sleep, some which apply to older adults more so than young adults, including pain, which may also affect how physically active an individual is. Future research should address this issue by taking into account reasons for sleep troubles and low physical activity.

Another limitation of the present study is the fact that the nighttime sleep measure was a combination subjective and objective sleep measure. Because no experimenter was physically present to observe when the subject got in and out of bed for the last time each night and each morning, it is not possible to know exactly what minutes estimated as sleep were true nighttime sleep minutes. Further, because subjects frequently failed to report nighttime sleep or misestimated nighttime and daytime sleep times relative to accelerometer estimates, sleep logs could not be the sole determinant of nighttime sleep (Appendix B). If subjects in this study had slept in the lab and exact times subjects got into and out of bed for the last time could be determined, the nighttime sleep metric would be more objective and accurate. However, one advantage to having subjects sleep at home as opposed to in a laboratory setting is that measured sleep may be more representative of their typical sleep habits (Ajilore, Stickgold, Rittenhouse, & Hobson, 1995). The goal of the present study was to examine the typical sleep habits of the subjects that participated in the study.

5.2 CLINICAL RELEVANCE

This dissertation has focused on the influence of sleep on cognition in healthy aging, but in the interest of informing interventions in healthy older adults, it is worthwhile to acknowledge the efficacy of treating sleep disorders and its impact on cognition. Treatment of **obstructive sleep apnea syndrome** with continuous positive airway pressure has been associated with significant improvements in performance on executive control tasks (see Jones & Harrison (2001) for a review). Naegele et al. (1998) showed improvements in a range of tasks thought to be sensitive to frontal lobe function, including the Wisconsin card sorting task, the Stroop task, and a long-term visual memory task. Neau et al. (1996) found significant improvement Trails B, but not Trails A. Given that Trails B involves executive control, more so than Trails A, treatment to improve disordered sleep may have specific benefits to executive control and the PFC.

Patients with Alzheimer’s disease often have disturbed sleep, sleep disorders, and exhibit decreased slow-wave sleep (Bliwise, 2004; Loewenstein et al., 1982). This may be the result of disruption in circadian rhythms (Y. H. Wu & Swaab, 2007). Given that sleep treatments have been effective in improving cognition in non-demented patients with sleep disorders, it is important that future studies investigate whether sleep treatments would aid in improving dementia symptoms in patients with memory disorders. A recent study (Westerberg et al., 2010) demonstrated a significant positive relationship between measures of sleep quality and memory performance in patients with mild cognitive impairment- an intermediate stage between normal aging and Alzheimer’s disease. This points to the possibility that symptoms of mild cognitive impairment may be alleviated with improvements in sleep.

5.3 GENERAL CONCLUSIONS

Overall, the present findings reveal compelling evidence to suggest that sleep may play an important role in cognitive decline. The current study suggests that sleep quality, and under some circumstances, sleep quantity, influence cognition on a range of tasks. These findings suggest that improvements in sleep may lead to improvements in cognitive performance in young and older adults. More research focused on the ameliorating effects of sleep treatment on cognition is needed to determine whether changes in sleep as a lifestyle factor may improve cognition in older adults. Further, there ought to be a greater public awareness about the importance of sleep hygiene in cognitive function. There is a common misconception that less sleep is associated with increased productivity. However, good sleep hygiene may translate into higher cognitive function that may influence performance on everyday activities relevant to individuals of all ages.

APPENDIX A

GLOSSARY TERMS

Retrieval success: Refers to old/new effects typically found in parietal regions reflecting successful memory recovery. Retrieval success is often operationalized as differences between brain activity elicited by correctly categorized studied items and brain activity elicited by correctly categorized new items presented at test

Slow-wave sleep: Non-REM sleep stages (3 and 4) in which low-frequency delta EEG activity is the highest.

Sleep quality: Sleep measures based on time spent lying in bed, including sleep efficiency (proportion of time spent lying down asleep), wake after sleep onset and sleep latency (time it takes to fall asleep)

Sleep efficiency: Proportion of time spent asleep versus time spent lying down

Executive control: Mechanism responsible for goal-oriented processes that involve selection of relevant and inhibition of irrelevant information and actions and the monitoring and updating of information.

Episodic memory retrieval: Recovery of memories for personally experienced events usually involving some recollection of details. In an experimental paradigm, studied information must exceed working memory capacity and be cleared from working memory prior to retrieval

Sleep architecture: Refers to sleep stages and other sleep phenomena measured with EEG

Obstructive Sleep Apnea Syndrome: Sleep disorder characterized by frequent breathing cessation leading to brief arousals

APPENDIX B

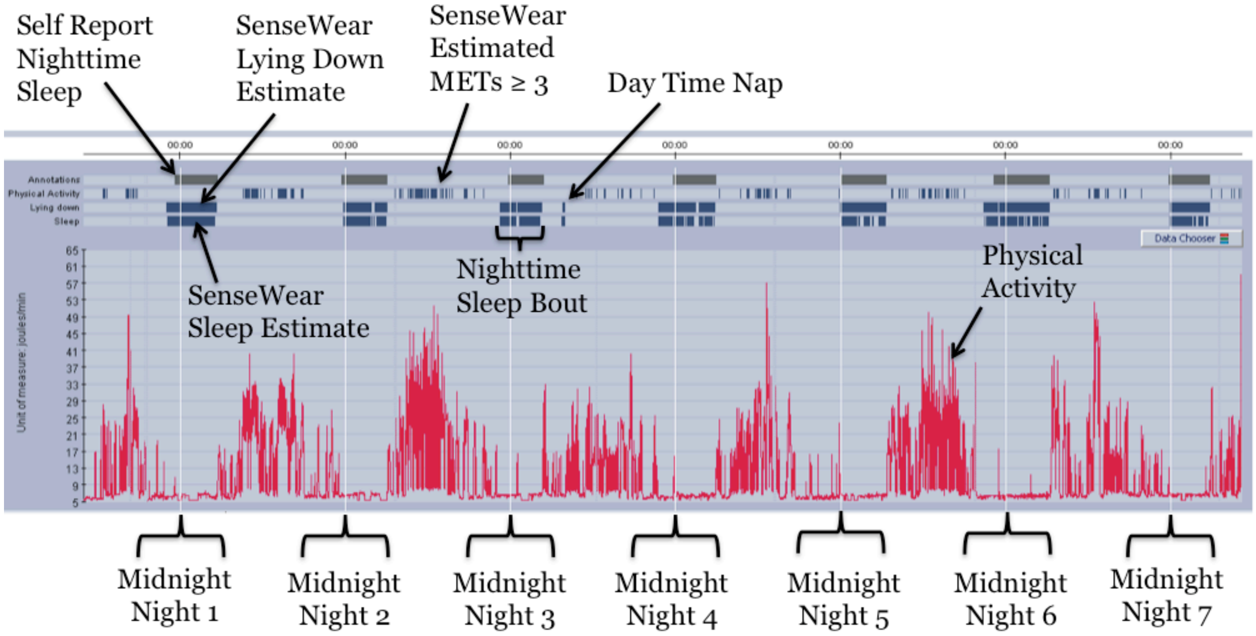
NIGHTTIME SLEEP FROM ACCELEROMETERS

Nighttime sleep was determined from sleep logs and activity levels. Self-report nighttime sleep and daytime naps from the sleep diary were incorporated into the subjects' accelerometer data files to distinguish nighttime sleep from naps. Because subjects frequently misestimated when they were sleeping or failed to report nighttime sleep, self-report sleep logs did not solely determine the block of time chosen for nighttime sleep versus daytime naps (example in Figure 21). Each subjects' accelerometer dataset was visually inspected to identify the nighttime sleep bout.

Figure 21 displays an example graph of accelerometer data; A) showing a week of sleep bouts and physical activity for a subject whose self-report sleep was consistent with accelerometer sleep estimates; B) showing a week of sleep bouts and physical activity for a subject who misestimated their nighttime sleep and nap time. (Self-report nighttime sleep bout did not overlap with accelerometer estimated lying down or sleep bout).

If there was a nap close to bedtime, it was considered a nap if it was either logged as a nap by the subject, or was outside of their nighttime lying down bout and outside of the time they said they went to sleep *and* was followed by (evening naps) or preceded by (morning naps) a cluster of peaks in physical activity. It was important to distinguish these naps close to bedtime from nighttime sleep because older adults are more likely to nap close to bedtime than young adults (Yoon, Kripke, Youngstedt, & Elliott, 2003).

A)



B)

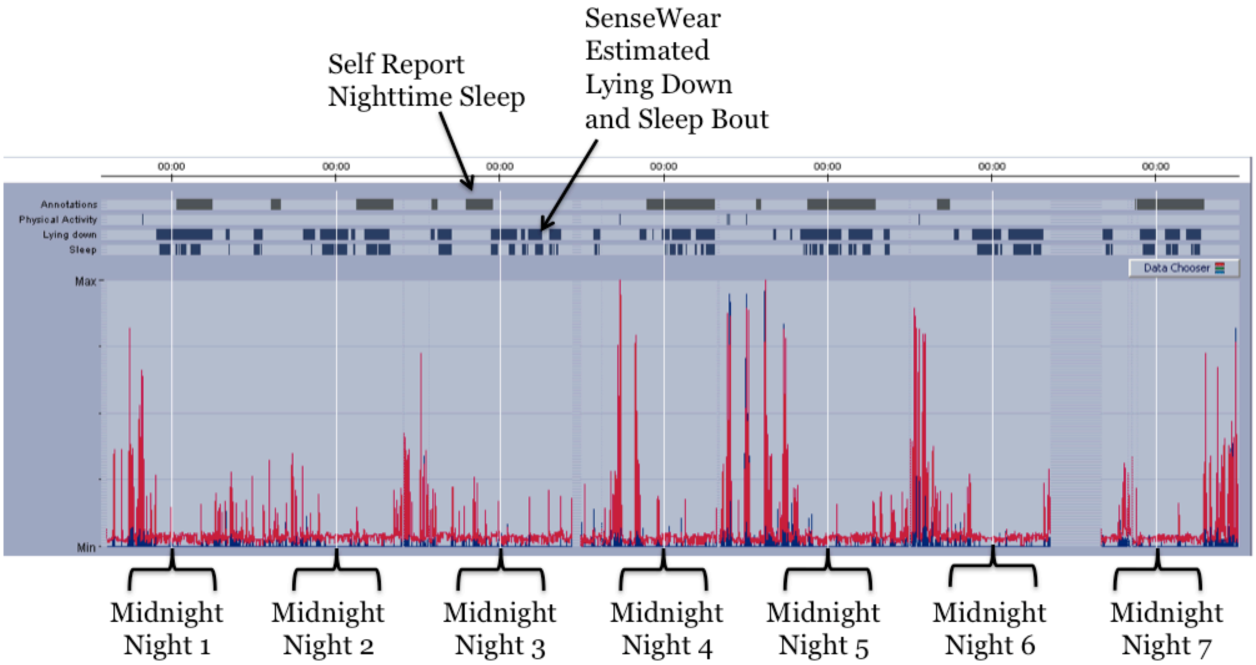


Figure 21. Example graph of accelerometer data with self-report sleep logs

APPENDIX C

OUTLIERS

C.1 TRAILS B

One outlier was identified with Trails B. This subject had a very long Trails B time (269 seconds) and low sleep efficiency, exaggerating the relationship between these two factors. The Trails B value was well outside of 3 standard deviations from the mean. With this outlier, the correlation between nighttime sleep and Trails B was r = -0.237, p = 0.013 (Figure 22A). Without the outlier, the correlation remained significant, r = -0.20, p = 0.037 (Figure 22B). The regression and mediation analyses involving Trails B and sleep efficiency remained significant regardless of whether this subject was included or not. This subject was however, excluded from all analyses to avoid biasing the remainder of the analyses in the direction of a significant relationship.

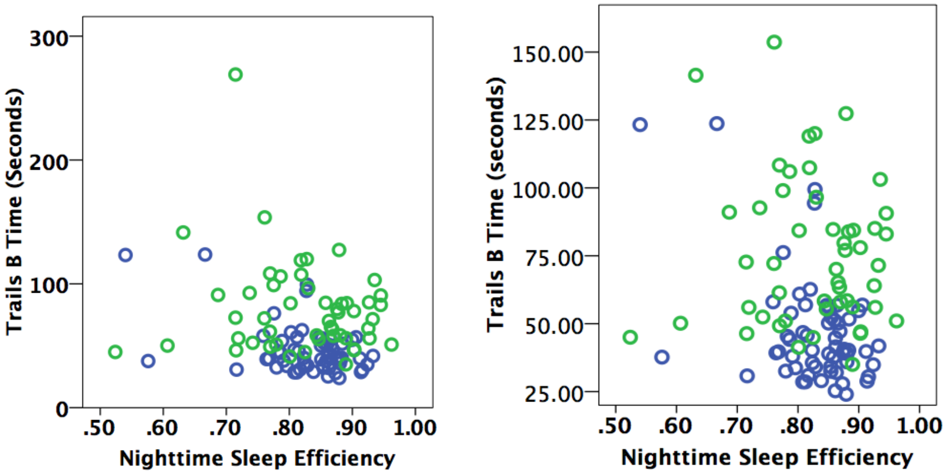


Figure 22. Scatterplots of Trails B performance with and without outlier

C.2 STERNBERG WORKING MEMORY

Three subjects with performance below 10% correct accuracy on the Sternberg working memory task in the 2-letter condition were detected, one of them being a clear outlier in relation to sleep efficiency. Scatterplots of 2-letter and 5-letter accuracy as a function of nighttime sleep efficiency, with (top panel) and without (bottom panel) subjects who performed below 10% accuracy are displayed in Figure 23. Removal of the outliers resulted in sleep efficiency being a marginally significant predictor of 2-letter accuracy, $\beta = 0.183$, R^2 Change = 0.031, $F(1,101) = 3.262$, $p = 0.074$. The relationship between nighttime sleep efficiency and 5-letter accuracy, however remained significant, $\beta = 0.244$, R^2 Change = 0.054, $F(1,101) = 6.215$, $p = 0.014$.

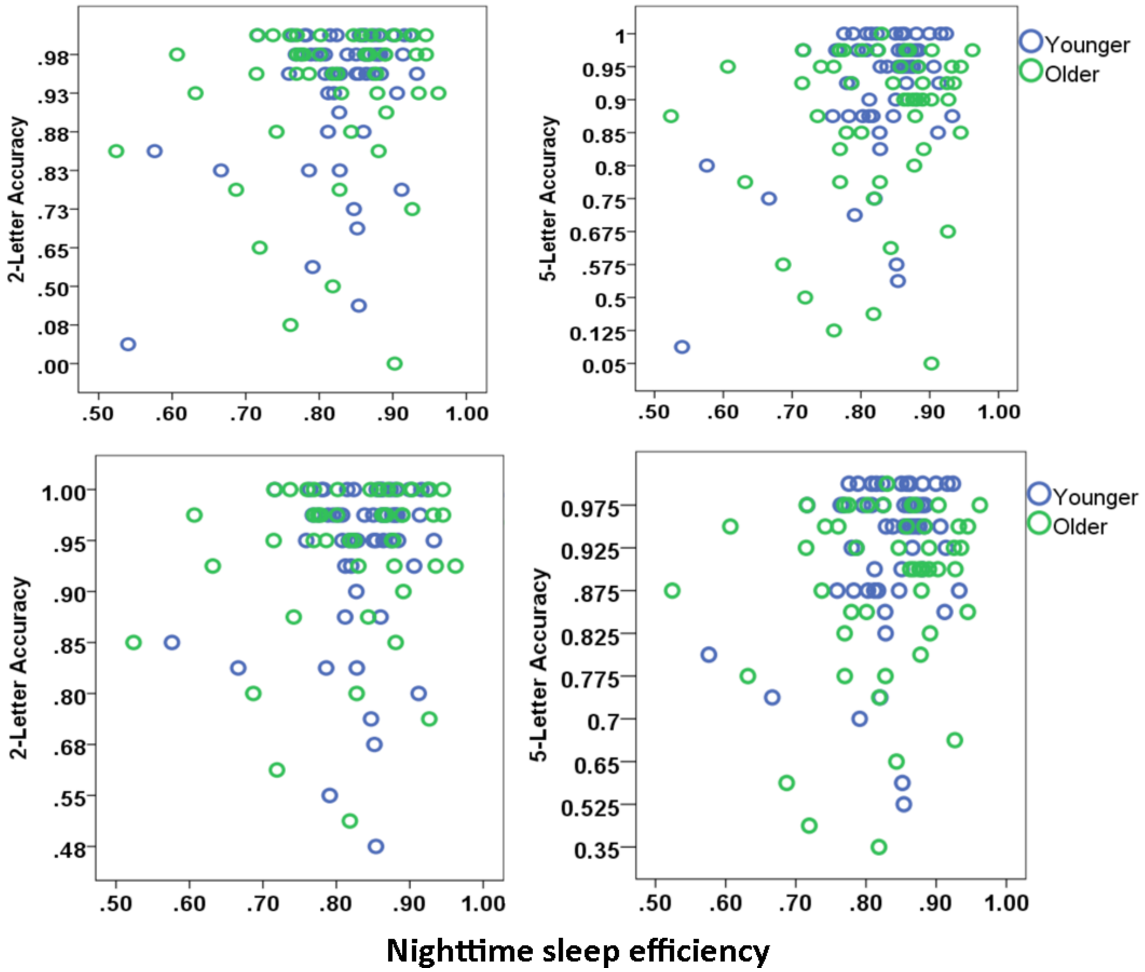


Figure 23. Scatterplots of Sternberg working memory performance with and without outliers

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