TESTING THE ROLE OF VIGILANT ATTENTION AS A MEDIATING PROCESS FOR COGNITIVE DEFICITS DUE TO SLEEP DEPRIVATION

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ABSTRACT

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Sleep deprivation impairs lower-level cognition such as vigilant attention. However, the effect of sleep deprivation on higher-order cognition, such as problem solving or working memory, is not well understood. One prominent theory, referred to as the attention-mediated theory, posits that deficits in higher-order cognition can be entirely attributable to deficits in vigilant attention, as attention is a global process required for nearly all cognitive tasks. Across four of the largest sleep deprivation studies ever conducted, we investigated the effect of sleep deprivation on vigilant attention and a broadly relevant component of higher-order cognition called placekeeping. Placekeeping is important for problem solving and linear thinking, even more so than working memory capacity. In the evening, participants completed UNRAVEL, a measure of placekeeping ability and memory maintenance, and the Psychomotor Vigilance Task (PVT), a standard measure of vigilant attention, as a baseline assessment of performance. Participants were then randomly assigned to sleep at home for the night or to remain awake in the laboratory overnight. In the morning, all participants completed UNRAVEL and PVT again. In Experiment 1, we show that vigilant attention cannot fully account for deficits in placekeeping or memory maintenance after sleep deprivation. In Experiment 2, we show that the ability to manage proactive interference, a potentially important process of memory maintenance, did not show a significant deficit due to sleep deprivation. Experiments 3 and 4 investigate two interventions, caffeine and brief naps, and the extent to which they mitigate cognitive deficits due to sleep deprivation. Caffeine selectively benefitted vigilant attention but had no effect on

placekeeping for the majority of participants. A brief nap during a period of sleep deprivation did not enhance vigilant attention or placekeeping performance; however, different aspects of sleep architecture during the naps were related to performance on the two tasks. Collectively, findings across the four studies do not support the attention-mediated theory; vigilant attention does not completely underlie deficits in placekeeping or memory maintenance after sleep deprivation. Instead, sleep deprivation appears to directly impair placekeeping and memory maintenance and may cause domain-specific deficits to cognition.

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KEY TO ABBREVIATIONS

ANOVA	Analysis of Variance
EEG	Electroencephalography
EOG	Electrooculography
EMG	Electromyography
PFC	Prefrontal Cortex
PVT	Psychomotor Vigilance Task
REM	Rapid Eye Movements
SWS	Slow Wave Sleep
TSD	Total Sleep Deprivation

INTRODUCTION

Insufficient sleep is extremely common and has even been deemed a public health epidemic (Centers for Disease Control and Prevention). Nonetheless, certain occupations, such as medical or military personnel, regularly demand individuals to remain awake for long periods of time with little or no sleep at all. Despite the prevalence of sleep loss, it is not entirely clear what effects total sleep deprivation (TSD), a period of 24 hours or more with no sleep, has on cognitive function. The effects of TSD on lower-level cognition, especially vigilant attention, have received much focus and it is well-established that TSD impairs such processes. However, the effects of TSD on components of higher-order cognition, such as problem solving, working memory, and inhibitory control, are relatively understudied and not well understood. Specifically, it is debated whether TSD directly impairs higher-order cognition or whether higher-order processes are selectively spared; in which case, decrements on cognitive tasks are solely driven by global vigilant attention impairments after TSD.

Furthermore, it is not clear how to mitigate cognitive deficits due to TSD. Two of the most common interventions for TSD are caffeine and naps. However, the majority of research utilizing these interventions has focused on how caffeine or naps affect vigilant attention. The reasoning behind this focus on vigilant attention is that if TSD exclusively affects vigilant attention, then interventions need only target this one cognitive domain. However, if TSD directly impairs higher-order processes, then an understanding of how interventions mitigate deficits in higher-order cognition is crucial, yet is currently lacking. Thus, there is a gap in the literature concerning higher-order cognition, both in terms of how TSD affects components of higher-order cognition and in terms of how caffeine and naps affect higher-order processes in sleep-deprived individuals.

This gap in the literature concerning higher-order cognition may be due, to a significant extent, to pervasive methodological limitations within the literature that have severely complicated the understanding of how TSD and interventions affect higher-order processes. The goal of this dissertation is to use methodologically sound approaches to investigate how TSD affects vigilant attention and a broadly relevant component of higher-order cognition – placekeeping ability. Specifically, we aim to test whether deficits in vigilant attention underly deficits in placekeeping ability after TSD, as would be predicted by the prominent attention-mediated theory of TSD. Additionally, we aim to examine how caffeine and naps affect vigilant attention and placekeeping ability after a period of TSD.

EFFECTS OF SLEEP DEPRIVATION ON COGNITION

Sleep deprivation is known to impair lower-level processes, particularly vigilant attention (Doran, Van Dongen, & Dinges, 2001; Graw, Kräuchi, Knoblauch, Wirz-Justice, & Cajochen, 2004). At the forefront of sleep deprivation research is the Psychomotor Vigilance Task (PVT; Wilkinson, & Houghton, 1982; Dinges & Powell, 1985), which assesses sustained attention and vigilance. The PVT is considered the gold standard task for assessing cognitive deficits due to TSD and is widely used throughout sleep deprivation research. During the PVT, individuals make simple behavioral responses (e.g. mouse click) as quickly as possible in response to the appearance of a stimulus (e.g. red dot). The PVT is a useful task for sleep deprivation research because it is resistant to practice or learning effects (Dinges, et al., 1997; Jewett, et al., 1999) and can be administered multiple times to the same individual. The PVT is also sensitive to effects of sleep loss and time-on-task effects can be captured within 10 minutes (Lim & Dinges, 2008).

To a large extent due to the PVT, the effects of TSD on vigilant attention are well characterized. One of the hallmarks of TSD is an increase in lapses of attention (De Havas,

Parimal, Soon, & Chee, 2012; Chuah, Venkatraman, Dinges, & Chee, 2006; Doran, Van Dongen, & Dinges, 2001; Graw et al., 2004; Jewett, Dijk, et al., 1999), which are most often defined as reaction times longer than 500 ms. TSD also broadly increases reaction times on the PVT, demonstrating that even non-lapse performance is impaired (De Havas, Parimal, Soon, & Chee, 2012; Doran, Van Dongen, & Dinges, 2001). In addition, variability in reaction times increases after TSD (De Havas, Parimal, Soon, & Chee, 2012; Chuah, Venkatraman, Dinges, & Chee, 2006; Doran, Van Dongen, & Dinges, 2001; Van Dongen, Baynard, Maislin, & Dinges, 2004). Increases in variability reflect less consistent performance within an individual as well as trait-like vulnerability to TSD such that some individuals are severely affected by TSD; whereas, others are resilient to TSD. Lastly, performance deteriorates with time-on-task, suggestive of a gradual waning of vigilant attention over time (Jewett, Dijk, et al., 1999).

Although the effects of TSD on vigilant attention are established, the effects of TSD on higher-order cognition is much less clear. Several studies have found that TSD impairs aspects of higher-order cognition, including working memory (Chee et al., 2006; Chee & Choo, 2004; Choo, Lee, Venkatraman, Sheu, & Chee, 2005; Durmer, & Dinges, 2005; Habeck, et al., 2004; Mu et al., 2005; Smith, McEvoy, & Gevins, 2002), executive function (Nilsson et al., 2005), inhibitory control (Chuah, Venkatraman, Dinges, & Chee, 2006), task switching (Wimmer, Hoffmann, Bonato, & Moffitt, 1992), verbal learning (Drummond, Meloy, Yanagi, Orff, & Brown, 2005), top-down emotion regulation (Yoo, Gujar, Hu, Jolesz, & Walker, 2007), and complex attention (Drummond, Gillin, & Brown, 2001). However, several other studies have found that TSD had no effect on working memory (Nilsson et al., 2005; Tucker, Whitney, Belenky, Hinson, & Van Dongen, 2010; Wimmer, Hoffmann, Bonato, & Moffitt, 1992), inhibitory control (Binks, Waters, & Hurry, 1999); verbal fluency (Binks, Waters, & Hurry,

1999; Tucker, et al., 2010), cognitive flexibility and set shifting (Binks, Waters, & Hurry, 1999), resistance to interference (Tucker, et al., 2010), and information processing (Binks, Waters, & Hurry, 1999). Thus, there are conflicting findings regarding how TSD affects higher-order cognition. These conflicting findings even extend to the same processes, such as working memory and inhibitory control.

To summarize, TSD has clear and well-defined deficits on vigilant attention as measured by the PVT – a widely used task in sleep deprivation research. One of the most common findings is that TSD increases lapses in attention. However, the effect of TSD on aspects of higher-order cognition is mixed.

INTERVENTIONS FOR SLEEP DEPRIVATION

Interventions that reduce cognitive deficits and performance errors associated with TSD are highly sought after. Two of the most frequently studied interventions for TSD are caffeine and naps. Both caffeine and naps have been shown to benefit vigilant attention and alertness under conditions of TSD (Kamimori, Johnson, Thorne, & Belenky, 2005; Killgore, Kahn-Greene, Grugle, Killgore, & Balkin, 2009; Killgore, Rupp, Grugle, Reichardt, & Balkin, 2008; McLellan et al., 2005; Wesensten, Killgore, & Balkin, 2005; Dinges, Orne, Whitehouse, & Orne, 1987; Jewett, Dijk, et al., 1999; Vgontzas et al., 2007). However, there is no clear consensus about how these interventions affect components of higher-order cognition.

Caffeine

One of the most widely used interventions for TSD is caffeine. Caffeine is a stimulant that is known to reduce sleepiness and fatigue. Across periods of wakefulness, extracellular adenosine builds up, a byproduct of energy utilization, and decreases neuronal activity and

increases sleepiness (Basheer, Strecker, Thakkar, & McCarley, 2004; Huang, Urade, & Hayaishi, 2011; Porkka-Heiskanen, Strecker, & McCarley, 2000; Scammell, 2001; Strecker, et al., 2000). When caffeine is consumed, it binds to adenosine receptors in the brain and acts as an antagonist, helping to keep individuals awake and focused by temporarily relieving drowsiness (Fredholm, et al., 1999; Huang, Urade, & Hayaishi, 2011). The consumption of caffeine (up to 400 mg daily) is considered safe for adults (Mayo Clinic) and caffeine has a long half-life, approximately 5 hours (Institute of Medicine, 2001). Thus, caffeine may benefit cognition by reducing drowsiness and increasing concentration and can do so over long durations.

Indeed, numerous studies have found that caffeine is beneficial for vigilant attention under conditions of TSD (Kamimori, et al., 2005; Killgore, et al., 2009; Killgore, Rupp, Grugle, Reichardt, & Balkin, 2008; McLellan et al., 2005; Wesensten, Killgore, & Balkin, 2005; Wesensten et al., 2002; Wesensten et al., 2004). Studies using electroencephalography (EEG) have shown that caffeine reduces microsleeps, stage 1 or stage 2 sleep lasting several seconds in duration (Beaumont et al., 2001), and increases beta power activity, which is an indication of enhanced alertness (Patat et al., 2000). Thus, caffeine benefits vigilant attention performance under conditions of TSD and changes neural activity indicative of enhanced alertness.

Despite the consistent effects of caffeine on lower-level processes, the effects of caffeine on higher-order cognition are much more mixed. Positive effects of caffeine have been found for tasks assessing problem solving (Killgore, et al., 2009) and quantitative reasoning (Wesensten, Killgore, & Balkin, 2005). Slow release caffeine has been found to benefit additional domains including information processing, working memory, divided attention, and reasoning (Beaumonet et al., 2001). However, there are also several studies showing that caffeine did not benefit higher-order cognition. Caffeine had little to no effect on mitigating sleep-deprived

performance on tasks assessing problem solving (Killgore, et al., 2009), cognitive flexibility and set shifting (Killgore, et al., 2009; Wesensten, Killgore, & Balkin, 2005), inhibitory control (Wesensten, Killgore, & Balkin, 2005), working memory (Wesensten et al., 2002), and verbal fluency (Wesensten, Killgore, & Balkin, 2005). When caffeine-related benefits have been found on these tasks, it was in only one outcome measure. For example, one study found a benefit of caffeine only in the 'learning to learn' dimension on the Wisconsin Card Sorting Task but caffeine had no effect on any other outcome measure in the same task: number of correctly sorted cards, number of errors, number of preservative responses, or number of categories completed (Wesensten, Killgore, & Balkin, 2005). Importantly, these mixed effects of caffeine cannot be explained by dose of caffeine because studies that found positive effects of caffeine have used similar dosages to studies that found no benefit of caffeine. Thus, the effect of caffeine on higher-order cognition is ambiguous and more research is needed to determine whether caffeine is beneficial for higher-order processes.

Naps

A second widely studied intervention for mitigating cognitive deficits from TSD is naps. Napping is a promising intervention since it directly restores some of the sleep debt that accumulates over extended periods of wakefulness. During sleep, there is a reuptake of adenosine that may be region specific. Brain areas that are more active during wakefulness may experience faster adenosine reuptake during sleep (Porkka-Heiskanen, et al., 2000). Thus, areas like the prefrontal cortex (PFC) may especially benefit from a nap because this area tends to be one of the most active during wakefulness (Maquet, et al., 1990). Therefore, a nap may help neuronal functioning by decreasing levels of extracellular adenosine, particularly in cortical areas

like the PFC which tend to be the most active during wakefulness and which also tend to be implicated in higher-order task performance (Miller, 2000).

In addition to adenosine reuptake during sleep, naps may also benefit cognitive performance during TSD by helping to stabilize memories for newly learned tasks. Slow wave sleep (SWS) has been linked to cortical reorganization, a process important for memory consolidation (Marshall & Born, 2007; Steriade & Amzica, 1998, Stickgold, 2005; Walker, 2009; Walker & Stickgold, 2004). Slow oscillations generated during SWS are thought to be important for both synaptic stability and plasticity required for memory organization, including enhancing, stabilizing, or integrating memories into previously established neural networks (Abraham & Robins, 2005; Steriade & Amzica, 1998). Thus, a nap that includes SWS may help organize newly formed memories, such as those associated with learning a new cognitive task during an experimental protocol.

Thus, there are a few different mechanisms that could explain why naps during a period of TSD would mitigate cognitive deficits. However, it is unclear how long of a nap is needed before observable benefits appear. Indeed, the vast majority of studies that have examined the effects of naps during TSD have used long nap durations, between 2 and 4 hours (Dinges, Orne, Whitehouse, & Orne, 1987; Jewett, Dijk, et al., 1999; Macchi, Boulos, Ranney, Simmons, & Campbell, 2002; Naitoh, Englund, & Ryman, 1982; Vgontzas et al., 2007). However, research investigating the effect of brief naps (< 2 hours) is much more limited (Gillberg, 1984; Hilditch, Centofanti, Dorrian, & Banks, 2016; Lumley, 1986).

Long naps, between 2 and 4 hours, (Dinges, Orne, Whitehouse, & Orne, 1987; Jewett, Dijk, et al., 1999; Macchi, Boulos, Ranney, Simmons, & Campbell, 2002; Naitoh, Englund, & Ryman, 1982; Vgontzas et al., 2007) and brief 10 and 60 minute naps, (Gillberg, 1984; Hilditch,

et al., 2016), during TSD protocols have been shown to benefit vigilant attention relative to sleep-deprived participants with no nap. However, PVT performance after a 10 minute nap was only assessed up to 47 minutes post-nap, so it is unclear whether benefits would persist over longer durations of post-nap wakefulness (Hilditch, et al., 2016). On the other hand, the benefit of long naps on lower-level simple reaction time tasks can persist for up to 14 – 20 hours of additional wakefulness, indicating that naps can exert a beneficial effect on attention and vigilance disproportionate to the duration of the nap itself (Macchi, et al., 2002; Naitoh, Englund, & Ryman, 1982). There is also evidence suggesting that the dose-response curve for basic alertness and lower-level cognition from a nap starts to plateau or produce smaller and smaller benefits as the length of the nap increases (Jewett, Dijk, et al., 1999; Lumley, 1986). There is some evidence to suggest that a 60 minute nap may be the point at which alertness plateaus (Lumley, 1986) and may thus be the optimal nap duration to balance time constraints with performance improvements.

Research on the effect of naps on higher-order cognition during periods of TSD is much more limited. However, the research that has been done shows that naps may also benefit some aspects of higher-order cognition. Long naps (2 – 4 hours) have been found to benefit components of higher-order cognition including working memory (Dinges, Whitehouse, Orne, & Orne, 1988; Haslam, 1985; Macchi, Boulos, Ranney, Simmons, & Campbell, 2002; Webb, 1987), logical reasoning (Haslam, 1985), and cognitive ability (Haslam, 1985). Only one study that examined the effect of brief naps on higher-order cognition during TSD found that a 10 and a 30 minute nap was beneficial for maintaining performance on an associative learning task up to 32 minutes post-nap compared to participants who did not nap (Hilditch, et al., 2016). Together, these findings suggest that a nap during a period of TSD benefits both lower-level and some

higher-order processes. However, research on brief naps is largely understudied and more research is needed to understand the effect of brief naps on higher-order cognition when sleep-deprived.

Summary

In summary, caffeine benefits lower-level cognition – vigilant attention and alertness – for sleep-deprived individuals but has conflicting findings regarding components of higher-order cognition. On the other hand, naps show some promise in benefitting both lower-level and higher-order cognition but there is very little research investigating the effectiveness of brief naps, particularly with regards to higher-order cognition. Notably, the gap in the literature lies primarily with understanding how TSD and interventions affect higher-order processes. In the next section, we argue that the reason for this may be due to methodological limitations present within the sleep deprivation literature that make detecting and interpreting findings from higher-order tasks particularly challenging.

METHODOLOGICAL LIMITATIONS

There are three pervasive methodological limitations that plague sleep deprivation research: small sample sizes, lack of rested controls, and difficulty in isolating higher-order processes. These limitations have contributed to the lack of an understanding of how TSD affects higher-order cognition and how caffeine and naps affect cognitive performance when sleep-deprived.

The use of small sample sizes in sleep deprivation literature is extremely common. A meta-analysis of acute sleep deprivation (< 48 hours) found an average sample size of 21.3 participants across the 70 studies they analyzed (Lim & Dinges, 2010). The use of small samples

is particularly problematic for this literature because variability in performance increases after TSD (De Havas, Parimal, Soon, & Chee, 2012; Chuah, Venkatraman, Dinges, & Chee, 2006; Doran, Van Dongen, & Dinges, 2001; Van Dongen, Baynard, Maislin, & Dinges, 2004), and small samples may not provide the power or precision necessary to detect effects (Lim, Choo, & Chee, 2007). Detecting effects of TSD on higher-order cognition may be especially challenging given that higher-order tasks tend to exhibit practice or learning effects, which may obscure deficits due to TSD, and certain higher-order tasks (ex. Tower of Hanoi) can only be administered once to participants, after a period of TSD. As a result, no baseline assessment of performance can be established, making it difficult to know whether performance is truly impaired by TSD or whether there were baseline differences between groups.

Indeed, effect sizes of TSD on higher-order tasks tend to be smaller than for vigilant attention tasks, indicating that larger samples with more power are needed when testing higher-order tasks. A meta-analysis (Lim & Dinges, 2010) found that simple attention tasks had a large average effect size as indicated by Hedge's *g*, an effect size measure that corrects for small samples (lapses: g = -.762. reaction time: g = -.732). Working memory (accuracy: g = -.555. reaction time: g = - .515) and complex attention tasks (accuracy: g = -.479. reaction time: g = -.312) tended to have moderate effect sizes. Other domains had smaller effect sizes including short-term memory (recall: g = -.383, recognition: g = -.378) and reasoning (accuracy: g = -.125). Despite differences in effect sizes between cognitive domains, researchers have used effect sizes from simple attention tasks, which produce the largest effects of TSD, to justify the use of small samples when investigating higher-order tasks (Tucker, et al., 2010; Wesensten, Killgore, & Balkin, 2005). Thus, studies are likely under-powered in their ability to detect effects on higher-order tasks specifically. The broad reliance on small samples within sleep deprivation

literature suggests that our knowledge of how TSD affects aspects of higher-order cognition is not entirely fleshed out.

Another common issue plaguing TSD research is the lack of rested control participants. Assuming a task is suitable to be administrated multiple times to a participant, common practice in the literature is to conduct a within-subjects design with a baseline assessment of performance prior to TSD, followed by another assessment of performance after TSD. In the case of intervention research, some participants would also receive caffeine or a nap while others would receive placebo (no caffeine, no nap). Nevertheless, all participants are sleep-deprived over the course of the study. Very few studies include a separate group of rested control participants who complete the same experimental protocol as sleep-deprived participants but are given the opportunity to sleep during the night (for exceptions see Binks, Waters, & Hurry, 1999; Tucker et al., 2010; Wimmer, Hoffmann, Bonato, & Moffitt, 1992). As a result, it is impossible to parse effects due to TSD or the intervention and effects due to time or repeated administrations of the same task. For example, performance may change simply due to time-of-day, practice or learning effects, or loss of interest and effort with repeated exposure to the same task. Thus, rested control groups are necessary to provide a comparison of how performance after TSD compares to normal rested conditions.

The last methodological limitation is that no task perfectly captures a single cognitive construct. For example, a task that is designed to assess working memory will also inevitably measure other components that are important for performance, such as attention. Thus, if performance on a task designed to measure some aspect of higher-order cognition shows a deficit after TSD, it can be difficult to determine whether the deficit lies in the higher-order or lower-level process. The mixed findings regarding the effects of TSD on higher-order tasks may reflect

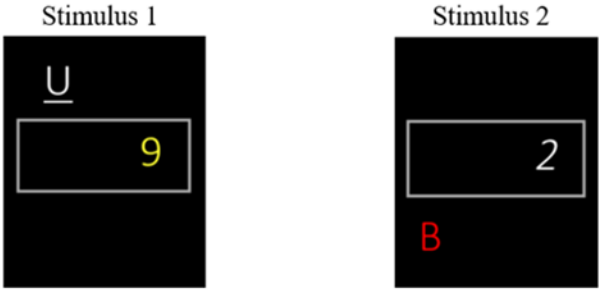
a complex combination of cognitive processes that are impaired or spared following TSD. One method to address this problem is structural equation modeling, in which several separate assessments are used to pull out a latent construct (ex. working memory). Another method is to assess multiple measures within the same task to isolate processes related to the construct of interest. Using this latter method, one study looked at performance on a working memory task and found that TSD overall increased reaction times and decreased accuracy. However, by further examining the linear relationship between reaction time and accuracy as memory set size increased, the researchers were able to parcel out working memory from non-working memory processes (Tucker, et al., 2010). The slope of this linear relationship reflected working memory processes; whereas, the intercept reflected non-working memory components such as probe encoding and motor execution. TSD affected the intercept but not the slope, suggesting that the actual working memory processes required for task performance were not affected by TSD. Instead, impairments were driven by deficits in non-executive processes. Thus, examining multiple measures within the same task has proven to be a useful method and, in this dissertation, this method will also be employed to isolate components of higher-order cognition.

In summary, there are several methodological limitations that exist within the sleep deprivation literature. These methodological limitations have contributed to a lack of an understanding of how TSD affects higher-order cognition. Given equivocal findings and the difficulty in establishing replicable effects for higher-order cognition, efforts should be made to use large sample sizes, include separate rested control groups, and isolate higher-order processes within a task or rule out effects due to other components of cognition which may affect task performance, such as attention.

In order to investigate effects of TSD and interventions on higher-order cognition, we use a task called UNRAVEL (Altmann et al., 2014, 2017). UNRAVEL measures placekeeping ability and includes multiple outcome measures which can be used to isolate a specific higher-order component of placekeeping ability called memory maintenance. Placekeeping is the ability to maintain place within a sequence containing substeps, while avoiding repetitions and omissions of those substeps. Placekeeping is related to general fluid intelligence (Gf) and problem solving, even more so than working memory capacity (Burgoyne, Hambrick, & Altmann, in press; Hambrick & Altmann, 2015). In the case of problem solving, for example, placekeeping is necessary to keep track of solution attempts so that unexplored paths are not omitted and already explored paths are not repeated. Thus, placekeeping is a broadly important component of higher-order cognition that is related to factors like Gf that predict real-world outcomes such as academic achievement and job performance.

The word UNRAVEL is an acronym in which each letter refers to a step that participants perform in a specific order (specified by the acronym). See Figure 1 for an example stimulus and a list of the decision rules. There is no information inherent in the task itself that indicates what step the participant is on; therefore, they must remember their place in the sequence. In addition, participants are occasionally interrupted from the task flow and must remember their place in the sequence prior to the interruption, despite interference and decay affecting memory maintenance. Thus, interruptions are used to assess memory maintenance processes that keep task-relevant representations active during the interruptions. To isolate memory maintenance, we compare two trial types that differ only in the need for memory maintenance. Post-interruption trials are preceded by an interruption; whereas, non-interruption trials are preceded by another trial. The

processing for the two trial types is identical except that post-interruption trials require recall of the step performed before the interruption, despite decay and interference during the interruption, and therefore depend on memory maintenance. Thus, non-interruption trials can be thought of as assessing general placekeeping ability while post-interruption trials uniquely assess memory maintenance.



Step	Rule	Answer to Stimulus 1	Answer to Stimulus 2
U	**U**nderlined or **I**talicized	U	I
N	**N**ear to or **F**ar from the start of the alphabet	F	N
R	**R**ed or **Y**ellow	Y	R
A	**A**bove or **B**elow the box	A	B
V	**V**owel or **C**onsonant	V	C
E	**E**ven or **O**dd	O	E
L	**L**ess than or **M**ore than 5	M	L

Figure 1. Above: Example of two randomly-generated stimuli from the UNRAVEL task. Below: The UNRAVEL rules that correspond to each step (letter) in the UNRAVEL acronym, and the correct keyboard responses for each rule based on the two stimuli above. The bolded letters represent the possible response options for each rule.

In a prior experiment, we found that TSD impaired performance on the UNRAVEL placekeeping task (Stepan, Fenn, & Altmann, 2019). Importantly, this experiment utilized large samples and a separate rested control group in addition to using the UNRAVEL placekeeping task. In the evening, participants completed UNRAVEL and were then randomly assigned to either a rested group (n = 112) or a sleep-deprived group (n = 122). Rested participants returned

home and were given the opportunity to sleep for the night; whereas, sleep-deprived participants remained awake in the laboratory overnight, continuously monitored by two trained research assistants. The following morning, rested participants returned to the laboratory and all participants completed UNRAVEL again.

We found that sleep-deprived participants (n = 18, 15%) were more likely to fail to meet a modest accuracy criterion that they had met the prior evening compared to rested participants (n = 1, 1%). Thus, TSD caused a breakdown in the ability or the willingness to perform the task as instructed, which they were able to do the previous evening. In the remaining sample, we found that sleep-deprived and rested participants performed similarly during the evening session, which was expected given random assignment to conditions. However, in the morning, sleep-deprived participants made more placekeeping errors – both in terms of post-interruption errors and non-interruption errors. Interestingly, there was a time-on-task effect within post-interruption errors such that sleep-deprived participants progressively made more errors across blocks of UNRAVEL that was not evident for rested participants. There was also a time-on-task effect for non-interruption errors but this increase was much smaller and did not differ by group, indicating that the underlying mechanism that caused the increase in errors is not the one that caused the increase in post-interruption errors for the sleep-deprived group. See Figure 2 for a depiction of the results.

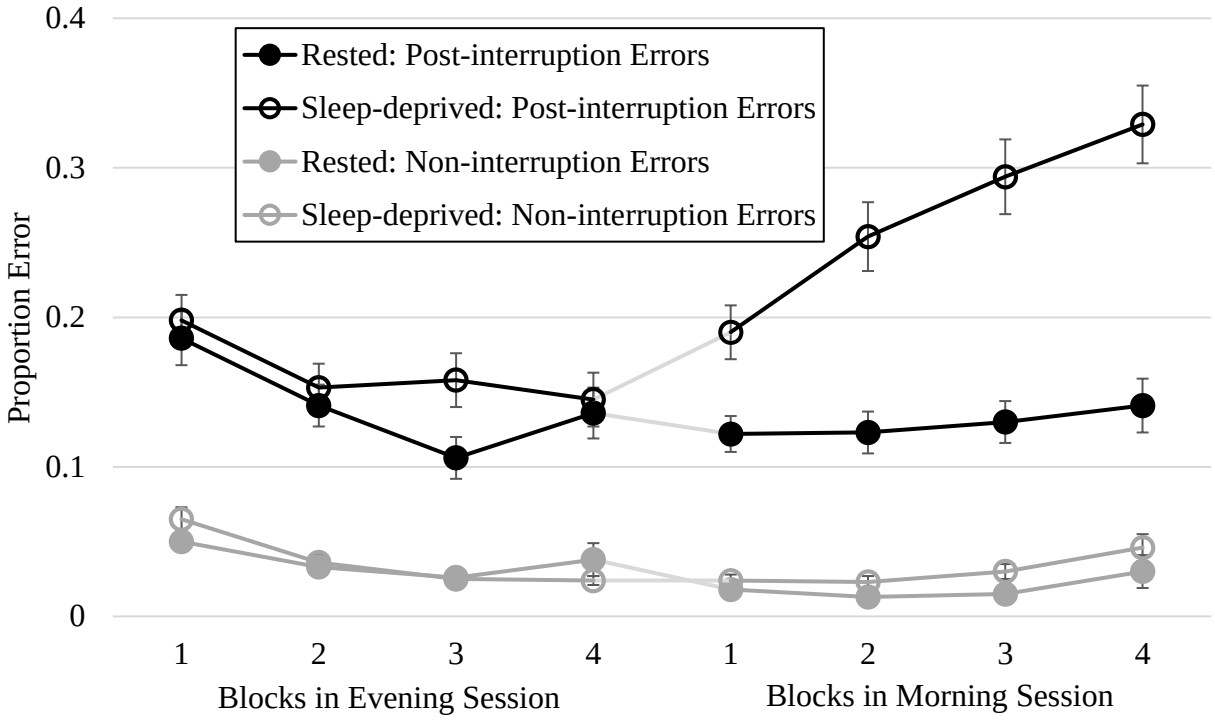


Figure 2. Proportion of post-interruption (black lines) and non-interruption (gray lines) errors across the four blocks of UNRAVEL in the evening session (left side) and morning session (right side) for the Rested and Sleep-deprived groups. Error bars are standard error of the mean.

The underlying mechanism for post-interruption errors may have been related to memory maintenance processes or could be explained by attention. Memory maintenance processes would imply that interference for past performance accumulated and resulted in deteriorating performance over time. An attention explanation would suggest that the time-on-task effect is the result of attention waning over time. Indeed, time-on-task effects have been observed on vigilant attention tasks like the PVT (Jewett, Dijk, et al., 1999). An attention-based effect should manifest on both trial types; however, an explicit test of attention was not included in this study and so the specific degree with which attention deficits affected the two trial types is unknown. Thus, there is evidence that TSD impairs performance on the UNRAVEL placekeeping task;

although, the precise processes that were impaired (attention vs. placekeeping and memory maintenance) are not entirely clear.

To summarize, the UNRAVEL task is a useful tool to study the effects of TSD and interventions on higher-order cognition. UNRAVEL assesses a broadly important component of higher-order cognition – placekeeping ability – and has multiple outcomes measures which can be used to isolate a specific component of placekeeping – memory maintenance. In a prior study, we demonstrated that TSD impairs performance on the UNRAVEL placekeeping task. Moreover, we detected processes unique to post-interruption errors which may be related to memory maintenance or vigilant attention. This very question, whether deficits in a higher-order cognitive task can be explained by vigilant attention deficits, is central to a prominent theory of TSD which will be covered in the next section.

ATTENTION-MEDIATED THEORY

One of the most prominent theories of TSD, which I will refer to as the attention-mediated theory, posits that vigilant attention is the only cognitive process directly impaired by TSD (Balkin, Rupp, Picchioni, & Wesensten, 2008; Doran et al., 2001). TSD-related impairments found on higher-order tasks simply reflect deficits in vigilant attention, because attention is a global process that is necessary for nearly all cognitive tasks (Sturm & Willmes, 2001; Sturm, Willmes, Orgass, & Hartje, 1997). Put another way, vigilant attention fully mediates the relationship between TSD and deficits on higher-order tasks.

The underlying mechanism driving vigilant attention deficits after TSD is state instability. Typically, wake and sleep are fixed states and the transition from one state to the other state is rapid and discrete (Saper, Scammell, & Lu, 2005). Instability in the wake state is

caused by competition from the sleep state – which becomes increasingly unstable as the amount of continued wakefulness accumulates (Doran, Van Dongen, & Dinges, 2001; Killgore, 2010; Graw et al., 2004). This competition is between a desire to maintain wakefulness and the homeostatic sleep drive, pushing the sleep-deprived individual towards sleep. The homeostatic sleep drive is an internal biochemical propensity to maintain homeostasis between sleep and wake. Over prolonged periods of wakefulness, the homeostatic sleep drive increases the pressure to sleep (Huang, Urade, & Hayaishi, 2011; Porkka-Heiskanen, Strecker, & McCarley, 2000; Scammell, 2001; Strecker, et al., 2000). This competition creates imbalance in the system, such that the individual is in a more transitional state between wake and sleep, which then causes lapses in attention (Yin, 2007). In some cases, involuntary transitions to a sleep state occur which causes severe lapses in attention called microsleeps – meaning an individual has briefly entered into the early stages of sleep (Kjellberg, 1977). Simple attention tasks, like the PVT, which assess reaction time to a randomly appearing stimulus are especially sensitive to state instability and microsleeps.

The attention-mediated theory is supported by evidence showing that vigilant attention is impaired by TSD and by evidence indicating that higher-order processes may be selectively spared following TSD. Decrements in vigilant attention are one of the most consistent findings in TSD research (De Havas, Parimal, Soon, & Chee, 2012; Chuah, Venkatraman, Dinges, & Chee, 2006; Goel, Rao, Durmer, & Dinges, 2009; Graw et al., 2004; Jewett, Doran, Van Dongen, & Dinges, 2001; Dijk, et al., 1999). Indeed, a meta-analysis found that vigilant attention was the cognitive domain most robustly impaired by TSD (Lim & Dinges, 2010). Furthermore, when higher-order and non-executive processes were dissociated within a task designed to assess higher-order cognition, the higher-order processes (i.e. resistance to proactive interference and

working memory scanning efficiency) were unaffected by TSD. Instead, TSD impaired the non-executive processes, such as probe encoding and motor execution (Tucker, et al., 2010). Thus, even though overall task performance on a higher-order task may be impaired by TSD, the impairment may not be driven by deficits in higher-order processes. Additionally, other work has found that intraindividual variability in reaction time on working memory tasks, as opposed to accuracy measures, is the best indicator of vulnerability to TSD, suggesting that deficits in attention – which typically manifest in reaction time measures – may underly much of the decline in working memory performance when sleep-deprived (Chee, & Chuah, 2008; Lim, Choo, & Chee, 2007). Thus, there is evidence to suggest that TSD reliably and robustly impairs basic vigilant attention processes but may spare higher-order processes.

OVERVIEW

The goal of this dissertation is to test the attention-mediated theory of TSD. To investigate this primary goal, we will also overcome methodological weaknesses in the literature by using large samples, including rested control groups, and isolating specific aspects of higher-order cognition. We investigate the effects of TSD on vigilant attention and a broadly relevant component of higher-order cognition, placekeeping ability. Prior work has shown that TSD impairs placekeeping ability, but the question remains as to whether those deficits can be fully explained by deficits in vigilant attention – as the attention-mediated theory would indicate.

We test the attention-mediated theory using two primary approaches across four methodologically sound experiments. The first approach (Experiments 1 and 2) is to use mediation models to quantify the extent to which vigilant attention mediates deficits in placekeeping. The second approach (Experiment 3 and 4) is to investigate how vigilant attention and placekeeping are affected by interventions for TSD. Experiment 1 will investigate whether

vigilant attention, as measured by the PVT, can fully account for deficits in placekeeping ability and memory maintenance after TSD. Experiment 2 will investigate the memory maintenance component of placekeeping more closely to assess whether vigilant attention or management of proactive interference mediates the relationship between TSD and memory maintenance deficits. Experiment 3 will investigate the effect of caffeine on vigilant attention and placekeeping. Specifically, if vigilant attention underlies all cognitive deficits due to TSD, then caffeine should have a similar effect on placekeeping as it does on vigilant attention. Finally, Experiment 4 will investigate the effect of brief naps and the aspects of sleep architecture during the naps that are related to vigilant attention and placekeeping performance. Together, this set of experiments will provide accumulating evidence that the attention-mediated theory does not adequately characterize TSD deficits on placekeeping and updated theories are needed to explain the direct effect of TSD on higher-order processes.

CHAPTER I: SLEEP DEPRIVATION IMPAIRS PROCEDURAL PLACEKEEPING: MORE THAN JUST LAPSES OF ATTENTION

Experiment 1

Total sleep deprivation (TSD) causes deficits in several domains of cognitive performance, particularly vigilant attention (Doran, Van Dongen, & Dinges, 2001; Graw, Kräuchi, Knoblauch, Wirz-Justice, & Cajochen, 2004) but also some higher-order processes such as working memory (Chee et al., 2006; Choo, Lee, Venkatraman, Sheu, & Chee, 2005) and placekeeping (Stepan, Fenn, & Altmann, 2019). *Placekeeping* is the ability to perform a set of steps or subtasks in a specified order without omissions or repetitions. As such, placekeeping incorporates a variety of memory operations, including memory for the set of steps or subtasks, and memory regarding which steps have been accomplished (Altmann, Trafton, & Hambrick, 2017). In turn, placekeeping supports many complex cognitive activities, including procedural performance and problem solving. In problem solving, for example, accurate placekeeping supports exploration of all candidate solutions (i.e., without omissions) without unproductive exploration of failed ones (i.e., without repetitions). Problem solving is a basis of fluid intelligence (Gf), and placekeeping is highly correlated with Gf (Hambrick & Altmann, 2015), even more so than is working memory capacity (Burgoyne, Hambrick, & Altmann, in press). Thus, placekeeping is a broadly relevant component of higher-order cognition, related to factors like Gf that predict real-world outcomes such as academic achievement and job performance.

Of interest here is whether effects of TSD on placekeeping, as a higher-order cognitive process with broad relevance, are direct or are mediated by vigilant attention. The question arises because vigilant attention is a core component of performance in many tasks (Sturm & Willmes, 2001; Sturm, et al., 1997). Accordingly, one theoretical view is that effects of TSD on vigilant

attention fully mediate effects of TSD on higher-order tasks (Balkin, Rupp, Picchioni, & Wesensten, 2008; Doran et al., 2001; Lim & Dinges, 2010). Supporting this view, effects of TSD are typically more robust for tasks that measure vigilant attention than for tasks that measure higher-order cognition (see Lim & Dinges, 2010, for a meta-analysis). Moreover, TSD can impair lower-level processes such as probe encoding and motor execution without affecting working memory (Tucker, et al., 2010), consistent with the possibility that it spares higher-order processes.

An opposing theoretical view is that TSD impairs higher-order processes directly, even if its effects are partially mediated by attention (Harrison & Horne, 2000). Supporting this view, neuroimaging studies often find that TSD affects activity in the PFC, which mediates higher-order processing (Duncan et al., 2000; Gray, Chabris, & Braver, 2003; Miller, 2000). The change is often a decrease in activity (Choo et al., 2005; Drummond, et al., 1999; Mu et al., 2005), but can also be an increase in activity, which is typically associated with relatively spared performance and interpreted as a compensatory response (Chee & Choo, 2004; Chuah, Venkatraman, Dinges, & Chee, 2006; Drummond & Brown, 2001; Drummond, Gillin, & Brown, 2001; Drummond, Meloy, Yanagi, Orff, & Brown, 2005). Thus, both views have support, but the question of full versus partial mediation by attention has not been directly tested.

We measured attention using the Psychomotor Vigilance Task (PVT; Dinges & Powell, 1985; Wilkinson & Houghton, 1982), because deficits in this task are the primary basis for the view that attention fully mediates effects of TSD (e.g., Lim & Dinges, 2010). We measured placekeeping using the UNRAVEL task (e.g., Altmann et al., 2017), which shows deficits due to TSD (Stepan et al., 2019). In this task, UNRAVEL is an acronym specifying a set of steps (one per letter) and the order in which to perform them (the order of the letters). On each trial, the

participant tries to perform the next step in the sequence, starting over with ‘U’ upon reaching ‘L’. The task environment provides no information about which step is correct, leaving the participant to keep track of where they are in the sequence. Placekeeping is made more challenging by periodic interruptions, which require the participant to remember the step performed before an interruption, in the face of decay and interference during the interruption. Interruptions allow us to isolate effects of TSD on memory maintenance processes that keep the target memory active during interruptions. To isolate these processes, we measure performance on post-interruption trials, which immediately follow interruptions, while controlling for performance on non-interruption trials, which immediately follow other trials, and which involve all the same cognitive operations as post-interruption trials, except for memory maintenance. The interruptions in this task were designed to represent the influence of a dynamic, interactive environment on performance of tasks that extend in time and also to capture effects of the “self-interruptions” that are an integral part of problem solving. Specifically, exploring a solution path or testing a hypothesis takes time and focus, and afterwards, if that path was a dead end, the solver must revisit the set of candidate solutions and ideally remember which failed and which are untested.

Participants performed UNRAVEL and the PVT twice, first in the evening and again the next morning. After the evening session, participants were randomly assigned either to sleep at home (Rested group) or to remain awake in the lab (Sleep-deprived group). Our analyses focused

on the morning session, with evening performance used to control for stable individual differences in ability to perform the tasks.

Method

Participants

Participants were Michigan State University undergraduates who were native English speakers. Individuals were eligible for participation if they had never been diagnosed with a memory or sleep disorder, were not color blind, and had no strong time-of-day preference (scores of 42–58 on the Morningness-Eveningness Questionnaire; Horne & Ostberg, 1975) or major sleep disturbances (scores of 0–10 on the sleep disturbance section of the Pittsburgh Sleep Quality Index; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Additionally, as part of the requirements of a larger study, participants reported no heart conditions and moderate caffeine use (up to 400 mg daily).

Participants slept a minimum of 6 hours the night before the study and woke up by 09:00. They also refrained from napping on the day of the study and did not consume any caffeine, alcohol, or drugs for 24 hours prior to the study. Participants also kept sleep diaries for five nights leading up to the study where they recorded their sleeping habits: time in bed, sleep onset time, number and duration of awakenings during the night, and time of awakening. Total sleep time (TST) was calculated using the duration between time in bed and time of awakening and subtracting sleep onset time and duration of all awakenings during the night. Sleep diary data, reported in Table 1[1], indicated that rested and sleep-deprived participants had similar amounts of sleep prior to the study. Table 2 summarizes actigraphy data from rested participants for the night between sessions. Comparison of Tables 1 and 2 suggests that Rested participants slept

[1] Four participants were missing sleep diaries and were not included in analyses

more prior to the study than during the night between sessions, but the difference could reflect over-estimation of self-reported TST using the sleep diaries compared to the objective actigraphy measure of TST for the night between sessions (Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008). Relationships with sleep between sessions for Rested participants and performance on UNRAVEL and PVT are reported in the supplemental online material (SOM).

Of an initial sample of 154 participants, 2 were excluded for attrition, 3 for noncompliance with instructions, 2 for technical problems, 2 for missing PVT data, and 7 for failing the evening UNRAVEL accuracy criterion. This left 138 participants (Rested [n = 61], Sleep-deprived [n = 77]) contributing data (18–25 years old[2], M_{age} = 19.18, SD = 1.34, 91 females).

[2] Demographic information for one participant was missing.

Table 1

Sleep characteristics from sleep diaries kept five nights prior to the study

	Average sleep time, 5 nights prior to study	Total sleep time, night before study	Time in bed, night before study	Time of awakening, day of study
Experiment 1				
Rested	7hrs 40min (58min)	7hrs 38min (1hr 14min)	23:53 (1hr 13min)	08:06 (55min)
Sleep-deprived	7hrs 39min (1hr 30min)	7hrs 46min (1hr)	00:10 (56min)	08:23 (52min)
Difference	$t(132)=.42$, $p=.67$	$t(132)=.55$, $p=.58$	$t(132)=1.55$, $p=.12$	$t(132)=1.82$, $p=.07$
Experiment 2				
Rested	7hrs 54min (58min)	7hrs 45min (1hr 3min)	00:05 (1hr 14min)	08:17 (54min)
Sleep-deprived	7hrs 45min (48min)	7hrs 33min (57min)	00:08 (1hr 3min)	08:08 (58min)
Difference	$t(236)=1.30$, $p=.20$	$t(234)=1.49$, $p=.14$	$t(234)=.32$, $p=.75$	$t(234)=1.09$, $p=.28$
Experiment 3				
Rested	7hrs 41min (57min)	7hrs 48min (1hr 53min)	00:00 (1hr 12min)	08:09 (52min)
Sleep-deprived	7hrs 54min (56min)	7hrs 55min (2hrs 34min)	00:17 (1hr 4min)	08:26 (53min)
Difference	$t(333)=1.94$, $p=.05$	$t(333)=.47$, $p=.64$	$t(333)=2.23$, $p=.03$	$t(333)=1.69$, $p=.09$
Experiment 4				
Rested	7hrs 55min (57min)	7hrs 46min (1hr 2min)	00:04 (1hr 12min)	08:16 (53min)
Sleep-deprived	7hrs 44min (47min)	7hrs 33min (56min)	00:07 (1hr 2min)	08:08 (57min)
Difference	$t(266)=1.73$, $p=.09$	$t(263)=1.72$, $p=.09$	$t(263)=.52$, $p=.61$	$t(263)=1.09$, $p=.28$

Note. Standard deviation in parenthesis.

Table 2

Sleep characteristics recorded from actigraphy monitors for the night between the evening and morning sessions in the Rested group

Total sleep time	Time spent in bed	Time spent awake	Number of awakenings	Sleep efficiency
Experiment 1				
5hrs 49min (51min)	6hrs 7min (53min)	18min (12min)	.67 (.86)	95.12% (3.12%)
Experiment 2				
5hrs 59min (51min)	6hrs 19min (51min)	19min (12min)	1.85 (5.12)	94.80% (3.06%)
Experiment 3				
5hrs 42min (1hr 20min)	6hrs 00min (1hr 2min)	18min (11min)	.77 (.97)	95.00% (3.01%)
Experiment 4				
5hrs 57min (52min)	6hrs 17min (52min)	20min (11min)	1.73 (4.84)	94.66% (3.03%)

Note. Standard deviation in parenthesis. Sleep efficiency is calculated by dividing the total sleep time by the time spent in bed.

Materials

UNRAVEL. UNRAVEL is an acronym in which each letter refers to a step that participants perform in a specified order (indicated by the order within the acronym). Each letter, or step, identifies a different two-alternative forced-choice decision rule to apply to a randomly generated stimulus. Figure 1 shows two sample stimuli and the seven decision rules. The stimulus contains no information about what step to perform and any rule can apply to any stimulus, so participants must remember where they are in the sequence. Participants perform the sequence in a loop, returning to ‘U’ when they reach ‘L’.

Performance is periodically interrupted by a typing task. Two strings of letters appear on the computer display, one string at a time, and the participant must type each string correctly into a box. Each string comprises the 14 UNRAVEL responses (Figure 1) presented in randomized order, which was designed to generate interference with remembering their place in the sequence once task flow resumes. In this sample, an interruption lasted about 20 seconds (M = 22.47, SD = 6.47). After an interruption, participants try to resume the UNRAVEL sequence where they left off prior to the interruption.

The measure of interest is *placekeeping errors*, meaning steps performed out of sequence. Placekeeping errors can be detected because every rule has unique response options, so we can determine which step the participant selected from any response. Placekeeping errors are coded with respect to the step performed on the previous trial. For example, if steps 'N,' 'R,' 'V,' and 'E' are performed in succession, 'V' would be an error because the 'A' step was skipped, but 'E' would not be an error because it correctly follows 'V.' We analyzed placekeeping errors separately for post-interruption trials, which immediately follow interruptions, and non-interruption trials, which immediately follow other trials. The two trial types measure the same set of cognitive operations except for memory maintenance, which is measured on post-interruption trials only. Memory maintenance is the ability to keep task relevant representations active across the interruptions, despite interference and decay affecting memory.

Errors applying the decision-rule can also occur (these are analyzed in the SOM). A correct trial is one on which there is neither a placekeeping error nor a decision-rule error. If fewer than 70% of trials in a block were correct, the participant was instructed to be more accurate at the end of the block. We coded a session as a failure if accuracy was below 70% on two or more blocks, on grounds that the participant did not follow the instruction to be more

accurate. We excluded participants who failed the evening session from all analyses because we could not be sure they understood the task.

There were four blocks of trials per session. Each block contained 66 trials on average (*SD* = 12) and exactly 10 interruptions. A session took about 35 minutes to complete (*M* = 36.13, *SD* = 9.25).

PVT. Participants monitored a blank computer screen for the appearance of a large red circle and were instructed to make a mouse click as quickly as possible when the circle appeared. Making a mouse click caused the circle to disappear and triggered feedback on reaction time. The circle appeared at random intervals between 1 and 10 seconds. The task lasted 10 minutes.

Procedure

Participants were recruited for a study on sleep deprivation and told they would either remain awake all night or be permitted to sleep. They arrived at 22:00 for the evening session and completed sleepiness and mood assessments (see SOM for task descriptions and analyses). Next, participants completed UNRAVEL, PVT, and other cognitive assessments that were part of a larger study. After completing all tasks (~2 hours), participants were randomly assigned to conditions. Researchers and participants were blind to condition until all evening testing was finished. Participants randomly assigned to the Rested group were given a Charge 2 activity monitor (Fitbit Inc., San Francisco, CA) to track their sleep, and then given a ride home.

Participants assigned to the Sleep-deprived group stayed awake overnight in the laboratory. Sleep-deprived participants were monitored throughout the entire night by two trained research assistants. The research assistants who stayed overnight were not the same researchers who ran the participants through the evening and morning sessions. Participants were

allowed to read, do homework, watch TV or movies, play board/card games, or engage in other quiet activities but were not permitted to engage in any activities that would activate the autonomic nervous system. Participants were permitted to consume any food or beverage that did not contain caffeine or alcohol. Every two hours (01:00, 03:00, 05:00, 07:00) participants were taken into a different testing room, seated at a different computer than the evening and morning sessions, and completed sleepiness and mood assessments. Participants were sleep-deprived for approximately 24 hours before starting the morning tasks.

At 08:30 the following morning, Rested participants returned and all participants completed the morning session, which included mood and sleepiness assessments, UNRAVEL, PVT, and other cognitive tasks associated with the larger study. The morning session lasted approximately 1.5 hours, at which time Sleep-deprived participants were given a ride home.

Also, as part of a larger study, participants consumed capsules containing either caffeine or placebo, distributed in double-blind fashion. Sleep-deprived participants consumed a capsule three times (00:30, 04:30, 08:30). Rested participants consumed a capsule when they returned to the lab at 08:30. We report results from participants who received only placebo for this study. Caffeine results are discussed in Experiment 3.

Results

PVT. The experimental effects are plotted in Figure 3. Means and standard errors are reported in Table 3. We performed an omnibus ANOVA on lapses with Group (Rested, Sleep-deprived) as a between-subjects factor and Session (Evening, Morning) as a within-subjects factor. There was a main effect of Group, $F(1, 136) = 5.96$, $p = .016$, $\eta_p^2 = .042$, with more lapses in the Sleep-deprived group than the Rested group. There was a main effect of Session, $F(1, 136) = 54.87$, $p < .001$, $\eta_p^2 = .277$, with more lapses in the morning than in the evening.

There was also a Group X Session interaction, $F(1, 136) = 19.73$, $p < .001$, $\eta_p^2 = .127$, which we examined by analyzing the Group effect separately for each session. In the evening, the Rested and Sleep-deprived groups performed similarly, $t(136) = 1.30$, $p = .195$, $d = 0.22$. In the morning, there were more lapses in the Sleep-deprived group, $t(136) = 3.68$, $p < .001$, $d = 0.63$. Note that the inclusion of a separate rested group for comparison allows us to dissociate the effect of TSD on lapses from circadian influences, which would similarly affect both groups.

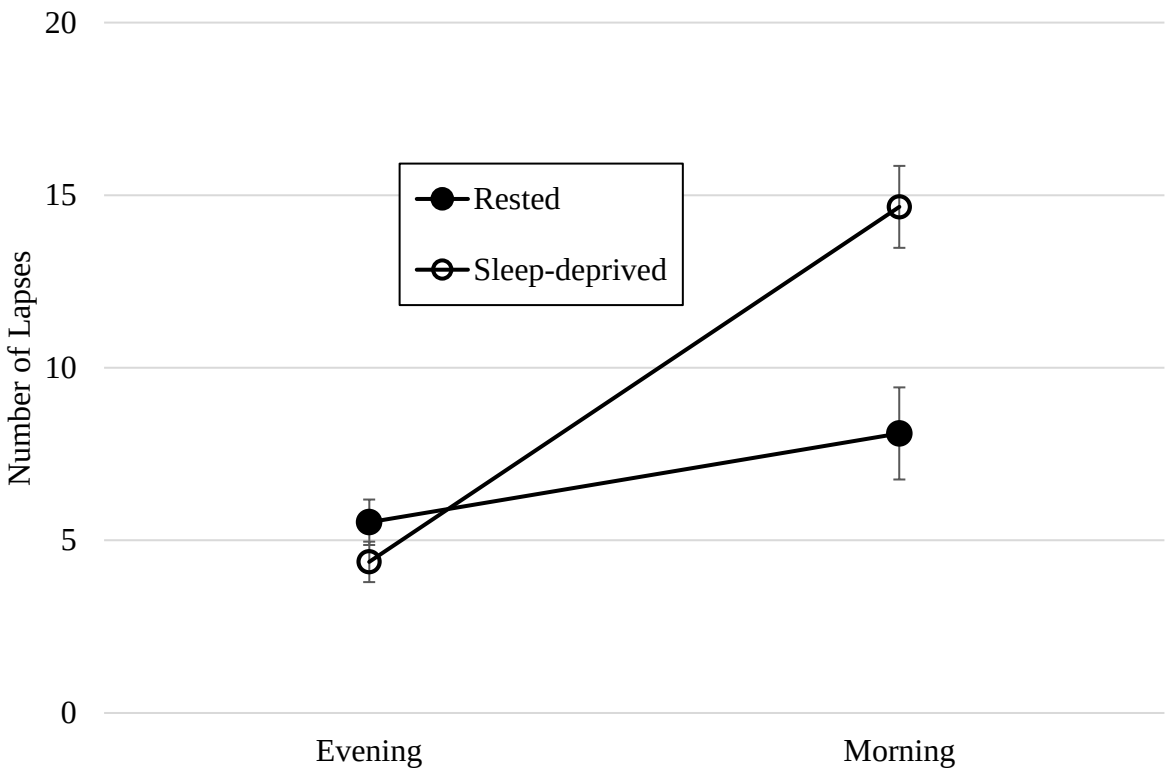


Figure 3. Number of lapses (reaction times greater than 500 ms) in the PVT, separated by Group (Rested, Sleep-deprived) and Session (Evening, Morning) for Experiment 1. Errors bars are standard error of the mean.

Table 3

PVT lapses and UNRAVEL placekeeping errors for Experiment 1

	Evening	Morning
	Lapses	
Rested	5.53 (0.66)	8.10 (1.33)
Sleep-deprived	4.38 (0.59)	14.66 (1.19)
	Post-interruption Errors	
Rested	.14 (.01)	.14 (.03)
Sleep-deprived	.15 (.01)	.29 (.02)
	Non-interruption Errors	
Rested	.03 (.005)	.01 (.02)
Sleep-deprived	.03 (.004)	.09 (.01)

Note. Standard error in parentheses.

UNRAVEL. Experimental effects are plotted in Figure 4. Means and standard errors are reported in Table 3. We performed an omnibus ANOVA on post-interruption errors with Group (Rested, Sleep-deprived) as a between-subjects factor and Session (Evening, Morning) as a within-subjects factor. There was a main effect of Group, $F(1, 136) = 10.08$, $p = .002$, $\eta_p^2 = .069$, with more errors in the Sleep-deprived group than the Rested group. There was a main effect of Session, $F(1, 136) = 21.70$, $p < .001$ $\eta_p^2 = .138$, with more errors in the morning than in the evening. Importantly, there was Group X Session interaction, $F(1, 136) = 21.94$, $p < .001$, $\eta_p^2 = .139$, which we examined by analyzing the Group effect separately for each session. In the

evening, the Rested and Sleep-deprived groups performed similarly, $t < 1$. In the morning, there were more errors in the Sleep-deprived group, $t(136) = 4.18$, $p < .001$, $d = 0.74$.

We performed the same omnibus ANOVA for non-interruption errors and found a similar pattern of results. There was a main effect of Group, $F(1, 136) = 10.21$, $p = .002$, $\eta_p^2 = .070$, with more errors in the Sleep-deprived group than in the Rested group. There was a marginal main effect of Session, $F(1, 136) = 3.66$, $p = .058$, $\eta_p^2 = .026$, with marginally more errors in the morning than in the evening. There was also a Group X Session interaction, $F(1, 136) = 11.85$, $p = .001$, $\eta_p^2 = .080$. The Groups performed similarly in the evening, $t < 1$. In the morning, there were more errors in the Sleep-deprived group, $t(136) = 3.43$, $p = .001$, $d = .62$.

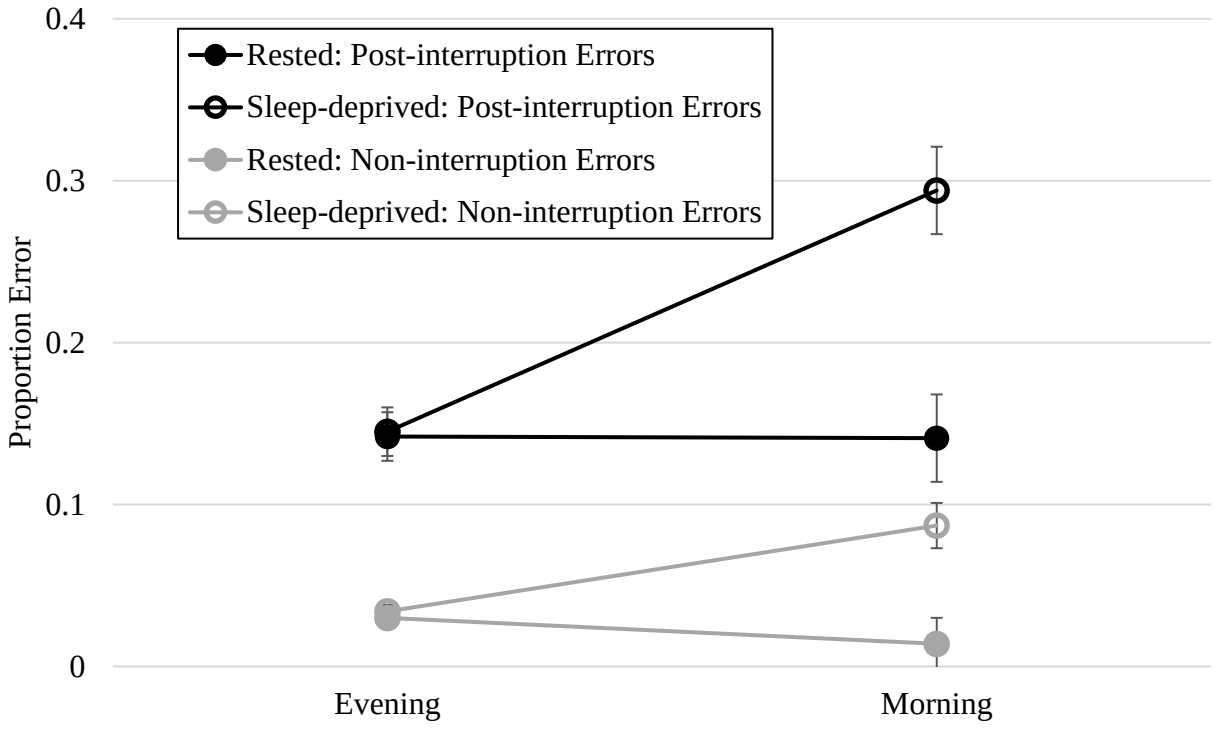


Figure 4. Proportion of post-interruption (black lines) and non-interruption errors (gray lines), separated by Group (Rested, Sleep-deprived) for Experiment 1. Errors bars are standard error of the mean.

Mediation Analyses. First, we report hierarchical regression analyses and then a mediation model using the approach described by Baron and Kenny (1986). We first confirmed that TSD affected vigilant attention (Path *a* in Figure 5). We regressed lapses in the morning session of the PVT against (1) evening lapses, to control for individual differences in attention, and (2) Group (Rested, Sleep-deprived). Table 4 shows the results. Both predictors were significant. The effect of evening lapses indicates reliable individual differences in attention. The effect of Group confirms an effect of TSD on attention, such that TSD increases lapses in attention.

Table 4

Hierarchical regression analysis for morning lapses in attention (Path a *in Figure 5) for Experiment 1*

	B	***SE*B**	***β***	***t***	***p***	***R*²**	**Δ *R*²**
Step 1							
Evening lapses in attention	0.61	.166	.291	3.69	< .001	.064	.064
Step 2							
Group (Rested, Sleep-deprived)	3.63	.860	.333	4.23	< .001	.174	.109

Note. Statistics are from the full model. *df:* Step 1 (1, 136), Step 2 (2, 135).

We then confirmed that TSD affected placekeeping without attention as a mediator (Path *c* in Figure 5). We regressed morning placekeeping errors against (1) evening placekeeping errors, to control for individual differences in placekeeping, and (2) Group, separately for post-interruption trials and non-interruption trials. Table 5 shows the results. Both predictors were significant, for both trial types. The effects of evening placekeeping errors indicate reliable individual differences in placekeeping. The effects of Group indicate unmediated effects of TSD

on placekeeping, such that TSD increases errors on post-interruption trials and non-interruption trials.

Table 5

Hierarchical regression analyses for morning placekeeping errors, unmediated by attention (Path c *in Figure 5), for Experiment 1*

	B	SE_B	β	*t*	*p*	R^2	ΔR^2
			Post-interruption trials				
Step 1 Evening placekeeping errors	0.91	.139	.463	6.56	< .001	.219	.219
Step 2 Group (Rested, Sleep-deprived)	0.08	.016	.330	4.68	< .001	.328	.109
			Non-interruption trials				
Step 1 Evening placekeeping errors	1.18	.280	.326	4.19	< .001	.116	.116
Step 2 Group (Rested, Sleep-deprived)	0.03	.010	.264	3.40	.001	.185	.070

Note. Statistics are from the full model. *df:* Step 1 (1, 136), Step 2 (2, 135).

We then tested the mediated effects of TSD on placekeeping. We regressed morning placekeeping errors against (1) evening placekeeping errors, (2) morning lapses, and (3) Group, separately for post-interruption and non-interruption trials. Table 6 shows the results. All three predictors were significant, for both trial types. The effects of morning lapses indicate that morning attention predicts morning placekeeping (Path *b* in Figure 5). The effects of Group indicate that TSD directly impairs placekeeping when the mediating effects of attention are removed from placekeeping ability (Path *c′* in Figure 5).

Table 6

Hierarchical regression analyses for morning placekeeping errors, mediated by morning lapses in attention (Paths b and c' in Figure 5), for Experiment 1

	B	SE_B	β	*t*	*p*	R^2	ΔR^2
			Post-interruption trials				
Step 1 Evening placekeeping errors	.774	.134	.393	5.76	< .001	.219	.219
Step 2 Morning lapses in attention	.006	.001	.310	4.34	< .001	.360	.141
Step 3 Group (Rested, Sleep-deprived)	.054	.016	.238	3.42	.001	.411	.051
			Non-interruption trials				
Step 1 Evening placekeeping errors	.919	.273	.255	3.37	.001	.116	.116
Step 2 Morning lapses in attention	.004	.001	.323	4.08	< .001	.249	.133
Step 3 Group (Rested, Sleep-deprived)	.022	.010	.171	2.22	.028	.275	.027

Note. Statistics are from the full model. *df:* Step 1 (1, 136), Step 2 (2, 135), Step 3 (3, 134).

Next, we compared the two models of TSD on placekeeping, one with and one without attention as a mediator (Paths *c* vs. *c'*). The models are shown in Figure 5. In the full model, sleep deprivation is the independent variable, placekeeping is the dependent variable, and attention is the mediator. By a Sobel test, the effect of TSD was smaller with attention as a mediator (Path *c'*) for post-interruption errors, $Z = 3.07$, $p = .002$, and non-interruption errors, $Z = 2.96$, $p = .003$. Together, these analyses support partial mediation, meaning that some, but not all, of the effect of TSD on placekeeping is mediated by attention.

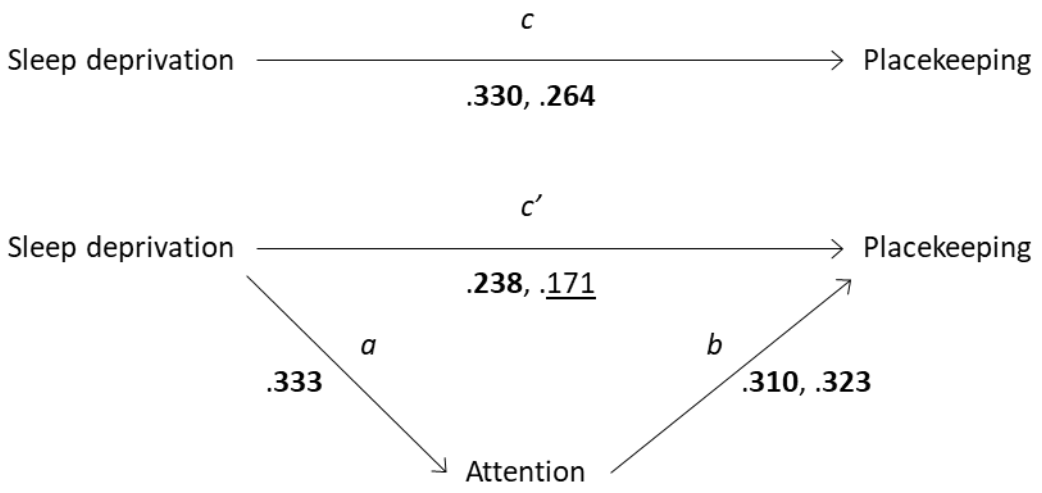


Figure 5. Mediation model with sleep deprivation as the independent variable, placekeeping as the dependent variable, and attention as the mediator. Numbers are standardized regression coefficients (β). Where two are present, the first is for post-interruption placekeeping trials and the second for non-interruption placekeeping trials. **Bold**, $p < .01$. Underline, $p < .05$.

Finally, we asked whether TSD directly affected the memory maintenance component of post-interruption trials. We conducted a hierarchical regression analysis on post-interruption errors in which we removed the variance associated with non-interruption errors. Non-interruption trials measure all the same cognitive operations as post-interruption trials, except those that maintain target information active in memory during interruptions. Thus, removing variance associated with non-interruption errors removes variance associated with all processes except memory maintenance. We regressed morning post-interruption placekeeping errors against (1) evening post-interruption placekeeping errors, (2) morning lapses in attention, (3) morning non-interruption placekeeping errors (the new predictor in this analysis), and (4) Group (Rested, Sleep-deprived). Table 7 shows the results. The effect of morning non-interruption placekeeping errors was significant, indicating that the two trial types were correlated. With this

effect removed, the effect of Group was still significant (p = .011), which is evidence that TSD directly affected memory maintenance specifically as well as placekeeping generally.

Table 7

Hierarchical regression analyses for morning post-interruption errors, mediated by morning lapses in attention, and controlling for non-interruption errors (Step 3), for Experiment 1

	B	SE_B	β	t	p	R^2	ΔR^2
Step 1							
Evening errors	.628	.116	.319	5.42	< .001	.219	.219
Step 2							
Morning lapses	.003	.001	.148	2.29	.023	.360	.141
Step 3							
Morning errors, non-interruption	.825	.113	.470	7.29	< .001	.558	.199
Step 4							
Group (Rested, Sleep-deprived)	.035	.014	.156	2.59	.011	.579	.021

Note. Statistics are from the full model. *df:* Step 1 (1, 136), Step 2 (2, 135), Step 3 (3, 134), Step 4 (4, 133).

Discussion

We tested the role of attention in the far-reaching cognitive deficits associated with TSD. One theory is that attention, as a core component of performance in many tasks, fully mediates the effects of TSD on higher-order processes (Balkin, et al., 2008; Doran et al., 2001; Lim & Dinges, 2010). An alternative theory is that attention may partially mediate these effects, but that TSD also has direct effects on higher-order processes (Harrison & Horne, 2000). We measured vigilant attention using the PVT, as a standard measure of attention deficits caused by TSD. We tested mediation with respect to placekeeping, a higher-order process involved in procedural performance, problem solving, and other cognitive activities that depend on keeping track of location in a sequence or hierarchy of steps or subtasks.

Our results uniformly support partial mediation and direct effects. Vigilant attention accounted for about 14% of the variance in effects of TSD on placekeeping (14.1% on post-interruption trials, 13.3% on non-interruption trials), but a direct effect of TSD on placekeeping remained, accounting for an additional 5.1% of variance on post-interruption trials and 2.7% on non-interruption trials. We also found a direct effect of TSD on memory maintenance processes, which support placekeeping by maintaining target information in an active state during interruptions. After controlling for performance on non-interruption trials, which require all the same cognitive operations as post-interruption trials except for memory maintenance, a direct effect of TSD remained, accounting for an additional 2.1% of variance on post-interruption trials.

A more thorough understanding of direct effects of TSD has important implications for intervention research aimed at mitigating deficits associated with sleep loss. Specifically, different or multiple interventions may be necessary to protect against costly errors associated with sleep loss. For example, these results suggest that an intervention that benefits vigilant attention, such as caffeine (Killgore, et al., 2009), may not reduce costly errors in procedural performance that have been linked to TSD (e.g., Navy Office of Information, 2017).

One limitation of the present design is that the PVT may not measure all relevant aspects of attention, and that additional indicators of attention could produce full mediation. However, the direct effect of TSD on memory maintenance controls for any attention process that plays a role in placekeeping generally but was not measured by the PVT, in that it removes the influence of any process active on non-interruption trials. Accordingly, to rule out full mediation would have required an indicator focused specifically on the role of attention in memory maintenance.

Another limitation is that our sample consisted of college-aged adults, who may differ from the general population in their response to TSD. For example, college-aged students may

need more sleep and therefore may be more affected by TSD. Indeed, in the week leading up to the study, participants averaged approximately 7hrs 40min of sleep per night, which is higher than the 2016 national average (Knutson et al., 2017). An important direction for sleep deprivation research generally is to make use of broader samples.

CHAPTER II: SLEEP DEPRIVATION DOES NOT AFFECT ABILITY TO MANAGE PROACTIVE INTERFERENCE

Experiment 2

One theoretical stance about TSD is that deficits in higher-order cognition are completely attributable to vigilant attention deficits (Balkin, Rupp, Picchioni, & Wesensten, 2008; Doran et al., 2001). Challenging this theory, there is accumulating evidence that TSD directly impairs placekeeping (Stepan, et al., 2019), an important procedural ability highly related to measures of fluid intelligence (Burgoyne, Hambrick, & Altmann, in press; Hambrick & Altmann, 2015). Importantly, these deficits in placekeeping cannot be solely explained by deficits in vigilant attention (Experiment 1). Furthermore, TSD appears to impair a specific component of placekeeping ability called memory maintenance. However, memory maintenance itself is a complex process involving component mechanisms and it is not clear what components of memory maintenance are affected by TSD.

Memory maintenance is the ability to keep task-relevant information active in working memory, despite interfering information, and is impaired under conditions of TSD. Sleep-deprived participants, but not rested, made progressively more post-interruption errors, reflective of memory maintenance failures, across the duration of the task (Stepan, et al., 2019). In addition, this time-on-task effect of TSD appeared to be unique to post-interruption trials because the time-on-task effect for non-interruption trials was far less pronounced and shared by rested participants. Furthermore, in Experiment 1, we isolated processes related to memory maintenance by controlling for vigilant attention and non-interruption trial performance (i.e. task-related processes not specific to memory maintenance) and found a direct effect of TSD on

post-interruption trial performance. Thus, TSD appears to directly impair memory maintenance processes.

The time-on-task effect for post-interruption trials and the direct effect of TSD on memory maintenance provide some insight into what component mechanism of memory maintenance is impaired by TSD. Vigilant attention is one possible mechanism as waning attention over time could explain the time-on-task effect. However, vigilant attention failed to fully account for memory maintenance deficits after TSD in Experiment 1; therefore, vigilant attention does not appear to be the component mechanism of memory maintenance that TSD directly impairs. Another candidate mechanism is proactive interference as a buildup of interference for past performance could also explain the time-on-task effect for post-interruption trials. Thus, resisting interference as the task progresses and more interruptions are experienced seems to be an important part of task performance related to memory maintenance.

Here, we investigated whether TSD impairs the ability to manage proactive interference and whether this ability is related to memory maintenance on the UNRAVEL task. In the evening, participants completed UNRAVEL and PVT and were then randomly assigned to either go home and sleep normally for the night or to remain awake overnight in the laboratory. In the morning, rested participants returned and all participants completed a proactive interference task, UNRAVEL, and PVT. We used regression analyses and mediation models to examine the extent to which the ability to manage proactive interference mediated the relationship between TSD and memory maintenance.

Method

Participants

Participant inclusion and exclusion criteria was the same as Experiment 1, except that there were no restrictions based on caffeine consumption or heart condition. Sleep diary data, reported in Table 1[3], indicated that rested and sleep-deprived participants had similar amounts of sleep prior to the study. Table 2 summarizes actigraphy data from rested participants for the night between sessions and correlations with morning performance are discussed in the SOM.

Of an initial sample of 334 participants, 45 were excluded for missing data, 25 for failing the evening UNRAVEL accuracy criterion, 9 for attrition, and 1 for noncompliance with instructions. This left 254 participants (Rested [n = 94], Sleep-deprived [n = 160]) contributing data (18–25 years old[4], M_{age} = 18.92 SD = 1.13, 163 females).

Materials

The materials are the same as Experiment 1 with the addition of a Proactive Interference Task, described below.

Proactive Interference Task. This task was used to assess the management of proactive interference, both resistance to a buildup of proactive interference and release from proactive interference. In this task, participants studied four lists containing ten words each. After each list, participants were asked to recall as many words as possible from the list they just saw, and not any previous lists. The first three lists were semantically related (e.g. animals) in order to generate proactive interference from previously studied lists. The fourth list was semantically

[3] Participants with missing sleep diaries were excluded from these analyses (n=18) and data from incomplete diaries (n=1) were used to the extent it could be.

[4] Due to experimenter error, demographic information for five participants is missing.

unrelated to the first three (e.g. musical instruments) and thus provided a release from the buildup of proactive interference (Wickens, Born, & Allen, 1963). Typical performance on this task results in the number of correctly recalled words decreasing in a linear fashion across the first three lists and then increasing again in the fourth list (Hasher, Chung, May, & Foong, 2002).

Participants were randomly assigned to one of two sets of lists. Set A consisted of animal words for the first three lists (e.g. badger, camel, rodent) and musical instruments for the fourth list (e.g. cello, fiddle, guitar). Set B consisted of words related to professions for the first three lists (florist, mason, surgeon) and fruits for the fourth list (e.g. mango, raspberry, fig). The three semantically related lists were presented in random order for each participant. The unrelated list was always presented last. The words within each list were also presented in random order. Lists were composed of single words containing ten or fewer letters. The ten most highly associated words (Van Overschelde, Rawson, & Dunlosky, 2004) from each category were not used. Lists within a set and across sets were matched for frequency.

Procedure

The procedure was the same as Experiment 1 with the following exceptions. Every hour during the night (01:00, 02:00, 03:00, 04:00, 05:00, 06:00, 07:00, 08:00) sleep-deprived participants completed sleepiness and mood assessments (discussed in the SOM). In the morning, all participants completed a task that assessed resistance to proactive interference before completing UNRAVEL and PVT. Additionally, participants were not administered pills at any point. Instead, as part of the requirements of a larger study, sleep-deprived participants were randomly assigned to a 0 min, 30 min, or 60 min nap opportunity during the night. Participants selected for the 30 or 60 min nap opportunity were set up with partial polysomnography (PSG) which involves placing electrodes onto the scalp and face to measure quantity and quality of

sleep during the nap. For the purposes of this experiment, we collapse across nap opportunity condition. See Experiment 4 for a detailed description of PSG and analyses pertaining to nap opportunity condition.

Results

Proactive Interference Task. For this task, we were interested in the ability to manage proactive interference. We calculated the slope of the best fit line for correct recall across the first three lists, which represented a buildup of proactive interference. A negative slope indicated a decline in correct recall with greater decline indicating less resistance to proactive interference buildup. We also calculated the slope of the line for correct recall from List 3 to List 4, which represented release from proactive interference. Here, a positive slope indicated greater release from proactive interference.

First, we compared the two list sets (A and B) to determine whether performance differed based on set. We performed a mixed ANOVA for correct recall with Set (A, B) as a between-subjects factor and List (1-4) as a within-subjects factor. There was no main effect of Set, $F(1, 252) = .08$, $p = .774$, $\eta_p^2 < .001$, or interaction between Set and List, $F(3, 756) = .35$, $p = .791$, $\eta_p^2 = .001$. We also compared the two slope measures, one representing resistance to proactive interference buildup and the other representing release from proactive interference. Independent samples t-test showed that there was no difference between sets for resistance to proactive interference buildup, $t(252) = .71$, $p = .476$, or release from proactive interference, $t(252) = -.40$, $p = .690$. Therefore, for all remaining analyses, we collapse across set.

Next, we compared correct recall performance between rested and sleep-deprived participants using a mixed ANOVA with Group (Rested, Sleep-Deprived) as a between-subjects

factor and List (1-4) as the within-subjects factor. The results are plotted in Figure 6 and reported in Table 8. There was a main effect of Group which showed that sleep-deprived participants (M = 5.07, SE = .09) correctly recalled fewer words than rested participants, (M = 5.42, SE = .11), $F(1, 252) = 6.03$, $p = .02$, $\eta_p^2 = .023$. There was also a main effect of List, $F(3, 756) = 117.37$, $p < .001$, $\eta_p^2 = .318$, but no Group X List interaction, $F(3, 756) = .83$, $p = .48$, $\eta_p^2 = .003$. The main effect of List reflects the expected proactive interference buildup and release effect. Pairwise comparisons showed that correct recall in List 2 (M = 4.86, SE = .09) was lower than in List 1 (M = 5.10, SE = .11), $t(253) = -2.17$, $p = .031$, and lower in List 3 (M = 4.44, SE = .09) than in List 2, $t(253) = -3.92$, $p < .001$, reflective of the buildup of proactive interference. Indeed, a polynomial trend analysis showed a significant linear decrease across the first three lists, $F(1, 252) = 33.54$, $p < .001$, $\eta^2 = .117$, but not a significant quadratic trend, $F(1, 252) = .70$, $p = .403$, $\eta^2 = .003$. Correct recall was higher in List 4 (M = 6.39, SE = .10) than List 3, $t(253) = 18.18$, $p < .001$, showing the typical release from proactive interference in the final list. A polynomial trend analysis confirmed that there was a significant linear increase from List 3 to List 4, $F(1, 252) = 321.79$, $p < .001$, $\eta^2 = .561$. Thus, this pattern of results suggests that both rested and sleep-deprived participants exhibited the expected performance trajectory for this task, except that correct recall for sleep-deprived performance was worse overall. However, the rate at which correct recall declined across the first three lists and rebounded in the fourth list was not different between groups, indicating that the degree of resistance to proactive interference buildup and release from proactive interference did not differ by group. Confirming this, independent sample t-tests showed no difference between groups for the slope representing resistance to proactive interference, $t(252) = .72$, $p = .470$, or the slope representing release from proactive interference, $t(252) = -1.36$, $p = .176$.

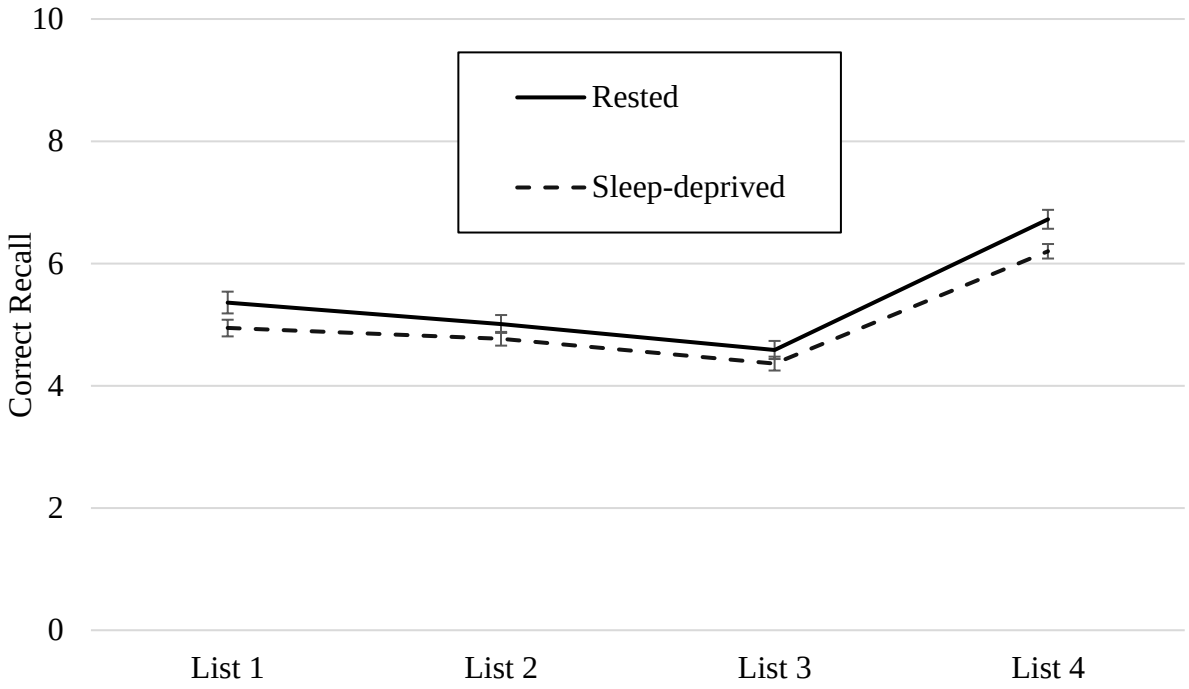


Figure 6. Number of words correctly recalled in the proactive interference task, separated by Group (Rested, Sleep-deprived), for Experiment 2. Errors bars are standard error of the mean.

Table 8

Correct recall on the proactive interference task, for Experiment 2

	List 1	**List 2**	**List 3**	**List 4**
Rested	5.36 (.18)	5.01 (.15)	4.59 (.15)	6.72 (.15)
Sleep-deprived	4.94 (.14)	4.77 (.11)	4.36 (.11)	6.20 (.12)

Note. Standard error in parentheses.

Lastly, we performed a reliability analysis. For each list, the ten words were split into two parcels containing five words each. Correct recall for each parcel was used to calculate Cronbach's alpha, a measure of internal reliability, for each list. For the reliability analysis, list refers to the actual set of words that made up a list and not the list order – which was randomized

for the first three list. For Set A, Cronbach's alpha was .188 for List 1, -.499 for List 2, -.185 for List 3, and .166 for List 4 (release list). For Set B, Cronbach's alpha was .345 for List 1, -.330 for List 2, -.169 for List 3, and .014 for List 4 (release list). Overall, reliability was low across all lists which may have influenced the effect of TSD on this task.

PVT. To establish basic effects of TSD on lapses of attention, we performed a mixed ANOVA with Group (Rested, Sleep-deprived) as a between-subjects factor and Session (Evening, Morning) as a within-subjects factor. Results are depicted in Figure 7 and reported in Table 9. There was no main effect of Group, $F(1, 252) = 2.24$, $p = .14$, $\eta_p^2 = .009$, but there was a main effect of Session, $F(1, 252) = 52.65$, $p < .001$, $\eta_p^2 = .173$, which was indicative of more lapses in the morning than in the evening. There was also a significant Group X Session interaction, $F(1, 252) = 53.65$, $p < .001$, $\eta_p^2 = .176$. To understand the interaction, we examined how performance changed from the evening to the morning session, separately for sleep-deprived and rested participants. Paired t-tests showed that sleep-deprived participants had more lapses in the morning than in the evening, $t(159) = 10.83$, $p < .001$; whereas, rested participants did not, $t(93) = -.06$, $p = .96$.

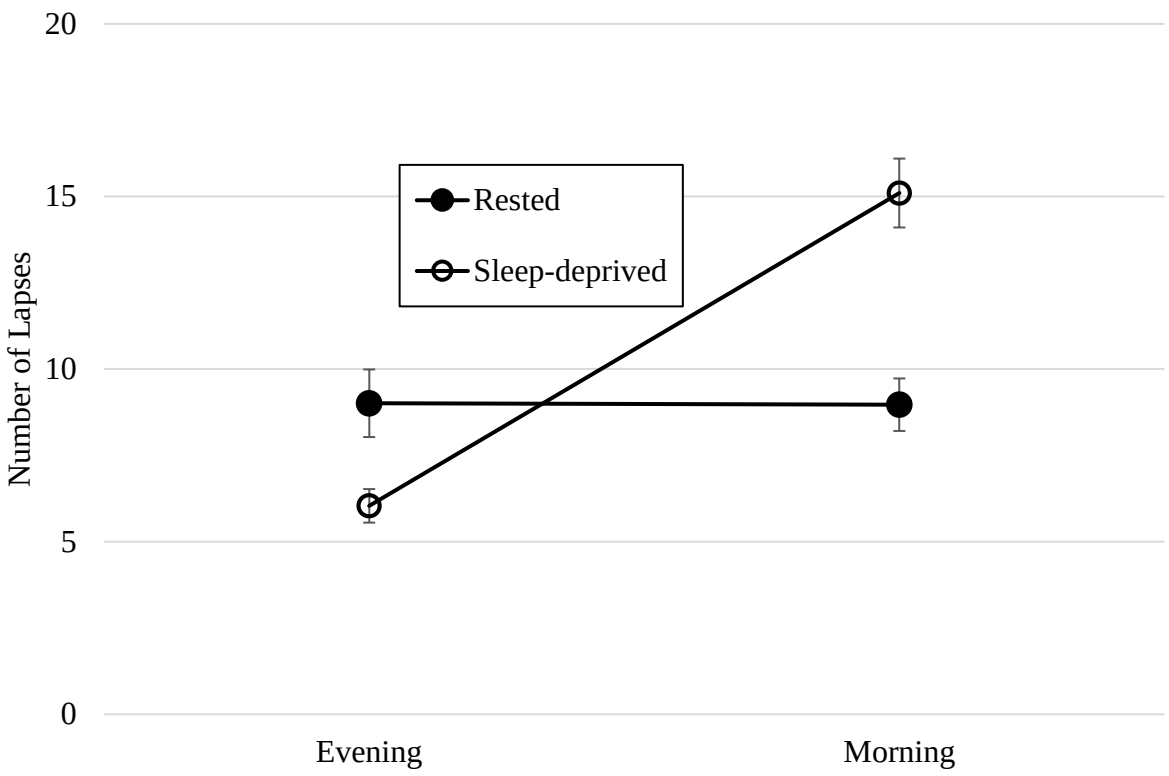


Figure 7. Number of lapses (reaction times greater than 500 ms) in the PVT, separately by rested and sleep-deprived participants, for Experiment 2. Errors bars are standard error of the mean.

Table 9

PVT lapses and UNRAVEL placekeeping errors for Experiment 2

	Evening	**Morning**
	Lapses	
Rested	9.01 (.98)	8.97 (.76)
Sleep-deprived	6.04 (.49)	15.10 (1.00)
	Post-interruption Errors	
Rested	.20 (.01)	.20 (.02)
Sleep-deprived	.16 (.01)	.27 (.02)
	Non-interruption Errors	
Rested	.04 (.005)	.03 (.01)
Sleep-deprived	.03 (.003)	.07 (.01)

Note. Standard error in parentheses.

UNRAVEL. We also looked at effects of TSD on placekeeping errors. Results are reported in Table 9 and displayed in Figure 8. First, we examined post-interruption errors using a mixed ANOVA with Group and Session as factors. There was no main effect of Group, $F(1, 252) = .93$, $p = .34$, $\eta_p^2 = .004$, but there was a main effect of Session, $F(1, 252) = 19.54$, $p < .001$, $\eta_p^2 = .072$, which indicated that more errors were made in the morning. Importantly, there was a Group X Session interaction, $F(1, 252) = 18.95$, $p < .001$, $\eta_p^2 = .070$. Paired t-tests showed that sleep-deprived participants made more post-interruption errors in the morning than they did

in the evening, $t(159) = 6.68$, $p < .001$; whereas, rested participants maintained performance from the evening to the morning session, $t(93) = .05$, $p = .96$.

Next, we examined non-interruption errors with a mixed ANOVA with factors Group and Session. There was no main effect of Group, $F(1, 252) = .84$, $p = .36$, $\eta_p^2 = .003$, or Session, $F(1, 252) = 2.76$, $p = .10$, $\eta_p^2 = .011$. There was, however, a Group X Session interaction, $F(1, 252) = 6.31$, $p = .01$, $\eta_p^2 = .024$. Similar to the findings for post-interruption errors, sleep-deprived participants made more non-interruption errors in the morning than they did in the evening, $t(159) = 3.08$, $p = .002$. Rested participants had a similar error rate in both sessions, $t(93) = -.70$, $p = .49$.

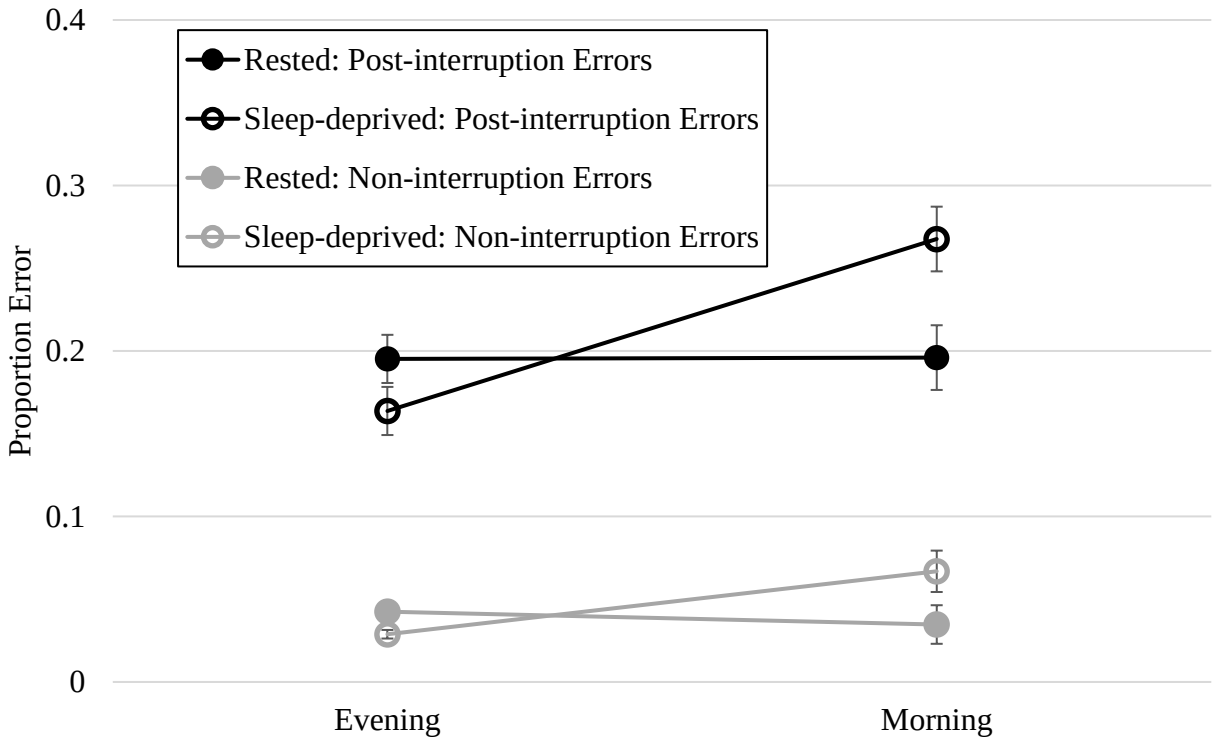


Figure 8. Proportion of placekeeping errors (post-interruption, non-interruption) in the UNRAVEL task, for Experiment 2. Errors bars are standard error of the mean.

Mediation Analyses. For the next set of analyses, we first use hierarchical regressions and then use mediation models to examine the extent to which the unique contribution of management of proactive interference explains deficits in memory maintenance after TSD. We use an approach described by Baron and Kenny (1986), which we also used for Experiment 1.

We first examined the effect of TSD on resistance to proactive interference (Path a_2 in Figure 9) and release from proactive interference (Path a_3 in Figure 9). We performed a regression on the slope measurements with Group (Rested, Sleep-deprived) as a predictor. There was not a significant effect of Group for either measure. Table 10 shows the results.

Table 10

Regression analysis for buildup (Path a_2 in Figure 9) and release of proactive interference (Path a_3), for Experiment 2

	B	***SE*B**	***β***	***t***	***p***	***R*²**	**Δ *R*²**
			Slope of proactive interference				
Group (Rested, Sleep-deprived)	.042	.058	.046	.72	.470	.002	.002
			Slope of release from proactive interference				
Group (Rested, Sleep-deprived)	-.150	.111	-.085	-1.36	.176	.007	.007

Note. df (1, 252).

Next, we examined the effect of TSD on vigilant attention (Path *a* in Figure 9). We performed a hierarchical regression for morning PVT lapses with (1) evening PVT lapses, to remove variability associated with individual differences in attention, and (2) Group as predictors. Table 11 shows the results. Both predictors were significant, indicating individual

differences in attention and an effect of TSD such that TSD increased morning lapses on the PVT.

Table 11

Hierarchical regression analysis for morning lapses in attention (Path a in Figure 9), for Experiment 2

	B	SE_B	β	*t*	*p*	R^2	ΔR^2
Step 1							
Evening lapses in attention	.754	.078	.510	9.63	< .001	.197	.197
Step 2							
Group (Rested, Sleep-deprived)	8.375	1.244	.357	6.73	< .001	.320	.123

Note. Statistics are from the full model. *df:* Step 1 (1, 252), Step 2 (2, 251).

Next, we performed hierarchical regressions for placekeeping performance, one for post-interruption trials and another for non-interruption trials (Path *c* in Figure 9). The predictors were (1) evening placekeeping errors, (2) morning non-interruption errors (only in the model for post-interruption trials) and (3) Group. Because we were specifically interested in the memory maintenance component of post-interruption errors, we used morning non-interruption errors as a predictor to control for task-related performance not unique to memory maintenance. The two trial types require identical processing except that post-interruption trials additionally measure memory maintenance. Thus, by removing variance associated with non-interruption trials, we can directly test effects on the memory maintenance component of post-interruption trials. Table 12 shows the results. All predictors were significant for both trial types. The effect of evening placekeeping errors reveals individual differences in placekeeping performance and the effect of group shows that TSD increased morning post-interruption and non-interruption errors. The

effect of morning non-interruption errors in the model for post-interruption trials reflects the shared processing involved in the two trial types.

Table 12

Hierarchical regression analyses for morning placekeeping errors, unmediated by attention or management of proactive interference (Path c in Figure 9), for Experiment 2

	B	***SE*B**	***β***	***t***	***p***	***R*²**	**Δ *R*²**
			Post-interruption trials				
Step 1 Evening placekeeping errors	.822	.064	.497	12.90	< .001	.303	.303
Step 2 Morning errors, non-interruption	.859	.060	.547	14.21	< .001	.619	.315
Step 3 Group (Rested, Sleep-deprived)	.035	.009	.150	3.90	< .001	.640	.022
			Non-interruption trials				
Step 1 Evening placekeeping errors	.773	.228	.211	3.39	.001	.035	.035
Step 2 Group (Rested, Sleep-deprived)	.043	.018	.144	2.31	.022	.055	.020

Note. Statistics are from the full model. *df:* Step 1 (1, 252), Step 2 (2, 251), Step 3 (3, 250).

We next start to examine possible mediators between TSD and placekeeping and begin by examining the mediating effects of vigilant attention (Path *b* in Figure 9). We performed hierarchical regressions, separately for post-interruption and non-interruption trials, with (1) evening placekeeping errors, (2) morning non-interruption errors (only in the model for post-interruption errors), (3) morning PVT lapses, and (4) Group. Table 13 shows the results. Lapses

was a significant predictor for both trial types, indicating that morning vigilant attention performance is important for placekeeping performance. The effect of group maintained a direct relationship to memory maintenance but was no longer significantly related to non-interruption trials.

Table 13

Hierarchical regression analyses for morning placekeeping errors, mediated by morning lapses in attention (Path b in Figure 9), for Experiment 2

	B	***SE*B**	***β***	***t***	***p***	***R²***	**Δ *R²***
			Post-interruption trials				
Step 1 Evening placekeeping errors	.791	.061	.479	12.96	< .001	.303	.303
Step 2 Morning errors, non-interruption	.780	.060	.497	13.06	< .001	.619	.315
Step 3 Morning lapses in attention	.004	.001	.200	5.12	< .001	.665	.047
Step 4 Group (Rested, Sleep-deprived)	.024	.009	.101	2.67	.01	.675	.009
			Non-interruption trials				
Step 1 Evening placekeeping errors	.711	.221	.194	3.22	.001	.035	.035
Step 2 Morning lapses in attention	.003	.001	.269	4.38	< .001	.118	.083
Step 3 Group (Rested, Sleep-deprived)	.010	.009	.071	1.13	.259	.122	.004

Note. Statistics are from the full model. *df:* Step 1 (1, 252), Step 2 (2, 251), Step 3 (3, 250), Step 4 (4, 249).

Next, we examined the mediating effects of resistance to proactive interference (Path b_2 in Figure 9) and release from proactive interference (Path b_3 in Figure 9) on the relationship between TSD and placekeeping. Specifically, we were interested in whether the slope of proactive interference or the slope of release from proactive interference mediated the effect of TSD on the memory maintenance component of post-interruption errors. The predictors were (1) evening placekeeping errors, (2) morning non-interruption errors (only in the model for post-interruption errors), (3) slope of buildup or release of proactive interference, and (4) Group. Table 14 shows the results for the buildup of proactive interference and Table 15 shows the results for the release from proactive interference. The slope of proactive interference was not significantly related to post-interruption trials but was significantly related to non-interruption trials, suggesting that participants who were more resistant to proactive interference tended to make more non-interruption errors. The slope of release from proactive interference was not significantly related to post-interruption or non-interruption trials.

Table 14

Hierarchical regression analyses for morning placekeeping errors, mediated by buildup of proactive interference (Path b_2 in Figure 9), for Experiment 2

	B	***SE*B**	***β***	***t***	***p***	***R²***	**Δ *R²***
			Post-interruption trials				
Step 1 Evening placekeeping errors	.833	.064	.504	12.98	< .001	.303	.303
Step 2 Morning errors, non-interruption	.872	.061	.556	14.25	< .001	.619	.315
Step 3 Slope of proactive interference	-.013	.010	-.050	-1.29	.199	.620	.002
Step 4 Group (Rested, Sleep-deprived)	.035	.009	.152	3.96	< .001	.643	.022
			Non-interruption trials				
Step 1 Evening placekeeping errors	.689	.228	.188	3.02	.003	.035	.035
Step 2 Slope of proactive interference	.025	.010	.153	2.48	.014	.061	.026
Step 3 Group (Rested, Sleep-deprived)	.020	.009	.133	2.15	.032	.078	.017

Note. Statistics are from the full model. *df:* Step 1 (1, 252), Step 2 (2, 251), Step 3 (3, 250), Step 4 (4, 249).

Table 15

Hierarchical regression analyses for morning placekeeping errors, mediated by release of proactive interference (Path b_3 in Figure 9), for Experiment 2

	B	***SE*B**	***β***	***t***	***p***	***R²***	**Δ *R²***
			Post-interruption trials				
Step 1 Evening placekeeping errors	.825	.064	.499	12.94	< .001	.303	.303
Step 2 Morning errors, non-interruption	.863	.061	.550	14.24	< .001	.619	.315
Step 3 Slope of release from proactive interference	.005	.005	.039	1.01	.312	.619	.001
Step 4 Group (Rested, Sleep-deprived)	.036	.009	.153	3.97	< .001	.642	.023
			Non-interruption trials				
Step 1 Evening placekeeping errors	.767	.228	.209	3.36	.001	.035	.035
Step 2 Slope of release from proactive interference	-.005	.005	-.063	-1.02	.310	.040	.006
Step 3 Group (Rested, Sleep-deprived)	.021	.009	.138	2.21	.028	.059	.018

Note. Statistics are from the full model. *df:* Step 1 (1, 252), Step 2 (2, 251), Step 3 (3, 250), Step 4 (4, 249).

Finally, we performed a hierarchical regression that contained both vigilant attention and management of proactive interference as mediators (Paths c_2' and c_3' in Figure 9). The predictors in this model were (1) evening placekeeping errors, (2) morning non-interruption errors (only in the model for post-interruption errors), (3) morning lapses, (4) slope of buildup or release of

proactive interference, and (5) Group. Results for proactive interference buildup are reported in Table 16 and results for release from proactive interference are reported in Table 17. Importantly, Group was still significant for post-interruption trials, indicating that neither vigilant attention nor resistance to proactive interference or release from proactive interference fully explained the effect of TSD on memory maintenance. For non-interruption trials, all factors were significant except for Group and the slope of release from proactive interference. Thus, TSD no longer directly affected non-interruption errors after controlling for vigilant attention and management of proactive interference.

Table 16

Hierarchical regression analyses for morning placekeeping errors, mediated by morning lapses in attention and buildup of proactive interference. Path c_2' in Figure 9, for Experiment 2

	B	***SE*B**	***β***	***t***	***p***	***R*²**	**Δ *R*²**
			Post-interruption trials				
Step 1 Evening placekeeping errors	.803	.061	.486	13.09	< .001	.303	.303
Step 2 Morning errors, non-interruption	.793	.060	.506	13.19	< .001	.619	.315
Step 3 Morning lapses	.004	.001	.203	5.19	< .001	.665	.047
Step 4 Slope of proactive interference	-.015	.009	-.058	-1.56	.121	.668	.003
Step 5 Group (Rested, Sleep-deprived)	.024	.009	.103	2.72	.007	.678	.010
			Non-interruption trials				
Step 1 Evening placekeeping errors	.642	.221	.175	2.90	.004	.035	.035
Step 2 Morning lapses	.003	.001	.257	4.20	< .001	.118	.083
Step 3 Slope of proactive interference	.021	.010	.130	2.18	.031	.135	.017
Step 4 Group (Rested, Sleep-deprived)	.010	.009	.065	1.04	.298	.139	.004

Note. Statistics are from the full model. *df:* Step 1 (1, 252), Step 2 (2, 251), Step 3 (3, 250), Step 4 (4, 249), Step 5 (5, 248).

Table 17

Hierarchical regression analyses for morning placekeeping errors, mediated by morning lapses in attention and release of proactive interference. Path c_3' in Figure 9, for Experiment 2

	B	***SE*B**	***β***	***t***	***p***	***R*²**	**Δ *R*²**
			Post-interruption trials				
Step 1 Evening placekeeping errors	.794	.061	.481	13.00	< .001	.303	.303
Step 2 Morning errors, non-interruption	.783	.060	.499	13.10	< .001	.619	.315
Step 3 Morning lapses	.004	.001	.200	5.11	< .001	.665	.047
Step 4 Slope of release from proactive interference	.005	.005	.037	1.02	.311	.666	.001
Step 5 Group (Rested, Sleep-deprived)	.024	.009	.104	2.74	.007	.676	.010
			Non-interruption trials				
Step 1 Evening placekeeping errors	.706	.221	.192	3.19	.002	.035	.035
Step 2 Morning lapses	.003	.001	.268	4.36	< .001	.118	.083
Step 3 Slope of release from proactive interference	-.005	.005	-.059	-1.00	.319	.122	.004
Step 4 Group (Rested, Sleep-deprived)	.010	.009	.065	1.05	.297	.126	.004

Note. Statistics are from the full model. *df:* Step 1 (1, 252), Step 2 (2, 251), Step 3 (3, 250), Step 4 (4, 249), Step 5 (5, 248).

Finally, we compared the model of TSD on placekeeping errors to the models containing the mediators. In the full models, TSD predicts morning placekeeping performance and vigilant attention and resistance to proactive interference or release from proactive interference are mediators. The full models are shown in Figure 9, in which the middle model contains resistance to proactive interference as a mediator and the bottom model contains release from proactive interference. The top model of Figure 9 shows the effect of TSD on post-interruption errors (β = .150, B = .035, *SE* = .009) and non-interruption errors (β = .144, B = .043, *SE* = .018) when no mediators are in the model (Path *c*). The effect of TSD on post-interruption errors dropped (β = .103, B = .024, *SE* = .009) when vigilant attention and resistance to proactive interference buildup were added as mediators (Path c_2' in Figure 9) and also when vigilant attention and release from proactive interference (β = .104, B = .024, *SE* = .009) were mediators (Path c_3' in Figure 9). The effect of TSD on non-interruption errors also dropped (β = .065, B = .010, *SE* = .009) when the mediators were added to the model (Paths c_2' and c_3' in Figure 9). A Sobel test, using the coefficients from Path *a* and Path *b* in Figure 9, showed that vigilant attention partially mediated the relationship between TSD and post-interruption errors, $Z = 3.47$, $p = .001$, and non-interruption errors, $Z = 2.77$, $p = .010$. The buildup of proactive interference (using the coefficients from Path a_2 and Path b_2 in Figure 9), however, did not significantly mediate the relationship between TSD and post-interruption errors, $Z = -.85$, $p = .393$, or non-interruption errors, $Z = .75$, $p = .451$. The release of proactive interference (using the coefficients from Path a_3 and Path b_3 in Figure 9), also did not significantly mediate the relationship between TSD and post-interruption errors, $Z = -1.00$, $p = .317$, or non-interruption errors, $Z = 1.00$, $p = .317$. The Sobel tests, in addition to the regression analyses, suggests that the ability to manage proactive interference does not mediate the effects of TSD on placekeeping.

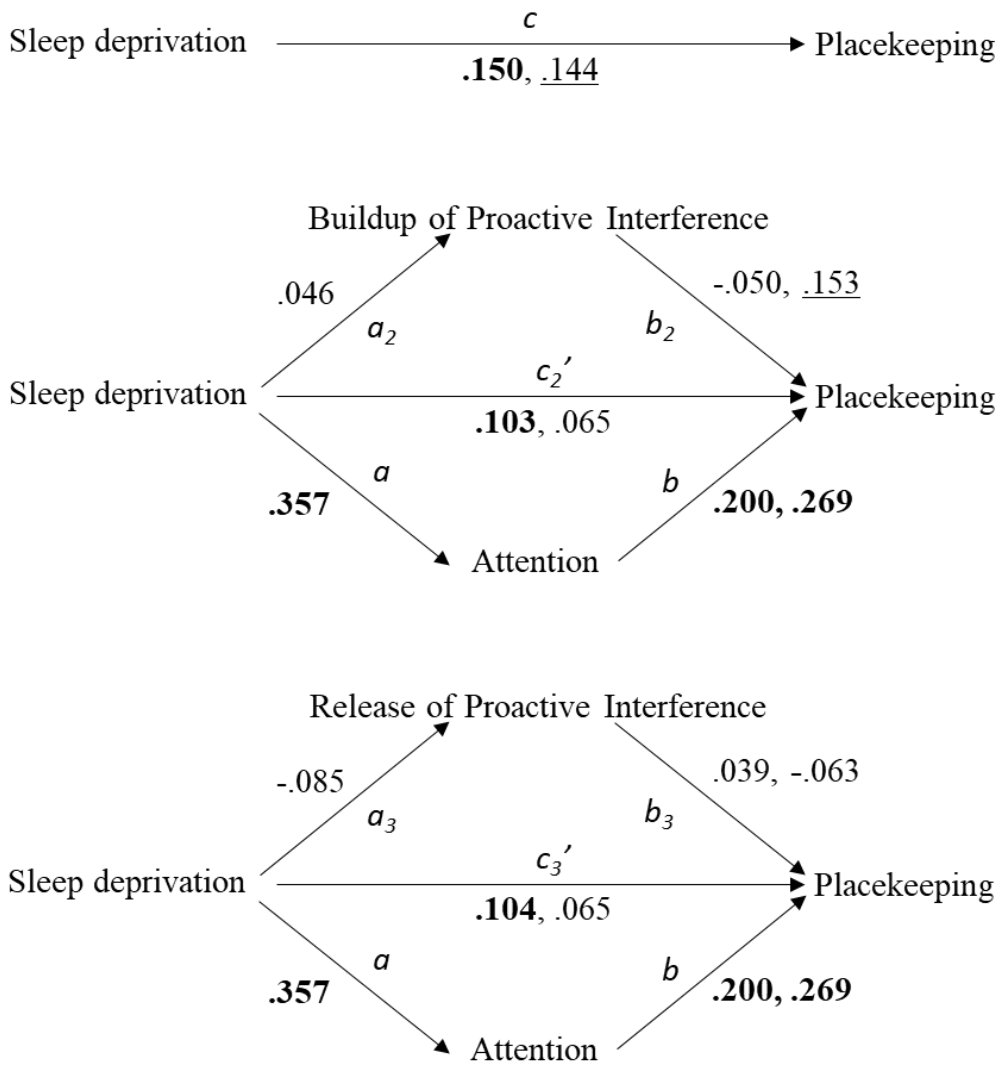


Figure 9. Mediation model with sleep deprivation as the independent variable, placekeeping as the dependent variable, and attention and management of proactive interference as mediators. The model in the middle contains the slope of proactive interference as the mediator and the model at the bottom contains the slope of the release from proactive interference as the mediator. Numbers are standardized regression coefficients (β). Where two regression coefficients are present, the first is for post-interruption placekeeping trials and the second for non-interruption placekeeping trials. **Bold**, $p < .01$. Underline, $p < .05$.

Discussion

Placekeeping, an important component of higher-order cognition, is impaired by TSD. In particular, the ability to keep task-relevant representations active in memory, an attribute of placekeeping that we refer to as memory maintenance, appears to be especially impaired by

TSD. However, the specific underlying mechanism of memory maintenance that TSD impairs is unclear. Here, we investigated whether the ability to manage proactive interference in episodic memory for past performance was the underlying mechanism affected by TSD. Using hierarchical regressions and mediation models, we show that the ability to manage proactive interference does not mediate the effect of TSD on memory maintenance.

Understanding what component mechanism of memory maintenance is impaired has important theoretical implications regarding what processes are impaired by TSD. For example, the attention-mediated theory posits that vigilant attention is the only cognitive process impaired by TSD. However, we replicated findings from Experiment 1, showing that vigilant attention only partially mediated the relationship between TSD and memory maintenance – indicating that TSD directly impairs higher-order processes. However, the ability to manage proactive interference, as measured using a standard buildup and release from proactive interference paradigm (Wickens, Born, & Allen, 1963), also did not explain the relationship between TSD and memory maintenance (performance on post-interruption trials after controlling for non-interruption trial performance). Sleep-deprived and rested participants showed a similar degree of buildup of proactive interference and a similar degree of release from proactive interference. Moreover, the ability to manage proactive interference did not mediate the relationship between TSD and memory maintenance. Therefore, managing proactive interference for past performance does not appear to be the underlying mechanism of memory maintenance impaired by TSD. This is consistent with another study which found that resistance to proactive interference in a working memory task was spared following TSD (Tucker, et al., 2010).

More research is needed to pinpoint what underlying mechanism of memory maintenance is impaired by TSD. An alternative hypothesis is that TSD impairs strategy development and

updating (for a meta-analysis see Harrison & Horne, 2000). Rested participants may develop more effective strategies to hold information in memory across interruptions in UNRAVEL; whereas, sleep-deprived participants may initially adopt ineffective strategies and may be less willing to switch their strategy, even if it is inappropriate. As motivation, self-monitoring, or the ability to avoid distraction declines – all of which have been linked to TSD (Harrison & Horne, 2000) – the ability to update one's strategy could be crucial for maintaining performance over time. Future work should continue to systematically examine these and alternative explanations for TSD related effects on memory maintenance.

One limitation of the present design is that the proactive interference task we used may not have been sensitive enough to capture deficits due to TSD. Although our task was based on a standard assessment of proactive interference (Wickens, Born, & Allen, 1963), this task is rather different from UNRAVEL. For example, the proactive interference effect requires participants to successfully encode the list words to elicit the typical decline in performance across the semantically related lists. Sleep-deprived participants may not have encoded the list words as well as rested participants, thereby artificially inflating our assessment of their ability to resist proactive interference buildup. Indeed, sleep-deprived participants showed overall less correct recall than rested participants.

In conclusion, the ability to manage proactive interference may be spared following TSD. However, vigilant attention does not completely explain deficits in memory maintenance after TSD. More research is needed to explore other potential underlying mechanisms of memory maintenance that may be affected by TSD. Nevertheless, the attention-mediated theory does not adequately characterize direct effects of TSD on aspects of higher-order cognition.

CHAPTER III: INTERVENTIONS FOR SLEEP DEPRIVATION

Experiment 3

Caffeine consistently benefits alertness, sustained attention, and vigilance under conditions of TSD (Beaumont et al., 2001; McLellan et al., 2005; Wesensten, et al., 2002). Sleep-deprived participants who receive caffeine have fewer attentional lapses on the PVT compared to sleep-deprived participants who receive placebo (Kamimori, et al., 2005; Killgore, et al., 2008; McLellan et al., 2005). Oftentimes, sleep-deprived performance with caffeine is similar to baseline levels in the same individual, suggesting that caffeine may eliminate vigilant attention impairments due to TSD. However, this interpretation should be treated with caution because rested control groups are infrequently used, making it difficult to know how performance of sleep-deprived individuals who have consumed caffeine compares to performance of rested individuals.

Although beneficial effects of caffeine on vigilant attention have been extensively explored in the literature, the extent to which caffeine affects aspects of higher-order cognition is much less clear. Caffeine benefitted sleep-deprived performance on certain tasks assessing problem solving (Killgore, et al., 2009) and reasoning and strategy development (Wesensten, Killgore, & Balkin, 2005). However, these tasks were administered only once to sleep-deprived individuals, with no rested baseline measure and no rested control group, so whether caffeine completely restored performance to rested levels or whether caffeine affected rested performance to the same extent as sleep-deprived performance, is unknown. Furthermore, caffeine did not improve performance on other tasks assessing problem solving (Killgore, et al., 2009; Wesensten, Killgore, & Balkin, 2005), inhibitory control (Wesensten, Killgore, & Balkin, 2005), working memory (Wesensten, et al., 2002), or verbal fluency (Wesensten, Killgore, & Balkin,

2005). Thus, there are mixed findings about the extent to which caffeine affects aspects of higher-order cognition. Even within the same experiment, some assessments of higher-order cognition were benefitted by caffeine; whereas, others were not. Mixed findings may reflect methodological limitations, such as the use of small sample sizes and infrequent use of rested control groups, that reduce the ability to detect effects on higher-order tasks.

The major aim of the present work was to assess the effects of caffeine comprehensively. We used a large sample (N = 348), a rested baseline measure, and a rested control group to assess performance on two distinct cognitive processes, one lower-level and one higher-level. The lower-level process is vigilant attention. The higher-level process is placekeeping.

Additionally, we addressed a novel question about whether the pattern of caffeine administration during a night of TSD influences performance. Specifically, if an individual performs a cognitive task after a night of TSD, is it more advantageous to administer multiple low doses of caffeine throughout the night or is caffeine more effective if given in a single acute dose shortly before task completion? While different caffeine administration patterns [i.e., multiple low doses (Kamimori, et al., 2005; Wyatt, Cajochen, Cecco, Czeisler, Dijk, 2004) or a single larger dose (Lieberman, Tharion, Shukitt-Hale, Speckman, Tulley, 2002; Penetar, McCann, Thorne, 1993; Killgore, McBride, Killgore, Balkin, 2006)] have been investigated in isolation, no study to date, to our knowledge, has directly compared the two administration patterns to determine if one is more effective than the other for mitigating cognitive deficits under conditions of TSD.

Participants performed a vigilant attention task and a placekeeping task, each at two time points. We assessed rested performance in the evening and assessed performance again the following morning after either 24 hours of TSD or a night of sleep. We used the PVT to measure

vigilant attention and the UNRAVEL task (Stepan et al., 2019) to measure placekeeping. We administered caffeine to approximately half of our rested participants and two-thirds of our sleep-deprived participants. Participants received either three doses of caffeine over the night (sleep-deprived only), a single dose of caffeine prior to the morning tasks (sleep-deprived and rested), or placebo (sleep-deprived and rested).

Method

Participants

Inclusion and exclusion criteria was the same as Experiment 1. Sleep diary data, reported in Table 1[5], indicated that sleep-deprived participants slept marginally more on the days leading up to the study, but sleep-deprived and rested participants had similar amounts of sleep the night before the study. Table 2 reports actigraphy data from rested participants for the night between sessions and correlations with morning performance are reported in the SOM.

Of an initial sample of 382 participants, 2 were excluded due to technical problems, 6 due to attrition, 7 due to experimenter error, 15 for failing the evening UNRAVEL accuracy criterion (see the Materials section), and 4 for missing data. Thus, we had a final sample of 348 participants (Rested [n = 129], Sleep-deprived [n = 219]; 18–26 years old[6], M = 19.05, SD = 1.27, 238 females). Participants were given course credit as compensation. This study was approved by Michigan State University's Institutional Review Board and informed consent was obtained from all participants. Data from the Placebo subgroup identified in the Procedure section are also reported in Experiment 1.

[5] Participants with missing sleep diaries were excluded from analyses (n = 13).
[6] Due to experimenter error, demographic information for two participants are missing.

Materials

The materials were the same as Experiment 1.

Procedure

The procedure was the same as Experiment 1 with the following exceptions. Participants were recruited for a study on sleep deprivation and caffeine. Three times throughout the night (00:30, 04:30, 08:30), sleep-deprived participants were given a capsule that contained either caffeine or placebo, according to which one of three subgroups they were randomly assigned to: Sustained (n = 71), Acute (n = 71), or Placebo (n = 77). Caffeine administration is detailed in Table 18. Capsules were distributed in a double-blind fashion; both participants and research assistants were blind to condition. The Acute and Sustained sleep-deprived subgroups were designed so that both subgroups would have similar levels of caffeine (approximately 180 mg and 160 mg, respectively) when the morning assessments began. Caffeine levels were estimated using a simulation based on a pharmacokinetic model of caffeine (Ritter & Yeh, 2016). Rested participants returned the next morning at 08:30 and were randomly given a capsule that either contained caffeine (n = 68) or placebo (n = 61). At 09:00, all participants began the morning session.

Table 18

Pattern and dose of caffeine administration

Condition	00:30	04:30	08:30
Rested: Acute	--	--	200 mg
Rested: Placebo	--	--	Placebo
Sleep-deprived: Sustained	100 mg	100 mg	100 mg
Sleep-deprived: Acute	Placebo	Placebo	200 mg
Sleep-deprived: Placebo	Placebo	Placebo	Placebo

Results

PVT. We conducted two sets of analyses, one to address each of our basic questions. The first analysis assessed effects of TSD and caffeine, collapsing over different caffeine administration schedules. The second assessed effects of caffeine administration schedule.

Effects of TSD and caffeine are plotted in Figure 10 and reported in Table 19. We analyzed the data with a 2 (Group: Rested vs. Sleep-deprived) X 2 (Pill: Caffeine vs. Placebo) X 2 (Session: Evening vs. Morning) mixed ANOVA with Group and Pill as between-subjects factors and Session as a within-subjects factor. There was a main effect of Group, with the Sleep-deprived group (M = 7.62, SE = .43) making more lapses than the Rested group (M = 5.99, SE = .49), $F(1, 318) = 6.27$, $p = .01$, $\eta_p^2 = .019$. There was also a main effect of Caffeine, with participants who received caffeine (M = 6.15, SE = .41) making fewer lapses than those who received placebo (M = 7.46, SE = .50), $F(1, 318) = 4.06$, $p = .045$, $\eta_p^2 = .013$. There was a main effect of Session, with more lapses made in the morning (M = 8.63, SE = .48) than the evening (M = 4.98, SE = .30), $F(1, 318) = 63.09$, $p < .001$, $\eta_p^2 = .166$.

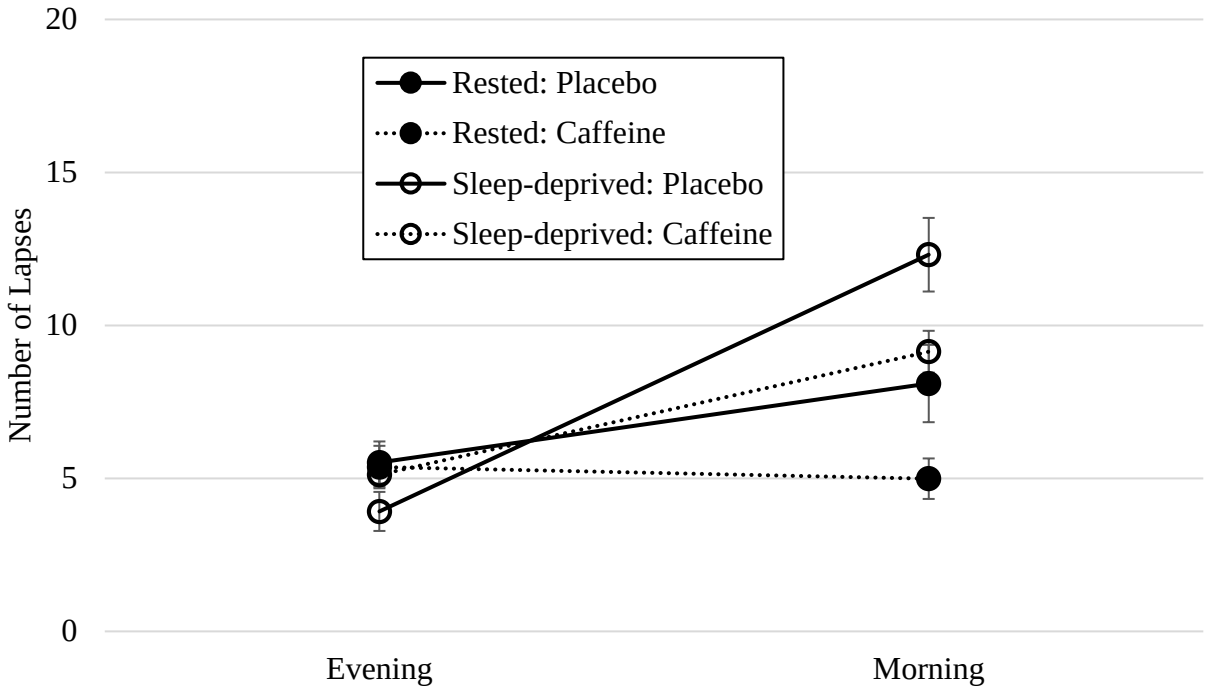


Figure 10. Number of lapses on the PVT, reaction times greater than 500 ms, within the Rested and Sleep-deprived groups, separated by whether that group received caffeine (dashed lines) or placebo (solid lines). Errors bars represent the standard error of the mean.

Table 19

PVT lapses and UNRAVEL placekeeping errors for Experiment 3

	Evening	**Morning**
	Lapses	
Rested: Placebo	5.52 (.69)	8.10 (1.26)
Rested: Caffeine	5.37 (.69)	4.99 (.66)
Sleep-deprived: Placebo	3.92 (.64)	12.31 (1.20)
Sleep-deprived: Caffeine	5.12 (.39)	9.14 (.68)
	Post-interruption Errors	
Rested: Placebo	.14 (.02)	.14 (.02)
Rested: Caffeine	.19 (.01)	.16 (.02)
Sleep-deprived: Placebo	.13 (.02)	.20 (.02)
Sleep-deprived: Caffeine	.15 (.01)	.19 (.01)
	Non-interruption Errors	
Rested: Placebo	.03 (.004)	.01 (.004)
Rested: Caffeine	.04 (.004)	.02 (.004)
Sleep-deprived: Placebo	.03 (.004)	.03 (.004)
Sleep-deprived: Caffeine	.03 (.003)	.02 (.003)

Note. Standard error in parentheses.

Importantly, these main effects were qualified by a Group X Session interaction, $F(1, 318) = 30.90$, $p < .001$, $\eta_p^2 = .089$, and a Pill X Session interaction, $F(1, 318) = 15.92$, $p < .001$, $\eta_p^2 = .048$. The Group X Pill X Session interaction was not significant, $F < 1$. To understand the two-way interactions, we examined the effects of Group and Caffeine separately within each session. The Rested group ($M = 5.44$, $SE = .49$) and the Sleep-deprived group ($M = 4.74$, $SE = .34$) performed similarly in the evening session, $t(320) = 1.22$, $p = .22$, but the Rested group ($M = 6.46$, $SE = .70$) made fewer lapses than the Sleep-deprived group ($M = 10.14$, $SE = .61$) in the morning session, $t(320) = 3.91$, $p < .001$. Participants who received caffeine ($M = 5.21$, $SE = .35$) and participants who received placebo ($M = 4.72$, $SE = .47$) performed similarly in the evening session, $t(320) = -.83$, $p = .41$, but participants who received caffeine ($M = 7.73$, $SE = .52$) made fewer lapses than participants who received placebo ($M = 10.20$, $SE = .89$) in the morning, $t(320) = 2.57$, $p = .01$. This pattern of results suggests that caffeine reduced lapses for both groups. That is, the benefit of caffeine was not specific to sleep-deprived individuals.

Given that caffeine reduced lapses in sleep-deprived participants, we were interested to determine whether caffeine completely or only partially mitigated effects of TSD. That is, we were interested in whether sleep-deprived participants who consumed caffeine performed similarly to rested participants who received placebo. We therefore compared morning PVT lapses for sleep-deprived participants who received caffeine with morning PVT lapses for rested participants who received placebo. There was no difference between the groups, $t(191) = .79$, $p = .43$. Thus, caffeine appears to restore sleep-deprived vigilant attention performance to rested levels.

To address our second question, we examined effects pertaining to caffeine administration schedule. Summary data for sleep-deprived participants are plotted in Figure 11

and reported in Table 20. We analyzed the data with a 3 (Administration: Sustained, Acute, Placebo) x 2 (Session: Evening vs. Morning) mixed ANOVA with Administration as a between-subjects factor and Session as a within-subjects factor. There was no main effect of administration, $F < 1$. There was a main effect of Session, with more lapses in the morning (M = 10.19, SE = .60) than the evening, (M = 4.72, SE = .34), $F(1, 190) = 93.32$, $p < .001$, $\eta_p^2 = .329$. Importantly, there was an Administration X Session interaction, $F(2, 190) = 6.47$, $p = .002$, $\eta_p^2 = .064$. To understand this interaction, we compared administration subgroups separately within each session. The three subgroups performed similarly in the evening, $F(2, 190) = 1.66$, $p = .19$, $\eta_p^2 = .017$, but there was a main effect of Administration in the morning, $F(2, 190) = 3.14$, $p = .046$, $\eta_p^2 = .032$. Post-hoc comparisons with a Bonferroni corrected p-value ($p < .017$) showed that the Placebo subgroup had marginally more lapses in the morning than the Acute subgroup, $p = .018$, but not more than the Sustained subgroup, $p = .06$. The Acute and Sustained subgroups did not differ from one another, $p = .59$.

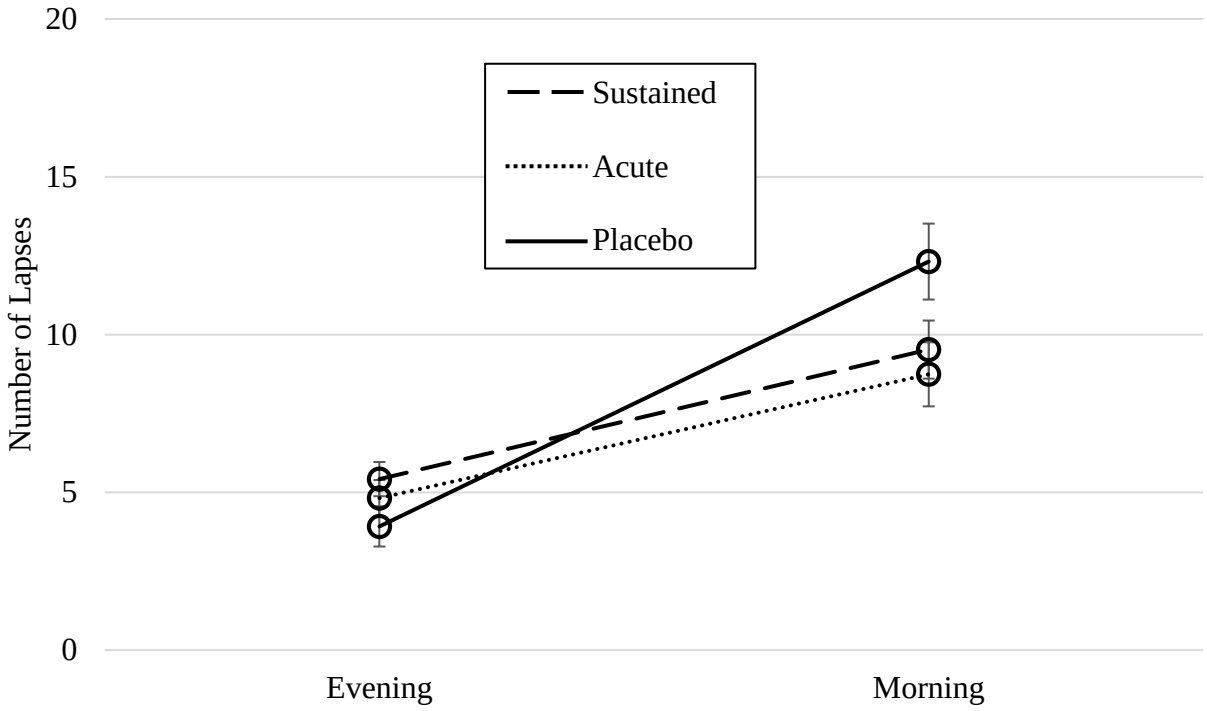


Figure 11. Number of lapses, reaction times greater than 500 ms, made within the three Sleep-deprived subgroups (Sustained, Acute, and Placebo). Errors bars represent the standard error of the mean.

Table 20

PVT lapses and UNRAVEL placekeeping errors in the Sleep-deprived group, separated by schedule of caffeine administration, for Experiment 3

	Evening	Morning
	Lapses	
Sustained	5.42 (.54)	9.52 (.92)
Acute	5.10 (.45)	6.82 (.62)
Placebo	4.72 (.47)	10.20 (.89)
	Post-interruption Errors	
Sustained	.15 (.01)	.19 (.02)
Acute	.14 (.01)	.18 (.02)
Placebo	.13 (.01)	.20 (.02)
	Non-interruption Errors	
Sustained	.03 (.003)	.02 (.005)
Acute	.03 (.003)	.03 (.01)
Placebo	.03 (.003)	.03 (.01)

Note. Standard error in parentheses.

UNRAVEL. First, we looked at the number of participants who failed the morning session of UNRAVEL. We considered this a task-level assessment of cognitive deficit following TSD because all participants were able to successfully perform the task in the evening. A

Fisher's Exact Test showed that more participants in the Sleep-deprived group (11.90%, $n = 26$) failed the morning session than participants in the Rested group (0%, $n = 0$), $p < .001$, 95% CI [.84, .93], replicating previous results. We next focused on the effect of caffeine on task-level failure in sleep-deprived participants. A Chi-Square analysis comparing task-level failure across the Placebo (20.80%, $n = 16$), Acute (8.50%, $n = 6$), and Sustained (5.60%, $n = 4$) subgroups showed an effect of subgroup, $\chi^2(2, n = 219) = 8.99$, $p = .01$. Follow-up Chi-Square analyses showed that the Placebo subgroup failed at a higher rate than both the Acute, $\chi^2(1, n = 148) = 4.44$, $p = .04$, and Sustained subgroups, $\chi^2(1, n = 148) = 7.25$, $p = .01$. Task-level failure between the Acute and Sustained subgroups did not differ from each other, $\chi^2(1, n = 142) = .43$, $p = .51$. Finally, two Fisher's Exact Tests comparing task-level failure in the Acute and Sustained subgroups with the Rested group showed that both the Acute, $p = .002$, 95% CI [.85, .98], and Sustained, $p = .02$, 95% CI [.89, 1.00], subgroups were more likely to fail the morning session than rested participants. Because participants included in these analyses were all able to perform the task the prior evening, these results indicate that a night of TSD made some participants either unable or unwilling to perform to the instructed criterion accuracy, and that caffeine mitigated this impairment, but not to the level of rested performance.

For all remaining UNRAVEL analyses, we excluded participants who failed the morning session and focused on participants who were willing and able to perform the task, according to the instructed accuracy criterion. As we did for the PVT data, we conducted two sets of analyses. The first assessed effects of TSD and caffeine, collapsing over different caffeine administration schedules. The second assessed effects of caffeine administration schedule.

Summary data on effects of TSD and caffeine on placekeeping performance are plotted in Figure 12 and reported in Table 17. We analyzed the data with a 2 (Group: Rested vs. Sleep-deprived) X 2 (Pill: Caffeine vs. Placebo) X 2 (Session: Evening vs. Morning) mixed ANOVA, with Group and Pill as between-subjects factors and Session as a within-subjects factor. For each type of placekeeping error (post-interruption and non-interruption), we first report notable results concerning effects of TSD and then report all results concerning effects of caffeine.

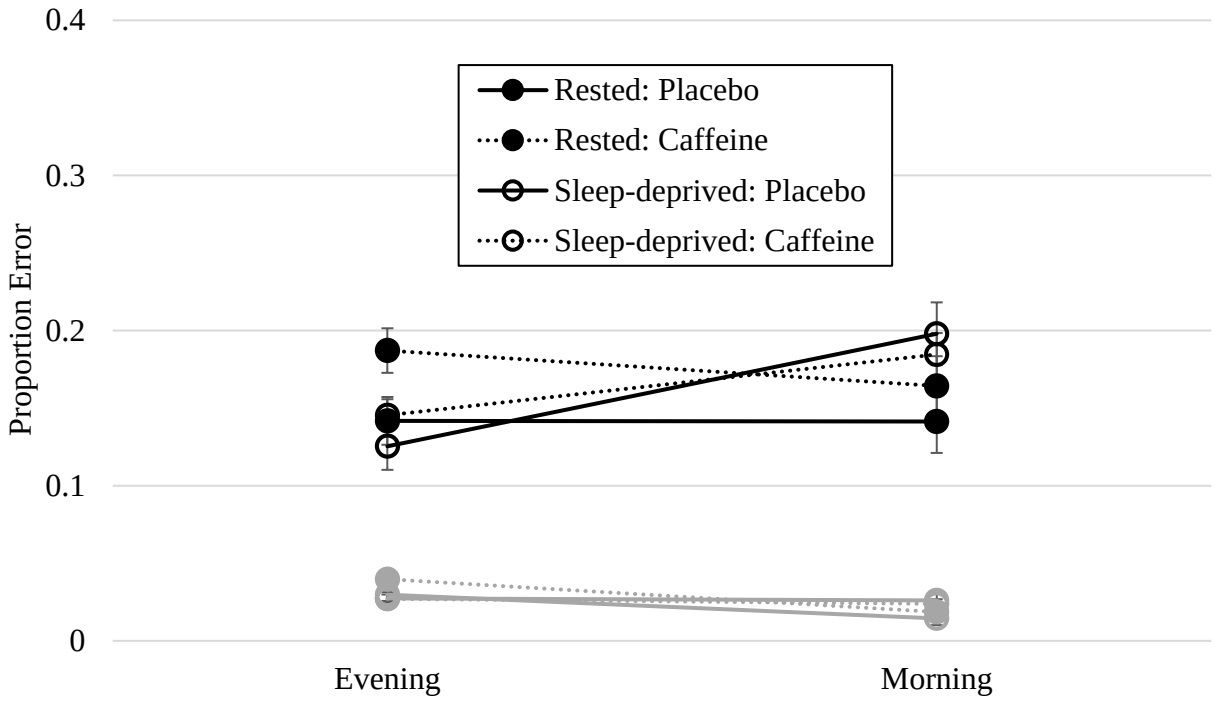


Figure 12. Proportion of post-interruption errors (black lines) and non-interruption errors (gray lines) in the Rested and Sleep-deprived groups, separated by whether that group received caffeine (dashed lines) or placebo (solid lines), for Experiment 3. Errors bars represent the standard error of the mean.

For post-interruption errors, there was no main effect of Group, $F(1, 318) = .11$, $p = .74$, $\eta_p^2 < .001$, but there was a main effect of Session, $F(1, 318) = 6.62$, $p = .01$, $\eta_p^2 = .020$, indicating that more errors were made in the morning. Of note was a Group X Session

interaction, $F(1, 318) = 15.38$, $p < .001$, $\eta_p^2 = .046$. To understand this interaction, we examined how performance changed from the evening to the morning session, separately for each group. Paired t-tests showed that sleep-deprived participants made more errors in the morning than the evening, $t(192) = 4.15$, $p < .001$, but rested participants did not, $t(128) = -1.25$, $p = .22$.

We next turn to the effects of caffeine on post-interruption errors. There was no main effect of Pill, $F(1, 318) = 1.81$, $p = .18$, $\eta_p^2 = .006$. There were also no interactions involving Pill: $F(1, 318) = 1.22$, $p = .27$, $\eta_p^2 = .004$ for the Group X Pill interaction, $F(1, 318) = 2.62$, $p = .11$, $\eta_p^2 = .008$ for the Pill X Session interaction, and $F(1, 318) = .10$, $p = .75$, $\eta_p^2 < .001$ for the Group X Pill X Session interaction.

For non-interruption errors, we again first examine the basic effects of TSD. There was no main effect of Group, $F(1, 318) = .02$, $p = .88$, $\eta_p^2 < .001$, but there was a main effect of Session, $F(1, 318) = 17.82$, $p < .001$, $\eta_p^2 = .053$, with fewer errors in the morning than in the evening. Of note was a Group X Session interaction, $F(1, 318) = 10.76$, $p = .001$, $\eta_p^2 = .033$. Paired t-tests showed that rested participants made fewer errors in the morning than in the evening, $t(128) = -5.50$, $p < .001$, and sleep-deprived participants made a similar number of errors in both sessions, $t(192) = -.85$, $p = .40$.

With regard to caffeine, there was no main effect of Pill on non-interruption errors, $F(1, 318) = .94$, $p = .33$, $\eta_p^2 = .003$. There were also no interactions involving Pill: $F(1, 318) = 1.90$, $p = .17$, $\eta_p^2 = .006$ for the Group X Pill interaction, $F(1, 318) = .64$, $p = .42$, $\eta_p^2 = .002$ for the Pill X Session interaction, and $F(1, 318) = .16$, $p = .69$, $\eta_p^2 < .001$ for the Group X Pill X Session interaction.

Summary data on effects of caffeine administration schedule for sleep-deprived participants are plotted in Figure 13 and reported in Table 18. We analyzed the data with a 3 (Administration: Sustained, Acute, Placebo) X 2 (Session: Evening vs. Morning) mixed ANOVA with Administration as a between-subjects factor and Session as a within-subjects factor. For post-interruption errors, there was no main effect of Administration, $F(2, 190) = .12$, $p = .89$, $\eta_p^2 = .001$, and no Administration X Session interaction, $F(2, 190) = .85$, $p = .43$, $\eta_p^2 = .009$. For non-interruption errors, there was also no main effect of Administration, $F(2, 190) = .14$, $p = .87$, $\eta_p^2 = .001$, and no Administration X Session interaction, $F(2, 190) = .20$, $p = .82$, $\eta_p^2 = .002$.

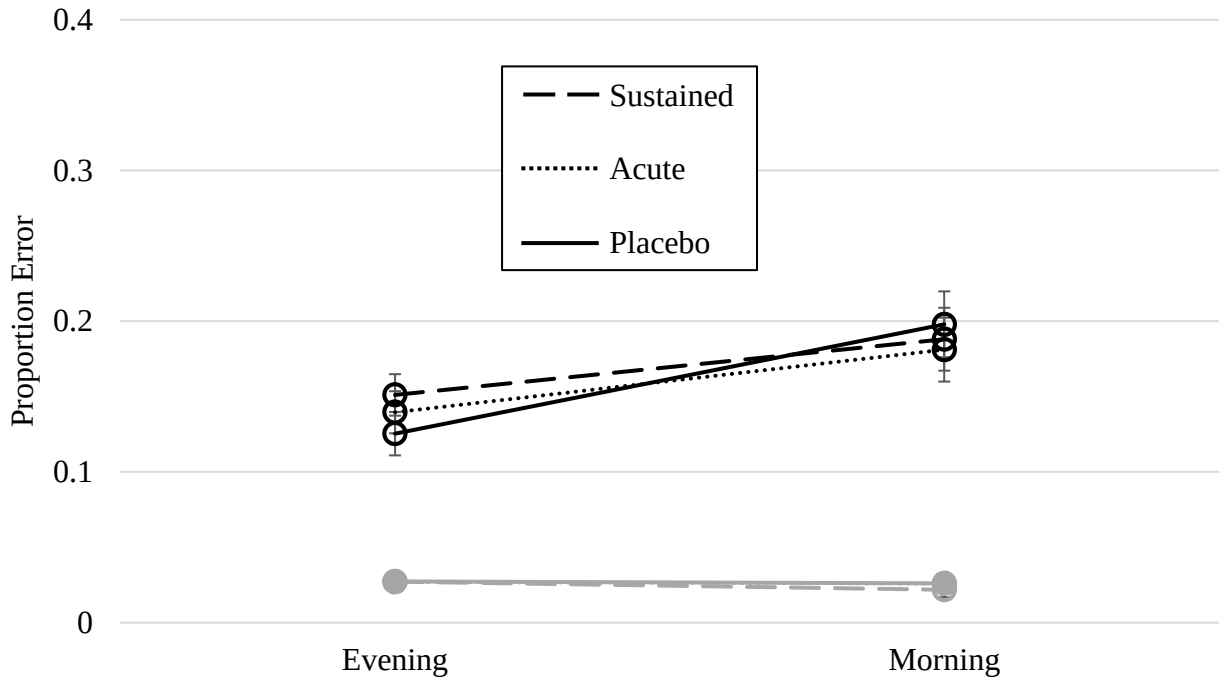


Figure 13. Proportion of post-interruption errors (black lines) and non-interruption errors (gray lines) in the three Sleep-deprived subgroups (Sustained, Acute, and Placebo) for Experiment 3. Errors bars represent standard error of the mean.

Discussion

The current study had two major aims: to understand effects of caffeine on different aspects of cognition in sleep-deprived individuals and to investigate the extent to which two patterns of caffeine administration affected cognitive performance. Using a large sample, baseline measures, and a rested control group, we found that caffeine affected vigilant attention similarly for sleep-deprived and rested participants but affected placekeeping only for participants who showed a general breakdown in ability or motivation to perform the placekeeping task. This selective benefit of caffeine is consistent with the view that TSD produces domain-specific deficits.

Our results extend and clarify prior work on the effects of caffeine on vigilant attention performance in two ways. First, we showed that participants who consumed caffeine made fewer lapses on the PVT than participants who received placebo, regardless of whether they were sleep-deprived or rested. Thus, caffeine nonspecifically benefitted vigilant attention. Perhaps more important, we found that sleep-deprived participants who received caffeine performed similarly to rested participants who received placebo, suggesting that caffeine eliminated vigilance decrements associated with TSD. Interestingly, the number of lapses increased from evening (baseline) to morning for all groups, suggesting that a general increase in lapses appears to be unassociated with TSD, although the magnitude of the increase is enhanced by TSD. Thus, including both a baseline measure and a rested control group in our design allowed us to show that caffeine nonspecifically benefits vigilant attention and that caffeine can eliminate vigilance deficits associated with TSD, rather than just mitigating them.

While caffeine provided clear benefits to vigilant attention performance on the PVT, it did not affect placekeeping performance in general, nor did it mitigate effects of TSD on

placekeeping performance for a majority of participants, namely those who were able to perform the UNRAVEL task at instructed levels of accuracy. Caffeine did reduce the proportion of individuals who failed to perform the task as instructed, though not to the level of the rested group. Task-level failure could reflect either an unwillingness or inability to perform the task as instructed, and it is unclear which of these processes, or both, were affected by caffeine. Indeed, moderate doses of caffeine (under 200mg), similar to the concentration in our participants when they completed the morning tasks, are known to increase both motivation and ability factors such as concentration (Garrett & Griffiths, 1997). However, caffeine had no effect on placekeeping errors for participants who passed the morning session. Thus, one explanation may be that caffeine only provides a benefit to participants who are highly susceptible to TSD but, for the majority of individuals, caffeine provides no benefit to placekeeping ability or memory maintenance.

The selective nature of caffeine, in that it improved vigilant attention but not placekeeping for most individuals, speaks to how TSD affects cognition more broadly. Theories vary on the precise deficits that arise from TSD and one theory is that TSD directly affects only vigilant attention, which subsequently causes deficits in other cognitive tasks (Balkin, Rupp, Picchioni, & Wesensten, 2008; Doran, Van Dongen, & Dinges, 2001; Lim & Dinges, 2010). In the context of the current study, if performance deficits on UNRAVEL were entirely due to impairments in vigilant attention, rather than actual placekeeping ability, then caffeine should benefit both PVT and UNRAVEL performance. Instead, we found that caffeine clearly benefitted PVT performance but had no discernable effect on UNRAVEL for the majority of participants. This pattern of results suggests that TSD directly impairs aspects of higher-order cognition and may have domain-specific cognitive deficits (Chuah, Venkatraman, & Dinges,

Chee; Harrison & Horne, 2000; Mu, Nahas, & Johnson, 2005). These results are also consistent with the findings from Experiments 1 and 2 which showed that vigilant attention, as measured by the PVT, could not entirely account for performance on UNRAVEL after TSD.

Our second goal was to compare how two different patterns of caffeine administration affected performance. Specifically, we tested whether maintaining a stable level of alertness throughout a period of TSD via multiple, smaller doses of caffeine would differ from a qualitative shift in alertness achieved via a single dose of caffeine, while holding overall caffeine level constant. The two patterns of caffeine administration were equally effective for vigilant attention performance and did not differ from each other on either cognitive task, suggesting that pattern of administration may not be a crucial factor in the effectiveness of caffeine. One caveat is that the 200 mg dose in the Acute subgroup may not have been enough to achieve a qualitative shift in alertness. We chose doses that seemed the likeliest to reap the positive benefits of caffeine such as enhanced alertness, motivation, and concentration (Garrett & Griffiths, 1997) while minimizing negative side effects associated with larger doses such as anxiety and dizziness (MedlinePlus, 2019). Thus, further research is needed to determine how the interplay between dose and pattern of administration can be used to optimize the benefits of caffeine on cognition.

In conclusion, caffeine had limited success reversing performance impairments specific to TSD. In terms of vigilant attention, caffeine improved performance to rested levels, but improved rested performance by a similar amount. In terms of placekeeping, a broadly relevant higher-order cognitive process, caffeine affected performance at the margins, reducing the proportion of participants who were unwilling or unable to perform the task but having no effect on the large majority of participants who were willing and able to perform the task. These selective benefits are inconsistent with the theory that vigilant attention underlies all cognitive

deficits due to TSD. Instead, these results suggest that TSD produces domain-specific cognitive impairments, some of which may be mitigated by caffeine and some not. In future work it will be important to clarify whether caffeine affects motivation, ability, or both and to develop a more complete inventory of tasks that show general performance benefits regardless of sleep loss and those that show benefits specifically under conditions of TSD, even if only at the margins.

Experiment 4

Sleep deprivation is a common occurrence amongst professions where the cost of failure is high, such as for medical and military personnel. Therefore, interventions aimed at mitigating cognitive deficits due to TSD are highly sought after. However, there has not been much success at mitigating higher-order cognitive deficits due to TSD. In Experiment 3, we found that caffeine benefitted lower-level vigilant attention but had no effect on placekeeping for a majority of participants. Placekeeping is a broadly relevant aspect of higher-order cognition that is related to problem solving, fluid intelligence, and linear thinking (Burgoyne, Hambrick, & Altmann, in press; Hambrick & Altmann, 2015). Although caffeine was not beneficial for placekeeping ability, it is possible that a short interval of sleep during a period of TSD will mitigate deficits for both lower-level and higher-order cognition. However, most of the research on naps has focused on lengthy nap durations, commonly between 2 – 4 hours (Dinges, Orne, Whitehouse, & Orne, 1987; Jewett, Dijk, et al., 1999; Macchi, Boulos, Ranney, Simmons, & Campbell, 2002; Naitoh, Englund, & Ryman, 1982; Vgontzas et al., 2007), and there is little research investigating the effectiveness of brief naps (under 2 hours) during a period of otherwise TSD. Here, we investigate the effect of a brief nap opportunity (30 or 60 minutes) during a period of TSD on vigilant attention and placekeeping performance.

Naps of any length have generally been found to benefit lower-level processes. Long naps, between 2 and 4 hours (Dinges, Orne, Whitehouse, & Orne, 1987; Jewett, Dijk, et al., 1999; Macchi, Boulos, Ranney, Simmons, & Campbell, 2002; Naitoh, Englund, & Ryman, 1982; Vgontzas et al., 2007), and brief naps, under 1 hour (Gillberg, 1984; Hilditch, Centofanti, Dorrian, & Banks, 2016; Lumley, 1986), during a TSD protocol have been found to benefit alertness and vigilant attention. Moreover, there is evidence to suggest that the benefit of a nap

on alertness can persist for several hours of wakefulness after the nap (Naitoh, Englund, & Ryman, 1982). Thus, a nap may be a particularly viable intervention for vigilant attention because the benefit of a nap can extend well past the duration of the nap itself.

In addition to benefitting lower-level processes, naps have also been shown to benefit higher-order cognition. Long naps have been found to benefit working memory (Dinges, Whitehouse, Orne, & Orne, 1988; Haslam, 1985; Macchi, Boulos, Ranney, Simmons, & Campbell, 2002; Webb, 1987), logical reasoning (Haslam, 1985), and cognitive ability (Haslam, 1985). A brief nap of either 10 or 30 minutes helped to maintain performance on an associative learning task compared to a TSD period with no nap (Hilditch, et al., 2016). Collectively, these findings suggest that naps, both long and brief, may be beneficial for vigilant attention as well as some aspects of higher-order cognition when sleep-deprived. However, this conclusion should also be treated with caution since research investigating brief naps and higher-order cognition is extremely limited. More research is needed to develop a better understanding of how brief naps of different durations affect cognition in sleep-deprived individuals.

By investigating the effect of brief naps and sleep architecture, we also aim to test the attention-mediated theory of TSD. This theory posits that placekeeping deficits, representing higher-order cognition, are due to decrements in vigilant attention after TSD (Balkin, et al., 2008; Doran et al., 2001; Lim & Dinges, 2010). By using polysomnography (PSG) to record aspects of sleep architecture while participants nap, we can determine which sleep variables are related to vigilant attention performance and whether these are the same variables related to placekeeping performance. If vigilant attention underlies placekeeping deficits then we would predict that similar sleep variables will correlate with both PVT and UNRAVEL performance, because the same underlying process (vigilant attention) is impaired for both. However, if

vigilant attention does not completely underlie deficits in placekeeping, then we would predict that different aspects of sleep architecture will correlate with PVT and UNRAVEL performance. Thus, investigating brief naps and sleep architecture during a nap is important for understanding how to mitigate cognitive deficits due to TSD and for testing theoretical predictions of the attention-mediated theory of TSD.

In the current study, we investigated the effect of a brief nap opportunity (30 or 60 minutes) during a period of TSD on vigilant attention and placekeeping. Participants performed UNRAVEL and PVT in the evening at baseline and again the following morning after a night of sleep or TSD. Sleep-deprived participants also randomly received either a 0, 30, or 60 minute nap opportunity during the night. Participants who napped were set up with partial PSG to assess sleep architecture.

Method

Participants

Inclusion and exclusion criteria was the same as Experiment 2. Sleep diary data, reported in Table 1[7], indicated that rested participants slept marginally more in the days leading up to the study and the night prior to the study than sleep-deprived participants. Table 2 summarizes actigraphy data from rested participants for the night between sessions and correlations with morning performance are reported in the SOM.

Of an initial sample of 334 participants, 15 were excluded for missing data, 25 for failing the evening UNRAVEL accuracy criterion, 9 for attrition, and 1 for noncompliance with

[7] Participants with missing sleep diaries were excluded from analyses (n=16) and data from incomplete diaries (n=3) were used to the extent it could be.

instructions. This left 284 participants (Rested [n = 106], Sleep-deprived [n = 178]) contributing data (18–26 years old[8], M_{age} = 18.91 SD = 1.18, 181 females).

Materials

The materials were the same as Experiment 2.

Procedure

The procedure was the same as Experiment 2. Sleep-deprived participants were randomly assigned to a 0 min, 30 min, or 60 min nap opportunity during the night with the stipulation that all participants in a given session either received a nap opportunity (30 min, 60 min) or did not receive a nap opportunity (0 min). The start time of the nap opportunity was restricted between 04:00 and 06:00. Participants selected for the 30 or 60 min nap opportunity were set up with partial polysomnography (PSG). PSG setup involved taking scalp measurements in accordance with the international 10-20 system. There were 14 electrodes in total. Electroencephalographic (EEG) electrodes included: O1, O2, C3, C4, F3, F4, and FpZ. Additionally, there were two EOG leads and three EMG leads. Finally, reference electrodes (M1 and M2) were placed on the mastoids. Data was recorded continuously using the program Sleepware G3. Sleep architecture and awakenings were visually scored in 30 second epochs based on standard practices from the American Academy of Sleep Medicine manual version 2.5. Two trained coders scored each participant's data. The average agreement for scored sleep stages between the two coders was high 92% and we used one coder's data for the analyses.

[8] Due to experimenter error, demographic information for five participants is missing.

Sleep spindles were coded automatically in MatLab using an EEG toolbox to load the data from the Sleepware G3 program. C3 in reference to M2 was used to identify spindles. Spindle detection was based on the following standard criteria: duration greater than or equal to .5 seconds, frequency between 11-16 Hz, and within an epoch coded as stage 2.

Results

PVT. For the first set of analyses, we examined effects of TSD on lapses by performing an ANOVA with Group as a between-subjects factor and Session as a within-subjects factor. Results are plotted in Figure 14 and reported in Table 21. There was no main effect of Group, $F(1, 261) = .94$, $p = .33$, $\eta_p^2 = .004$. However, there was a main effect of Session, $F(1, 261) = 38.35$, $p < .001$, $\eta_p^2 = .128$, indicating that there were more lapses in the morning than in the evening, and a Group X Session interaction, $F(1, 261) = 50.07$, $p < .001$, $\eta_p^2 = .161$. To understand the interaction, we examined how performance changed from the evening to the morning session for rested and sleep-deprived participants, separately. Paired t-tests showed that sleep-deprived participants made more lapses over time, $t(160) = 10.36$, $p < .001$, but rested participants made a similar number of lapses during each session, $t(101) = -.59$, $p = .55$.

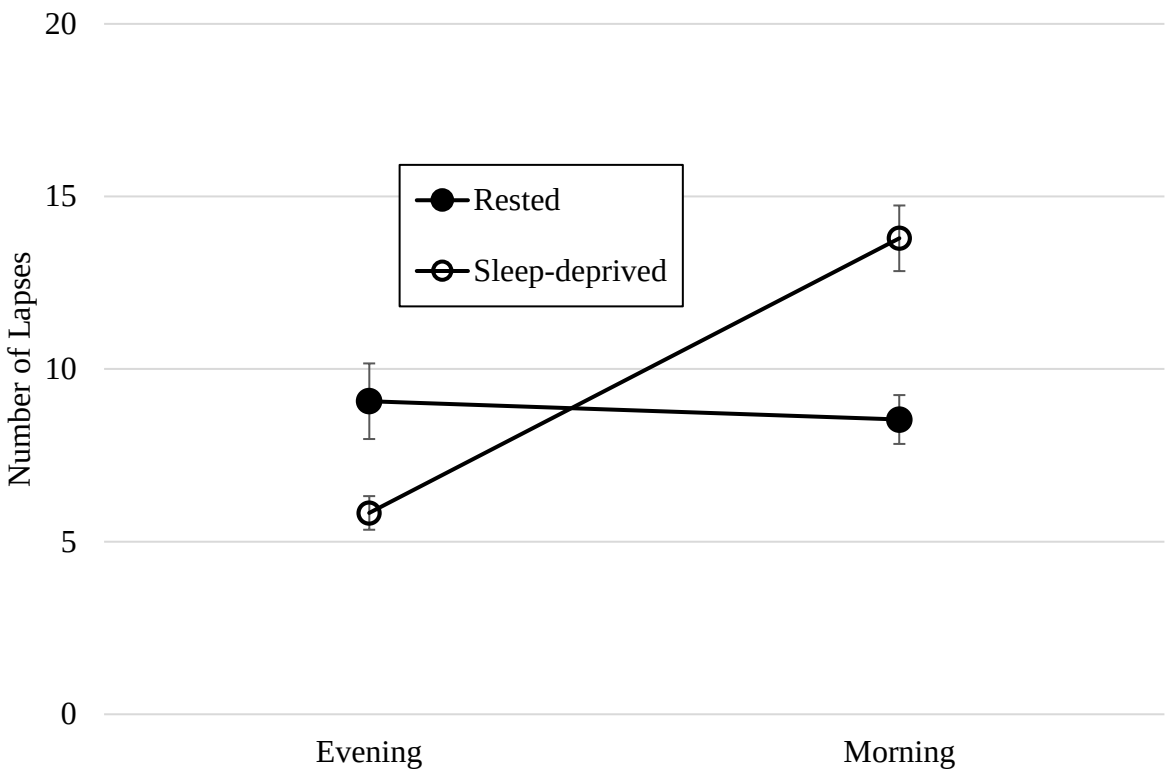


Figure 14. Number of lapses (reaction times greater than 500 ms) in the PVT, for Experiment 4. Errors bars are standard error of the mean.

Table 21

PVT lapses and UNRAVEL placekeeping errors for Experiment 4

	Evening	**Morning**
	Lapses	
Rested	9.07 (1.10)	8.54 (.71)
Sleep-deprived	5.83 (.49)	13.79 (.95)
	Post-interruption Errors	
Rested	.19 (.01)	.18 (.02)
Sleep-deprived	.15 (.01)	.21 (.01)
	Non-interruption Errors	
Rested	.04 (.003)	.02 (.002)
Sleep-deprived	.03 (.003)	.03 (.003)

Note. Standard error in parentheses.

For the second set of analyses, we look at nap effects within the Sleep-deprived group by conducting an ANOVA with Nap Opportunity (0, 30, 60 min) as a between-subjects factor and Session as a within-subjects factor. Results are shown in Figure 15 and reported in Table 22. There was a main effect of Session, $F(1, 158) = 107.30$, $p < .001$, $\eta_p^2 = .404$, with more lapses in the morning than the evening, but no main effect of Nap Opportunity, $F(2, 158) = .94$, $p = .40$, $\eta_p^2 = .012$, and no interaction, $F(2, 158) = .45$, $p = .64$, $\eta_p^2 = .006$.

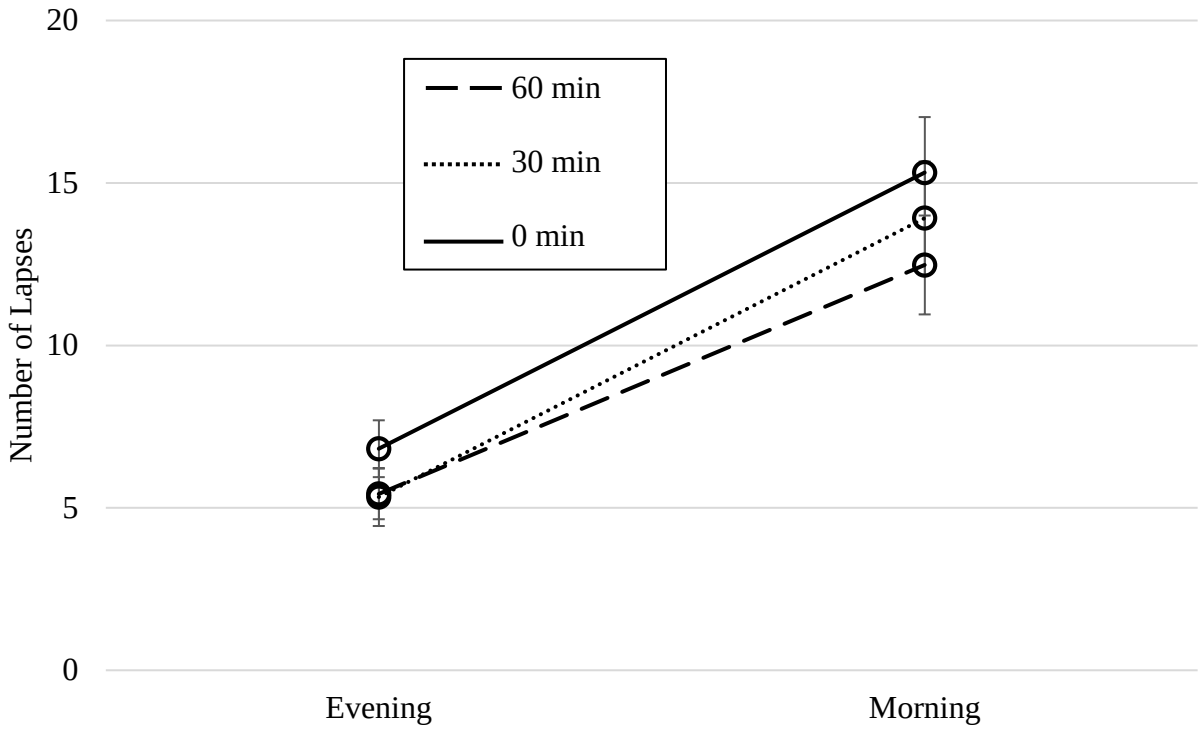


Figure 15. Number of lapses (reaction times greater than 500 ms) in the PVT, separated by nap opportunity condition within the Sleep-deprived group. Errors bars are standard error of the mean.

Table 22

PVT lapses and UNRAVEL placekeeping errors, separated by nap opportunity within the Sleep-deprived group, for Experiment 4

	Evening	Morning
	Lapses	
60 min	5.43 (.78)	12.48 (1.52)
30 min	5.33 (.89)	13.92 (1.74)
0 min	6.82 (.87)	15.32 (1.71)
	Post-interruption Errors	
60 min	.16 (.02)	.22 (.02)
30 min	.13 (.02)	.21 (.03)
0 min	.16 (.02)	.22 (.03)
	Non-interruption Errors	
60 min	.02 (.004)	.03 (.01)
30 min	.02 (.005)	.03 (.01)
0 min	.03 (.004)	.03 (.01)

Note. Standard error in parentheses.

UNRAVEL. First, we examined the likelihood of failing the morning session of UNRAVEL. We consider this a task-level assessment of deficit because these participants were all able to perform to the prespecified accuracy criterion the evening before. A Chi-Square analysis showed that sleep-deprived participants (9.60%, $n = 17$) were marginally more likely to fail the morning session than rested participants (3.80%, $n = 4$), $\chi^2(1, n = 284) = 3.24$, $p = .07$.

Next, we examined the effect of nap opportunity within the Sleep-deprived group. The 30 min nap opportunity (18.60%, $n = 11$) was more likely to fail compared to the 60 min nap opportunity (3.10%, $n = 2$), $\chi^2(1, n = 124) = 7.99$, $p = .01$, and was marginally more likely to fail compared to the 0 min nap opportunity (7.40%, $n = 4$), $\chi^2(1, n = 113) = 3.09$, $p = .08$. The 60 min and 0 min groups did not differ from each other, $\chi^2(1, n = 119) = 1.16$, $p = .28$. We also compared each of the nap opportunity groups to the rested group. The 60 min, $\chi^2(1, n = 171) = .06$, $p = .81$, and the 0 min, $\chi^2(1, n = 160) = 1.00$, $p = .32$, nap opportunity groups did not differ from the rested group. However, the 30 min nap opportunity group failed the morning session at a higher rate than rested participants, $\chi^2(1, n = 165) = 10.14$, $p = .001$. Thus, brief naps during the TSD period did not reduce the likelihood of failing the morning session of UNRAVEL and, in the case of the 30 min nap opportunity, actually increased the likelihood of failing.

For the remaining behavioral analyses, we excluded participants who failed the morning session. For our first set of analyses, we investigated the effects of TSD (collapsing across nap conditions) on errors, post-interruption and non-interruption, on the UNRAVEL task. We conducted a mixed ANOVA with Group (Rested, Sleep-deprived) as a between-subjects factor and Session (Evening, Morning) as a within-subjects factor. Summary data is plotted in Figure 16 and reported in Table 19. For our second set of analyses, we examined the effect of brief naps on error rates within the Sleep-deprived group. We performed ANOVAs with Nap Opportunity (0 min, 30 min, 60 min) as a between-subjects factor and Session as a within-subjects factor. Summary data for nap effects are shown in Figure 17 and reported in Table 20.

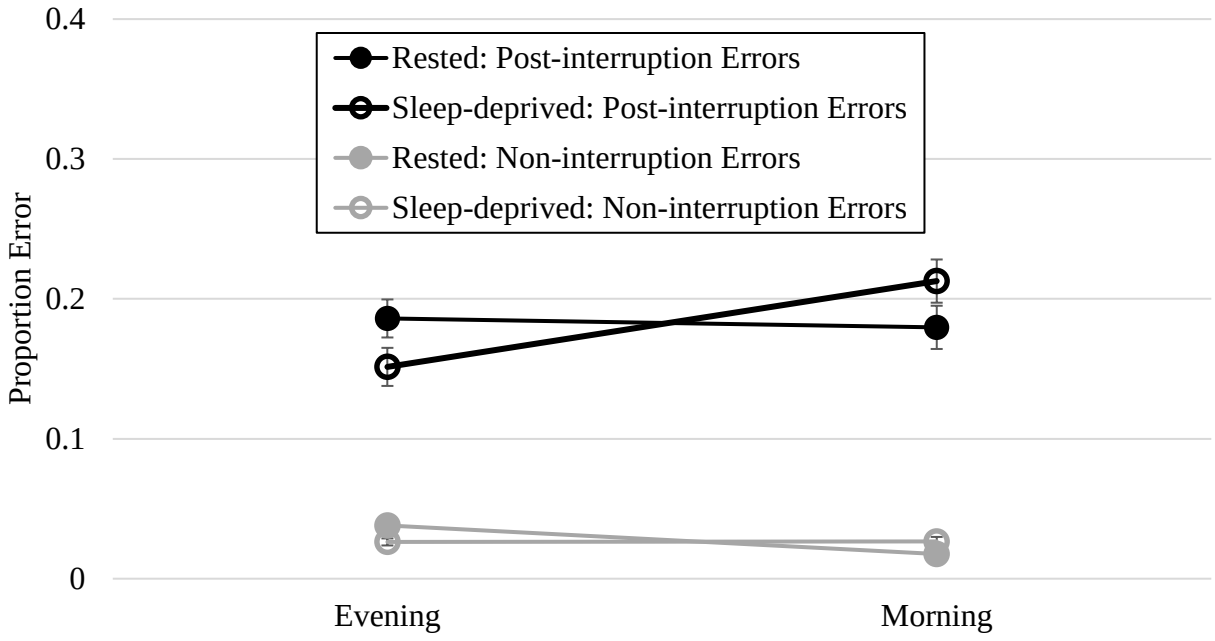


Figure 16. UNRAVEL placekeeping errors, post-interruption errors (black lines) and non-interruption errors (gray lines), for Experiment 4. Errors bars are standard error of the mean.

First, we looked at post-interruption errors. There was no main effect of Group, $F(1, 261) = .002$, $p = .964$, $\eta_p^2 < .001$, but there was a main effect of Session, $F(1, 261) = 10.25$, $p = .002$, $\eta_p^2 = .038$, indicating that participants made more post-interruption errors in the morning than in the evening. Importantly, there was also a Group X Session interaction, $F(1, 261) = 15.55$, $p < .001$, $\eta_p^2 = .056$. To understand this interaction, we used paired t-tests to examine how post-interruption errors changed from the evening to the morning session, separately for rested and sleep-deprived participants. Sleep-deprived participants made significantly more errors over time, $t(160) = 5.46$, $p < .001$, whereas rested participants did not show a significant change, $t(101) = -.52$, $p = .60$.

Next, we examined the effect of brief naps for sleep-deprived participants on post-interruption errors rates. There was a main effect of Session, $F(1, 158) = 29.64$, $p < .001$, $\eta_p^2 =$

.158, again showing that more errors were made in the morning. There was no main effect of Nap Opportunity, $F(2, 158) = .29$, $p = .75$, $\eta_p^2 = .004$, and no Nap Opportunity X Session interaction, $F(2, 158) = .16$, $p = .85$, $\eta_p^2 = .002$.

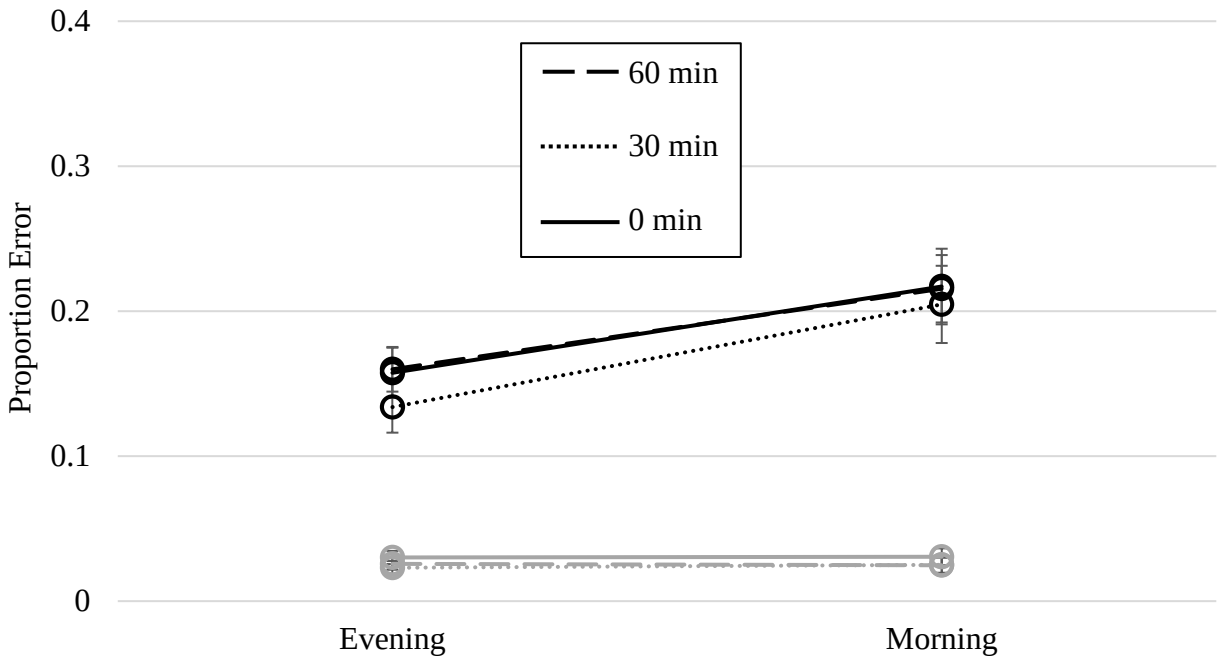


Figure 17. UNRAVEL placekeeping errors, post-interruption errors (black lines) and non-interruption errors (gray lines), separated by nap opportunity condition within the Sleep-deprived group, for Experiment 4. Errors bars are standard error of the mean.

We next turn to non-interruption errors and first examine the basic effects of TSD, collapsing across nap opportunity. Again, there was no main effect of Group, $F(1, 261) = .16$, $p = .69$, $\eta_p^2 = .001$, but there was a main effect of Session indicating that fewer errors were made in the morning, $F(1, 261) = 15.55$, $p < .001$, $\eta_p^2 = .056$. There was also a Group X Session interaction, $F(1, 261) = 17.00$, $p < .001$, $\eta_p^2 = .061$. To break down this interaction we examined how non-interruption errors changed from the evening to morning session, separately for rested and sleep-deprived participants. Paired t-tests showed that rested participants made fewer errors

over time, $t(101) = -6.57$, $p < .001$, whereas sleep-deprived participants showed similar performance across time, $t(160) = .11$, $p = .92$.

Finally, we examined effects of nap opportunity for sleep-deprived participants on non-interruption errors. There was no main effect of Nap Opportunity, $F(2, 158) = .66$, $p = .52$, $\eta_p^2 = .008$, or Session, $F(1, 158) = .02$, $p = .89$, $\eta_p^2 < .001$, and no interaction, $F(2, 158) = .06$, $p = .94$, $\eta_p^2 = .001$.

Polysomnography Data. Next, we examined sleep architecture from the PSG recordings while sleep-deprived participants slept during the naps[9]. First, we investigated differences in sleep architecture between the 30 and 60 min nap opportunity conditions. Summary data is reported in Table 21. Independent t-tests showed that, as expected, participants who received a 60 min nap opportunity spent more time asleep, $t(117) = 15.80$, $p < .001$, and more time in stage 2, $t(117) = 5.57$, $p < .001$, and stage 3, $t(117) = 8.95$, $p < .001$. Participants who received the 60 min nap opportunity also had a higher spindle count, $t(117) = 4.03$, $p < .001$, than participants who received a 30 min nap opportunity. There were no other differences in sleep architecture based on nap opportunity (see Table 23).

[9] Four participants did not sleep during the nap opportunity and are excluded from analyses.

Table 23

Sleep architecture from polysomnography recordings for the 30 and 60 min nap opportunity groups, from Experiment 4

	30 min nap opportunity	**60 min nap opportunity**	***t***	***p***
Total sleep time	25.99 (7.49)	52.11 (10.10)	15.80	< .001
Sleep latency	4.60 (4.79)	4.99 (5.38)	.42	.68
Stage 1 (min)	4.53 (3.78)	4.61 (3.66)	.12	.90
Stage 2 (min)	10.00 (3.67)	16.81 (8.41)	5.57	< .001
Stage 3 (min)	11.08 (8.02)	30.16 (13.94)	8.95	< .001
REM (min)	.38 (1.58)	.52 (2.22)	.40	.69
WASO	1.17 (2.08)	1.92 (4.01)	1.25	.21
Spindle count	29.89 (21.47)	48.20 (27.17)	4.03	< .001
Spindle density	2.83 (1.58)	3.14 (1.41)	1.14	.26
Average spindle duration (s)	.73 (.08)	.73 (.06)	.07	.95

Note. Standard deviation in parentheses.

Next, we investigated whether sleep architecture during the naps related to how performance changed on PVT and UNRAVEL after TSD. Specifically, we were interested in whether different aspects of sleep architecture helped to maintain vigilant attention and placekeeping performance when sleep-deprived. We collapsed across the 30 and 60 min nap opportunity conditions and performed separate hierarchical regressions for morning PVT lapses, morning post-interruption errors, and morning non-interruption errors. In the first step, we entered evening performance to control for individual differences. In the second step, we entered the sleep variables: total sleep time (TST), sleep latency, stage 1, stage 2, stage 3, REM, wake after sleep onset (WASO), spindle count, spindle density, and average spindle duration. Sleep

latency is the time from the start of the nap opportunity until sleep onset. WASO is a measure of how much time was spent awake after initial sleep onset. The effect of evening performance and significant sleep variables for each outcome (lapses, post-interruption errors, and non-interruption errors) are reported in Table 24.

First, we examined vigilant attention performance on the PVT. For PVT lapses, the predictors which were significantly related to morning performance were evening lapses, stage 3, and sleep latency. Evening lapses is an indication of individual differences in vigilant attention performance. The significant effect of stage 3 indicated that more time spent in stage 3 was related to fewer lapses in the morning. Finally, the significant effect of sleep latency indicated that more time until sleep onset was related to fewer lapses. All other sleep variables were not significantly related to morning lapses, $ts < 1.70$, $ps > .09$.

Next, we investigated placekeeping performance on UNRAVEL. For post-interruption errors, evening post-interruption errors and TST were significantly related to morning performance. The effect of TST indicated that more sleep was related to fewer post-interruption errors after TSD. For non-interruption errors, stage 3 was related to morning performance such that more stage 3 was related to fewer non-interruption errors. All other sleep variables were unrelated to post-interruption, $ts < 1.96$, $ps > .052$, and non-interruption errors, $ts < 1.51$, $ps > .13$.

Table 24

Regression analyses for morning lapses and placekeeping errors for participants who napped, for Experiment 4

	B	***SE*B**	***β***	***t***	***p***
			Lapses		
Evening lapses	1.13	.19	.50	5.93	< .001
Sleep latency	-.44	.22	-.18	2.04	.04
Stage 3 (min)	-.18	.08	-.22	2.26	.03
			Post-interruption errors		
Evening errors	1.02	.14	.57	7.32	< .001
Total sleep time	-.003	.001	-.22	2.23	.03
			Non-interruption errors		
Evening errors	.36	.47	.08	.77	.45
Stage 3 (min)	-.002	.001	-.25	2.21	.03

Note. Only significant sleep variables are reported

Discussion

Interventions for TSD are highly sought after, yet there has been little success in finding interventions that mitigate higher-order cognitive deficits due to TSD. There is evidence to suggest that a nap during a period of TSD may benefit both lower-level and higher-order cognition when sleep-deprived. However, studies have almost exclusively investigated nap durations between 2 and 4 hours (Dinges, Orne, Whitehouse, & Orne, 1987; Jewett, Dijk, et al., 1999; Macchi, Boulos, Ranney, Simmons, & Campbell, 2002; Naitoh, Englund, & Ryman, 1982; Vgontzas et al., 2007) which is not necessarily a feasible intervention. Here, we tested the effects of brief nap opportunities (30 and 60 minutes) during a period of TSD on vigilant attention and placekeeping. Participants who received a nap opportunity did not show a benefit in performance on either task; however, characteristics of sleep architecture measured using PSG correlated with

performance. In particular, the aspects of sleep architecture that correlated with vigilant attention were different than those that correlated with memory maintenance performance. This has important theoretical implications and provides further evidence that vigilant attention does not completely underlie deficits in placekeeping performance.

Receiving a nap opportunity had no benefit for cognitive performance after TSD. Participants in the 30 min nap opportunity were more likely to fail the morning session of UNRAVEL than participants in the 60 min nap opportunity; however, both groups failed at a similar rate to participants in the 0 min nap opportunity. Additionally, the 30 min nap opportunity was the only group which failed at a higher rate than rested participants. Thus, not only was there no evidence for a benefit of a brief nap, it appears that in some cases a brief nap could actually worsen performance. For participants who passed the morning session of UNRAVEL, nap opportunity had no effect on placekeeping performance. Nap opportunity also had no effect on vigilant attention performance on the PVT. Sleep-deprived participants in general showed an increase in post-interruption errors and the number of lapses after TSD; however, this increase was similar across all nap opportunity conditions. Together, these results suggest that receiving a brief nap opportunity during a period of TSD is not a beneficial intervention for cognitive deficits due to TSD and could instead exacerbate problems.

Although behavioral analyses did not reveal a benefit of nap opportunity condition for vigilant attention or placekeeping, polysomnography recordings during the nap indicated that there were specific aspects of sleep architecture during the naps that related to performance. A reduction in morning lapses was associated with more stage 3 sleep and a longer sleep latency. As wakefulness accumulates, we build up a greater need for sleep – particularly for stage 3 SWS (Wu, et al., 2006; Ferrara et al., 2002). Indeed, participants spent the largest proportion of their

allotted nap time in SWS (*M* = 48%, *SD* = 25%). Thus, SWS may have alleviated sleep pressure which, in turn, reduced lapses in attention under conditions of TSD. Sleep latency, the time from the start of the nap opportunity to sleep onset, is a standard measure of sleepiness, and a sleep latency of less than five minutes is associated with impaired performance (Carskadon, 1986; Carskadon & Dement, 1979). In the current study, sleep latency was within the performance decrement range (*M* = 4.81 min, *SD* = 5.10 min) as would be expected for sleep-deprived participants. Participants who fell asleep immediately were likely the most affected by TSD and were experiencing high amounts of sleepiness; whereas, participants who took longer to fall asleep may be more resilient to TSD.

Morning placekeeping performance was also associated with specific aspects of sleep architecture. A reduction in morning post-interruption errors was associated with more TST. Thus, memory maintenance – a component process of placekeeping that is uniquely involved in post-interruption trials – appears to not be sensitive to sleep stage composition but is affected by overall sleep duration. Reduced non-interruption errors, however, was specifically related to more stage 3 SWS. Thus, a common sleep variable, SWS, was related to non-interruption errors and lapses, reflecting shared processing between non-interruption trial and PVT performance. This shared processing may be related to basic alertness as other work has found that minutes of SWS during a nap was the best predictor of increased alertness (Lumley, et al., 1986).

Interestingly, the aspects of sleep architecture that related to vigilant attention performance were different from what related to memory maintenance. This pattern of results is more consistent with direct effects of TSD on memory maintenance than it is with vigilant attention underlying memory maintenance deficits. Otherwise, we would have expected more stage 3 and longer sleep latency, which promoted greater resilience to TSD with regards to PVT

performance, to also benefit performance on post-interruption trials if vigilant attention was solely implicated in both cases.

In conclusion, a brief nap opportunity during a period of TSD is likely not a viable intervention for cognitive deficits due to TSD. Indeed, one of the best predictors for memory maintenance performance was TST which suggests that longer nap durations may be required before clear performance benefits on higher-order cognition can be observed. Nonetheless, different aspects of sleep architecture were associated with vigilant attention and memory maintenance performance which is inconsistent with the attention-mediated theory.

CHAPTER IV: OVERALL DISCUSSION

The major aim of this dissertation was to test a prominent theory of TSD, referred to as the attention-mediated theory. This theory states that vigilant attention, a global process required for nearly all cognitive tasks (Sturm & Willmes, 2001; Sturm, et al., 1997), underlies deficits in higher-order cognition in sleep-deprived individuals (Balkin, et al., 2008; Doran et al., 2001; Lim & Dinges, 2010). To test this theory, we investigated effects of TSD on vigilant attention and a specific component of higher-order cognition – placekeeping – using two different methods. Experiments 1 and 2 utilized mediation models to quantify the extent to which vigilant attention mediated the relationship between TSD and placekeeping ability. Experiment 2 additionally investigated whether the ability to manage proactive interference mediated the relationship between TSD and an important component of placekeeping, memory maintenance. Experiments 3 and 4 utilized a different approach to testing the attention-mediated theory by exploring whether vigilant attention and placekeeping are differentially affected by caffeine and brief naps – two commonly used interventions for TSD. Across these four experiments, we accumulate converging evidence that the attention-mediated theory does not adequately explain deficits in placekeeping ability after TSD.

According to the attention-mediated theory, the mechanism driving vigilant attention deficits after TSD is state instability. State instability is the result of competition from the sleep state while the individual is trying to remain awake. As the amount of wakefulness increases, the homeostatic drive to sleep also increases. The homeostatic drive to sleep is an internal biochemical process which signals for the need to sleep and builds up in a linear fashion across periods of wakefulness. The signaling process is likely related to adenosine buildup from energy utilization during waking activity (Huang, Urade, & Hayaishi, 2011; Porkka-Heiskanen,

Strecker, & McCarley, 2000; Scammell, 2001; Strecker, et al., 2000). Thus, as the need for sleep increases, this causes instability between the wake and sleep states. The states then become less discrete and this causes lapses in attention to occur (Yin, 2007).

While deficits in vigilant attention after TSD are robust, it has been debated whether vigilant attention deficits are truly the only cognitive deficits directly caused by TSD. Here, we show evidence that TSD impairs placekeeping and memory maintenance and that vigilant attention does not completely explain these deficits. In Experiment 1, we found that, using a mediation model, vigilant attention partially explained the relationship between TSD and placekeeping and memory maintenance. Thus, vigilant attention is indeed impaired by TSD and is also necessary for placekeeping performance. Importantly, however, TSD maintained a direct relationship with placekeeping and memory maintenance after accounting for vigilant attention, indicating that placekeeping ability was directly impaired by TSD. Thus, Experiment 1 provided evidence against the attention-mediated theory by empirically showing that vigilant attention does not completely underlie deficits in placekeeping and memory maintenance after TSD.

In Experiment 2, we build upon the findings from Experiment 1 by testing whether the ability to manage proactive interference explains the direct relationship between TSD and memory maintenance. We again used a mediation model to quantify the relationships between TSD, vigilant attention, and management of proactive interference. We showed that vigilant attention did not fully explain the relationship between TSD and memory maintenance, replicating findings from Experiment 1. However, the ability to manage proactive interference was not significantly impaired by TSD and did not mediate the relationship between TSD and memory maintenance. Nonetheless, the findings from Experiment 2 corroborate Experiment 1 and add to the evidence against the attention-mediated theory.

In the next two experiments, we employed a different method to test the attention-mediated theory. We used interventions to mitigate effects of TSD and examined how vigilant attention and placekeeping responded to these interventions. The pattern of results that would be most consistent with the attention-mediated theory would be if vigilant attention, placekeeping, and memory maintenance responded similarly to an intervention. If vigilant attention completely underlies deficits in placekeeping and memory maintenance, then any intervention which benefits PVT performance should have a similar effect on UNRAVEL; because, in both cases the same underlying process is hypothesized to be impaired. If, however, the two tasks respond differently to an intervention then this would imply that placekeeping, not solely vigilant attention, is directly impaired by TSD. In Experiment 3, the intervention we tested was caffeine. We found that caffeine benefitted vigilant attention and restored PVT performance to that of rested levels. However, caffeine only benefitted UNRAVEL performance for participants at the margins – participants who were unwilling or unable to perform the task as instructed after TSD. Caffeine had no benefit on placekeeping for a majority of the sample. Thus, using a new method, we again found evidence inconsistent with the attention-mediated theory of TSD.

In Experiment 4, we investigated brief naps as an invention for TSD and examined the relationships between sleep architecture and cognitive performance. Shorter sleep latencies, an objective measure of increased sleepiness, was related to more attentional lapses. Sleepiness is an indication of high sleep pressure from the homeostatic sleep drive which generates competition with maintaining wakefulness. Thus, sleep-deprived individuals who were more affected by TSD and experiencing high amount of sleep pressure were also more likely to experience lapses in attention. More stage 3 SWS was related to fewer lapses and also fewer non-interruption errors, suggestive of common processing between the two tasks, possibly basic

alertness. Other work found that minutes of SWS in sleep-deprived individuals who received a nap was related to increased alertness (Lumley, et al., 1986). Post-interruption trials, a measure of memory maintenance, on the other hand, was only related to TST. Thus, memory maintenance performance appears to be sensitive to overall sleep duration but not sleep stage composition. This may reflect that progression through the sleep stages, rather than amount of time spent in any single stage, is important for this higher-order process. These findings are also not consistent with the attention-mediated theory since this theory would have predicted that the same sleep variables that related to PVT performance would also be related to post-interruption trial performance.

The findings from the four experiments provide converging evidence that the attention-mediated theory does not adequately explain deficits in placekeeping or memory maintenance under conditions of TSD. While vigilant attention is indeed important for UNRAVEL performance, our findings suggest that this is not the full picture. Instead, TSD appears to directly impair placekeeping and memory maintenance, over and above the influence of vigilant attention. An alternative theory which may account for these direct effects on higher-order cognition is a neuropsychological account of TSD. This theory posits that TSD produces direct and domain-specific impairments to cognition (Harrison & Horne, 2000). The degree of deficit in a certain domain of cognition depends on the extent to which TSD alters neural functioning in the brain regions or systems that underlie that cognitive process.

The degree to which a certain brain region is impaired by TSD may depend, in part, on how active that region is during waking activity. The prefrontal cortex (PFC) is often specifically implicated in this theory because the PFC tends to be particularly active during wakefulness (Maquet, et al., 1990). As a result, the PFC builds up a greater sleep need – particularly for SWS

(Wu, et al., 2006; Ferrara et al., 2002; Wilckens, Ferrarelli, Walker, & Buysse, 2018). It has been shown that there is local homeostasis achieved via SWS, such that areas involved in learning during wakefulness receive more slow wave activity during sleep (Huber, Ghilardi, Massimini, & Tononi, 2004). Moreover, SWS has been proposed to be important for cortical reorganization in the PFC (Steriade & Amzica, 1998). Slow oscillations generated during SWS are thought to be important for both synaptic stability and plasticity required for memory organization, including enhancing, stabilizing, or integrating memories into previously established neural networks (Abraham & Robins, 2005; Steriade & Amzica, 1998). Indeed, SWS has been linked to performance on tasks that engage the PFC in healthy older adults (Anderson & Horne, 2003) and increasing slow wave activity using transcranial electrical stimulation may enhance declarative memory (Barham, Enticott, Conduit, & Lum, 2016; Wilckens, et al., 2018). Thus, TSD may be particularly detrimental to the PFC and the tasks that engage it.

In support of this theory, the PFC frequently undergoes changes in response to TSD. Using positron-emission tomography (PET), TSD reduced glucose metabolism in frontal regions compared to rested baseline (Thomas, et al., 2000; Wu et al., 2006). In addition, neuroimaging studies often find that TSD decreases PFC activity (Mu et al., 2005; Choo, Lee, Venkatraman, Sheu, & Chee, 2005; Drummond, et al., 1999). However, several studies have also found increases in PFC activity following TSD. Increased activation after TSD often correlates with relatively more spared performance and is interpreted as a compensatory response (Chuah, Venkatraman, Dinges, & Chee, 2006; Drummond, Meloy, Yanagi, Orff, & Brown, 2005; Chee & Choo, 2004; Drummond, Gillin, & Brown, 2001, Drummond and Brown, 2001). For example, Chuah and colleagues (2006), found that TSD generally impaired inhibitory control, as assessed via the go-no go task, but that individuals who were more resistant to sleep-deprived

impairments also exhibited transient increases in activation in the ventrolateral PFC compared to their rested wakefulness state. Moreover, TSD may also reduce functional connectivity within areas of the PFC (Verweij, et al., 2014) as well as between the PFC and other brain regions, such as the amygdala (Yoo et al., 2007). Taken together, these findings suggest that the PFC may be particularly vulnerable to the effects of TSD and that cognitive processes directly controlled by the PFC, and also those that receive inputs from the PFC, may suffer as a result of TSD.

Given the wealth of neural evidence in support of the neuropsychological theory of TSD, one might expect that behavioral deficits on higher-order tasks would be more straightforward. However, pervasive methodological limitations may explain why behavioral findings tend to be more mixed for higher-order cognition. Indeed, we were able to detect and replicate the basic finding that TSD impairs placekeeping ability in all four experiments using large samples, including rested control groups, and isolating processes related to memory maintenance. Out of those methodological considerations, probably the one most violated and problematic is the use of small sample sizes. The use of small samples is likely a major contributor to why the attention-mediated theory has remained prominent. It tends to be much more difficult to detect effects on higher-order tasks, due to a number of reasons discussed in the introduction to this dissertation, and the use of small samples makes it even less likely. As a result, behavioral findings for higher-order cognition are more inconsistent than for vigilant attention which lends to the interpretation that higher-order cognition is not directly impaired by TSD.

In an attempt to assist researchers with future sleep deprivation studies, we determined what sample sizes would be sufficient to detect effects on vigilant attention and placekeeping using the effect sizes we obtained in the four experiments. We performed power analyses for each experiment for the two main UNRAVEL outcomes (post-interruption and non-interruption

errors) and for PVT lapses. The effect sizes used were from the Group (Rested, Sleep-deprived) X Session (Evening, Morning) interaction term. A priori power analyses were performed in G-Power 3.1.9.2 with alpha set at .05 and power set at .80 (Cohen, 2013). Summary information is reported in Table 25. An average sample size of 58 participants would be needed to detect a significant Group X Session effect for PVT lapses; whereas, sample sizes over twice as large on average are necessary to detect placekeeping deficits [post-interruption errors (n = 117.5) and non-interruption errors (n = 197)]. These sample sizes for placekeeping are in stark contrast to the average sample size in sleep deprivation experiments (n = 21.3, Lim & Dinges, 2010) and highlights how this methodological limitation has contributed to mixed findings for higher-order cognition. Higher-order tasks will vary in their sensitivity to TSD and may require larger or even smaller samples than what we recommend here; nonetheless, these recommended sample sizes are a useful starting point.

Table 25

Power analysis calculations for recommended sample sizes

	Post-interruption errors	Non-interruption errors	Lapses
Exp. 1	54 (η_p^2 = .139)	96 (η_p^2 = .080)	58 (η_p^2 = .127)
Exp 2.	110 (η_p^2 = .070)	324 (η_p^2 = .024)	42 (η_p^2 = .176)
Exp 3.	168 (η_p^2 = .046)	242 (η_p^2 = .032)	86 (η_p^2 = .089)
Exp 4.	138 (η_p^2 = .056)	126 (η_p^2 = .061)	46 (η_p^2 = .161)
Average	117.5	197	58

Note: Sample size is based on the effect size in parentheses.

In conclusion, we found converging evidence that TSD directly impairs placekeeping ability and memory maintenance – broadly important components of higher-order cognition – and that these deficits could not be entirely explained by deficits in vigilant attention. Thus, the attention-mediated theory does not sufficiently characterize higher-order cognitive deficits due to TSD. Alternatively, theories which posit that TSD produces domain-specific deficits to cognition, such as the neuropsychological account, have better explanatory power, especially for higher-order deficits in sleep-deprived individuals. Additionally, we show that caffeine is beneficial for vigilant attention decrements after TSD but that placekeeping deficits are more difficult to mitigate. Neither caffeine nor a brief nap opportunity was particularly beneficial for placekeeping performance. This is further evidence that TSD causes domain-specific deficits to cognition and, as a result, interventions may need to be specifically tailored to the task a sleep-deprived operator is expected to perform. Future research should continue to investigate which aspects of higher-order cognition are impaired by TSD and what other interventions can be used

to mitigate deficits. Importantly, future research needs to reform common, but unsatisfactory, practices in the field, particularly the use of small samples, if we are to build upon our understanding of how TSD and interventions for TSD affect higher-order cognition.

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