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PRINCIPAL INVESTIGATOR: Sean P.A. Drummond, Ph.D.

CONTRACTING ORGANIZATION: Veterans Medical Research Foundation
San Diego, CA 92161

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**5. AUTHOR(S)**  
Sean P.A. Drummond, Ph.D.

E-Mail: Drummond@ucsd.edu

**6. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**  
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San Diego, CA 92161

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**14. ABSTRACT:** An ever-increasing number of military personnel and civilians alike must work daily without adequate sleep. Although considerable data show that sleep deprivation alters many aspects of behavior, little is known about changes in the brain substrate underlying the behavioral effects, and even less is known about the cerebral effects of recovery sleep. The overarching objective of this study is to investigate the effects of 2 full nights of sleep loss (66 hours total) and 2 full nights of recovery sleep on cognitive performance and brain function. We have studied 40 individuals for 6 nights and 6 days. Over the course of this period, subjects received 4 polysomnograms and 10 functional magnetic resonance imaging (FMRI) sessions. During the FMRI sessions, functional brain imaging data was collected while subjects performed each of 3 cognitive tasks. These data provide a rich amount of information concerning the effects of prolonged total sleep deprivation and recovery sleep on cognitive performance and the cerebral underpinnings of that performance. Early analyses of these data are revealing the course of deterioration and recovery in cognitive performance, the specific component processes of cognition affected by sleep deprivation, and the changes in brain function associated with sleep deprivation. We have also initially reported distinct patterns of recovery for different sleep parameters after sleep deprivation, and the possibility of using the FMRI measures to identify neural correlates of vulnerability and resilience to sleep deprivation.

**15. SUBJECT TERMS**  
Sleep, sleep deprivation, functional magnetic resonance imaging, cognition, performance

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INTRODUCTION:
An ever-increasing number of military personnel and civilians alike must work daily without adequate sleep. Although considerable data show that sleep deprivation alters many aspects of behavior, including motor skills and cognitive performance, little is known about changes in the brain substrate underlying the behavioral effects. Even less is known about the cerebral effects of recovery sleep. The overarching objective of this study is to investigate the effects of 2 full nights of sleep loss (about 66 hours total) and 2 full nights of recovery sleep on cognitive performance and brain function. To accomplish this goal, we will study 40 individuals for 6 nights and 6 days. Over the course of this period, subjects will receive 4 polysomnograms and 10 functional magnetic resonance imaging (FMRI) sessions. During the FMRI sessions, functional brain imaging data will be collected while subjects perform each of 3 cognitive tasks: sustained attention, arithmetic working memory, and verbal learning. Together, these data will provide a rich amount of information concerning the effects of prolonged total sleep deprivation and recovery sleep on cognitive performance and the cerebral underpinnings of that performance. In addition to the 40 individuals in the sleep deprivation protocol, we will recruit 10 separate individuals to serve as control subjects who will participate only in the FMRI portion of the protocol, not the sleep or sleep deprivation portions. These data will allow us to determine the effects on FMRI measures of brain activation due to repeated measurements, independent of any sleep or sleep deprivation-related effects. Preliminary analyses of the sleep deprivation data are revealing the course of deterioration and recovery in cognitive performance and the specific component processes of cognition affected by sleep deprivation. We have also initially reported distinct patterns of recovery for different sleep parameters after sleep deprivation, and the possibility of using the FMRI measures to identify neural correlates of vulnerability and resilience to sleep deprivation.

BODY:
As of the end of Year 4 of this project, July 15 2006, we have completed the main sleep deprivation portion of the protocol and all related items from the Statement of Work. In addition, we have completed more than half of the subjects planned for the control arm of the study.

In total, approximately 700 individuals have been initially screened for the main sleep deprivation study. Fifty-one (51) were determined to be preliminarily eligible and signed informed consent to participate in the main sleep deprivation protocol. Of those, 40 (18 females) have fully completed the study. Of those who did not complete, 6 voluntarily withdrew for personal reasons prior to the first experimental night, 4 were withdrawn due to further screening determining they were ineligible, and 1 subject voluntarily withdrew because he was unwilling to remain awake after approximately 20 hours of sleep deprivation.

Six (6), subjects have completed the control arm of this study. As reported last year, in recruiting subjects for the control arm, we found that the majority of individuals prefer to participate in the main sleep deprivation protocol, because 1) the compensation is considerably greater, and 2) it requires less travel (since participants live in the lab rather than appear for two separate appointments each day). Thus, we decided to complete all 40 subjects in the sleep deprivation protocol prior to continuing the control arm. We are now actively recruiting subjects for this control arm and will complete this item in the Statement of Work by the end of the No Cost Extension period (July 2007).
The 46 subjects who have completed both arms of this study represent 1380 separate functional MRI scans (10 sessions/subject x 3 cognitive task scans/session) and 460 anatomical MRI scans. Each functional scan requires approximately 10-12 hours to fully process and prepare the data for group level analyses.

This year, we have continued to publish conference abstracts and to report preliminary analyses at scientific conferences. Furthermore, we have submitted three manuscripts for peer-reviewed publication (two have been accepted for publication) and are currently preparing four others. In addition to the abstracts and manuscripts, Dr. Drummond gave a platform presentation at the 2006 Military Health Research Forum in San Juan, Puerto Rico that reported data from this study. He has also presented these data during invited presentations at the University of Arizona and at the National Institutes of Health.

All submitted manuscripts and abstracts are included in the appendix. Nonetheless, a few are briefly described here. The first paper to be accepted for publication described the effects of sleep deprivation and recovery sleep on inhibitory abilities. The results showed that sleep deprivation significantly impairs one’s ability to stop oneself from performing an action, even when that action is inappropriate, but that a single night of recovery sleep restores this ability. This has implications for operational settings where a war fighter may need to withhold what is an otherwise over-trained automatic response. A second paper uses newly developed analytical techniques to examine functional connectivity within the brain. This paper reports that a network of brain regions responsible for learning new information is altered by sleep deprivation. Some of these alterations appear to allow individuals to continue to learn despite sleep loss. One of the papers in preparation (anticipated submission in August 2006) uses computational modeling to examine the specific aspects of working memory performance that are impaired by sleep deprivation. Results of that analysis show that the working memory buffer is most severely impacted. Importantly, though, we identified individual differences in which component cognitive processes of working memory were impaired by sleep deprivation. This approach to understanding the effects of sleep deprivation on cognitive function may allow us to develop individualized management tools for mitigating and/or overcoming the effects of sleep loss. Finally, we have recently submitted a manuscript describing the effects of sleep deprivation on decision making. We found that while overall accuracy of specific decisions did not change with sleep deprivation, the way information is used to make those decisions did change. Along with a conference presentation on risk preference during decision making, these data may help improve the way commanders and other war fighters make decisions. In addition to peer-reviewed manuscripts, we presented six abstracts at this year’s Associated Professional Sleep Societies meeting. Of these six, five received platform presentations and all three that were eligible for awards received one. Three of these seven abstracts are among the manuscripts outlined above and we anticipate turning the others into manuscripts in the future.

**KEY RESEARCH ACCOMPLISHMENTS:**

- Forty (40) subjects have completed the sleep deprivation protocol
- Six (6) subjects have completed the control arm of the protocol
- Three (3) papers have been submitted for peer-reviewed publication
REPORTABLE OUTCOMES:

1. Three (3) manuscripts accepted and/or submitted (Ref 1-3)
2. Three (3) manuscripts in preparation (the first will be submitted in August 2006)
3. Seven (7) abstract presentations at the Associated Professional Sleep Societies meeting in June 2005 (Ref 4-9)
   a. Five earned platform presentations (Ref 4-8)
   b. Three were awarded merit-based awards from the Sleep Research Society (Refs 4, 7-8)
4. Three (3) invited talks (Ref 10-12), including at the 2006 Military Health Research Forum

CONCLUSIONS:

Overall, we have completed all of the items in the Statement of Work related to the sleep deprivation portion of this study. We will complete the control arm of the study during the next year. Specifically, we completed 40 subjects through the week-long sleep deprivation protocol and have completed 6 (of 10) though the control arm of the study. This represents over 1300 individual functional magnetic resonance imaging scans. Over the four years of the study, we have produced 15 conference abstracts (8 were platform presentations and 7 received merit-based awards), 8 invited presentations at international meetings, 3 submitted manuscripts, and 3 in-preparation manuscripts. During the next year, we will complete the control arm of the study and continue to analyze data and submit manuscripts for peer-reviewed publication.

REFERENCES:


3. Dickinson, D.L., Drummond, S.P.A. The Effects of Total Sleep Deprivation on Bayesian Updating (submitted)


APPENDICES:

We have included the page proofs from reference 1 and 2 and a PDF of preprint of reference 3. We have also included reprints of the abstracts. These were copied from a PDF version of the journal and complied into a single document. Thus, the formatting reflects the journal, but these are not the exact journal pages.
Effects of two nights sleep deprivation and two nights recovery sleep on response inhibition

SEAN P. A. DRUMMOND 1, MARTIN P. PAULUS 2 and SUSAN F. TAPERT 1

1Psychology Service and 2Psychiatry Service, VA San Diego Healthcare System, Department of Psychiatry, University of California San Diego, San Diego, CA, USA

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SUMMARY

This study examined the effects of two nights of total sleep deprivation (TSD) and two nights of recovery sleep on response inhibition. Thirty-eight young, healthy adults performed a Go-NoGo task at 14:00 after: (1) a normal night of sleep; (2) each of two consecutive nights of TSD; and (3) each of two consecutive nights of recovery sleep; they also performed the task at 05:00 during the first night of sleep deprivation. We hypothesized that TSD would lead to an impaired ability to withhold a response that would be reversed with recovery sleep. Subjects did experience a significant increase in false positive responses throughout all of TSD, errors of omission (i.e. missed ‘go’ targets) were not significant until after the second night of TSD. Both components (withholding a response and automatic responding) of the task returned to baseline levels after one night of recovery sleep. These data suggest that individuals experience difficulty in withholding an inappropriate response during TSD, even when they are able to attend to the incoming stimuli and respond accurately to appropriate stimuli.

KEYWORDS

INTRODUCTION

Response inhibition is the cognitive process necessary to stop oneself from engaging in a prepotent response when that reaction is not appropriate. Response inhibition involves two cognitive components: attention to incoming stimuli and prevention of an automatic response (Lezak et al., 2004). Poor response inhibition has been reported as one of the cognitive symptoms of a variety of conditions, such as schizophrenia (Weisbrod et al., 2000), substance use disorders (Fillmore, 2003), and attention deficit/hyperactivity disorder (Willcutt et al., 2005).

Response inhibition is often measured with a Go–NoGo task. Such a task requires frequent automatic responding to stimuli interspersed with the need to withhold a response from a specific, less frequently occurring, stimulus. It is well established that sleep deprivation can affect performance such that automatic responding is slowed and more variable during sleep deprivation (Doran et al., 2001; Dorrian et al., 2005).

The effect of sleep deprivation on withholding a prepotent or automatic response, though, has not been extensively studied. The few published studies in this area have reported inconsistent results. One reason for the inconsistency is that most studies have used fairly complex cognitive tasks involving a number of demands beyond withholding a response. For example, some studies have employed stimulus-response incompatibility paradigms that required not only inhibition of an automatic response but also initiation of a less salient response (Harrison and Horne, 1998; Jennings et al., 2003; Smulders et al., 1997). Studies have also used complex choice reaction time tasks (Jennings et al., 2003; Smulders et al., 1997), negative priming (Harrison and Espelid, 2004), or tasks with vague inhibitory demands (Fallone et al., 2001). Another reason for the inconsistent findings is that with a few exceptions, the aims of these studies were not specifically to examine response inhibition. Rather, withholding a response was but one part of a larger set of cognitive demands, all of which influenced the behavioral outcome.

Thus, it remains unclear whether total sleep deprivation (TSD) affects the ability to withhold a response specifically or whether errors of commission result from deficits in other task demands. Here, we used a Go–NoGo task to address this issue.
This task is ideal for focusing on withholding of an automatic response because of the simplicity of the design. Subjects performed the task at baseline, three times during TSD, and after each of two nights of recovery sleep. We hypothesized that (a) TSD would impair response withholding; (b) this impairment would be greater than that seen for automatic responding; and (c) recovery sleep would reverse the expected performance decrements.

METHODS

Subjects and conditions

Thirty-eight young healthy adults (18 females; age: 24.1 ± 5.0; education: 15.3 ± 1.6) free of medical and psychiatric disorders participated in this study after providing written informed consent. All subjects reported habitually obtaining 7–9 h of sleep. They completed sleep diaries and wore actigraphs for 1 week before the study to verify adherence to a regular sleep–wake schedule. After an adaptation night in the laboratory, subjects returned the next night and were then sequestered in the laboratory until completion of the study. The subjects slept according to their normal schedule on night 2, underwent TSD for the next two nights (about 64 h total), and then were given two nights of recovery sleep (again, according to their habitual sleep–wake schedule).

Testing procedures

At 14:00 on each day starting after night 2, plus at 05:00 during the first TSD night, subjects performed a Go–NoGo task. Thus, the task was administered at an average of 21.75, 30.75 and 54.75 h TSD (standard deviation of each = 0.44 h), as well as 6.75 ± 0.44 h after waking on the baseline day and after each recovery night. The computer-administered task involved viewing stimuli presented individually in the center of the screen in a semi-random order for 200 ms with a 1300 ms interstimulus interval. A total of 181 stimuli were shown during the 4.5 min task. Stimuli consisted of two geometric shapes in each of two sizes (see Fig. 1 for examples). Subjects were instructed to respond ‘as fast as possible’ with a button press on the keyboard to all shapes except the target shape and to withhold a response for the target shape. The task directions emphasized both speed and accuracy of responding. To develop a prepotent tendency to respond positively with a button press, the need to respond quickly was emphasized repeatedly in the directions, 68.5% of the stimuli were ‘go’ stimuli, and the ‘NoGo’ stimulus shared a perceptual feature in common with two of the Go shapes (size or geometric shape, respectively).

Six different versions of the test were constructed. A previous pilot study, not designed as a direct control for this study, with 21 subjects from the same demographic as those reported here examined the practice effects and comparability of task versions. In that pilot, each subject took five of the six different versions of the Go–NoGo task, once each on five separate days after normal sleep. These test administration days were either consecutive or included two non-testing days (i.e. Saturday and Sunday) when the 5-day testing period included a weekend. Briefly, with respect to practice effects, only false positive rate showed a main effect of time (P = 0.018), with an improvement from test 1 to test 2, and no significant changes thereafter. Overall, these data suggest that the practice effects for this task are

Figure 1. Examples of task stimuli. Each row shows the stimuli from 1 of the 6 matched versions of the task. In each case, the first three shapes represented ‘go’ stimuli where subjects were required to press a button as quickly as possible when they appeared. The far right shape was the ‘NoGo’ stimulus where subjects were required to withhold a response. Note that to increase the tendency to respond with a button press, the NoGo shape shared a perceptual feature with each of two Go shapes (size or geometric shapes, respectively). While the shapes are shown in gray scale here, the actual stimuli were in color (all shapes of a given version were the same color).
modest and largely resolved after the first administration (Table 1). With respect to version compatibility, analyzes showed no differences in any version of the task on any variable (Table 2).

**Data analysis**

The outcome variables for task performance included (1) hit rate (correct button press for Go stimuli); (2) response time (RT) for correct hits; and (3) false positive rate (error of commission for NoGo stimuli). Automatic responding was measured with hit rate and RT for hits, while response withholding was measured with false positive rate (i.e. errors of commission). All variables were analyzed with one-way repeated measures ANOVA. Post hoc follow-up tests were done with Dunnett’s test corrections using the baseline scores as the comparator. Hit RT data for six subjects was lost due to technical errors, so \( n = 32 \) for that analysis.

**RESULTS**

Figure 2 shows the results of the three outcome variables. Each variable showed a significant effect of Time in the omnibus ANOVA \( (P < 0.001 \) with Greenhouse-Geisser correction). Hit rates were significantly different from baseline only after two nights TSD (55.75 h). Hit RT was significantly slower than baseline after both 31.75 and 55.75 h TSD. False positive rates, on the other hand, were elevated during all TSD testing sessions. Each of these variables returned to baseline values after one night of recovery sleep. Hit RT and false positive rates continued to decline after the second recovery night, but this change was significant only for hit RT.

**Table 1** Practice effects from a previous pilot study

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<thead>
<tr>
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<th>Time 4</th>
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<td>0.99</td>
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<tr>
<td>False +</td>
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<td></td>
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<td>62.08</td>
<td>49.76</td>
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Data for each variable are presented as mean (top) and standard deviation (bottom).

**Table 2** Version comparability from a previous pilot study

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<td>Hit RT (ms)</td>
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Data for each variable are presented as mean (top) and standard deviation (bottom).
DISCUSSION

Here, we report the effects of two nights TSD and two nights of recovery sleep on response inhibition as measured by a Go–NoGo task. Given the simple nature of the task design, we were able to more directly test the effects of TSD on the ability to stop oneself from performing an automatic response than many previous studies examining inhibition during TSD. We found that throughout TSD, subjects showed an impaired ability to withhold an automatic response. In contrast, hit rates remained stable early in TSD and only showed significant declines after the second night of TSD. This pattern suggests that during most of TSD subjects could initiate a response normally when appropriate (although somewhat slower than usual), but the inability to withhold an inappropriate response was impaired. Performance on all outcome variables returned to baseline levels after a single night of recovery sleep.

The main goal of this report was to evaluate whether the ability to withhold a response is impaired by TSD. As stated above, these data suggest that is indeed the case. One possible explanation for why subjects made more errors of commission than errors of omission during TSD may be they sacrificed accuracy in favor of speed. The emphasis on speed in the task directions may have led subjects to emphasize this outcome over the need to not respond during the NoGo stimuli. However, the RT data does not support this hypothesis. Such a focus on speed over accuracy should have favored intact RTs during correct hits with TSD. However, as Fig. 2 shows, that is not the case since RTs actually slowed during TSD.

The fact that both automatic responding and withholding a response were impaired during TSD (albeit at different rates) raises the possibility that both functions rely on the same cognitive processes and/or brain regions. While it is clear that the automatic responding component of this task requires attention, it remains unclear whether withholding a response also relies mainly on the attention system or an inhibitory system independent of attention. Manly and colleagues, through a series of experiments, argue that both task components require endogenous attention (Manly et al., 1999). Evidence for this includes the fact that subjects scoring high on a measure of ‘absent mindedness’, but not those scoring low, showed greater false positive rates when the task was made longer or the proportion of NoGo stimuli was reduced (both manipulations should increase attentional demands). Additionally, they found that faster hit RTs were correlated with increased false positives and suggested this means that ‘inefficient’ use of attention or an ‘inattentive approach to the task’ produces both speeding of responses and errors of commission (Manly et al., 1999). However, given that there are many different types of attention (e.g. sustained, selective, spatial, divided, etc.) that each engage different brain regions (Itti et al., 2005; Posner, 2004), possibly the two very different behaviors of automatic responding and withholding a response rely on distinct aspects of the attention system. Consistent with this idea are the facts that (a) during TSD our subjects showed a slowing of RT to Go stimuli along with an increase in false positive responding; and (b) both variables showed reversals after Recovery sleep. These relationships are opposite those of Manly et al. If Manly et al.’s findings argue in favor of a single attention process underlying both types of responding, our data would have to be seen as arguing against that idea. Thus, our data may suggest that TSD produces a dissociation between the types of attention responsible for automatic responding and response withholding that Manly et al.’s manipulations did not.

Moreover, consistent with the notion that automatic responding and withholding a response may rely on at least slightly different cognitive processes is the fact that each seems to activate different regions within the prefrontal cortex. The vulnerability of the prefrontal cortex to TSD has long been debated (Binks et al., 1999; Harrison and Horne, 1996; Horne, 1993; Wimmer et al., 1992). The prefrontal cortex, though, is composed of many sub-regions, and it is likely those regions respond somewhat differently to TSD. The region within the prefrontal cortex most commonly implicated in response withholding during neuroimaging and lesion studies is the right ventral prefrontal cortex, typically within the inferior frontal gyrus (Aron et al., 2004; Fassbender et al., 2004; Kelly et al., 2004; Matthews et al., 2005). This suggests that impaired response withholding during TSD may result from impaired function of this specific region. Automatic responding, on the other hand, typically activates sustained attention regions within the right dorsolateral prefrontal cortex (Culham et al., 2001; Yamasaki et al., 2002). Impaired automatic responding during TSD, then, may relate to impaired function of this region, possibly due to an impaired ability to appropriately allocate cognitive resources to within the brain (Drummond et al., 2005). Significant errors of omission were not evidenced here until after two nights TSD. However, if a more subtle deficit in resource allocation was present earlier in TSD, that may have contributed to potential dysfunction within the prefrontal region required for successful inhibition. A caveat to this possible consequence of TSD is that some tasks rely less on the prefrontal cortex after sufficient practice (Beauchamp et al., 2003; Sayala et al., 2005). If that occurs for response withholding, then the task may rely more heavily on other brain systems, such the posterior portion of the attention system.

The simplicity of the task design, while largely a strength, did not allow us to evaluate all aspects of response withholding. Specifically, we only examined motor inhibition, as opposed to speech inhibition. We also did not evaluate the ability to stop a response that has already been initiated, as can be done with the Stop Task (Brown and Braver, 2005; Matthews et al., 2005). However, as described above, our aim focused on the ability to withhold a motor response and this Go–NoGo task allowed us to do that relatively free of other cognitive demands. A second limitation is that we did not use a pure measure of sustained attention (e.g. the PVT) to contrast with response withholding. However, given the emphasis on speed, the Go stimuli here served as a reaction time task for which we could assess both errors of omission.
and speed, the two most common measures used in sustained attention analyzes. Another limitation of the study is the lack of an explicit control group who received all study procedures except TSD. While our pilot data provide information regarding practice effects, this is an imperfect control. Nonetheless, it is interesting to note that the practice effects in the pilot study were in the opposite direction of the TSD effects seen here, suggesting that the true TSD effects may be even greater than what we report.

In summary, we utilized a Go–NoGo task to assess the impact of two nights TSD and two nights of recovery sleep on the ability to withhold a motor response. The design of our cognitive task allowed us to study this outside the context of more complex cognitive demands. We found that subjects experienced significant impairment in response withholding throughout all of TSD, while automatic responding was not significant until after the second night of TSD. Both components of the task returned to baseline levels after one night of recovery sleep. These data suggest that individuals experience difficulty in withholding an inappropriate response during TSD, even when they are able to attend to incoming stimuli and respond accurately to appropriate stimuli. Thus, operational settings might consider installing safeguards to prevent mistakes and accidents from occurring as a result specifically of impaired response withholding among sleep deprived personnel.

ACKNOWLEDGEMENTS

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REFERENCES


The impact of sleep deprivation and task difficulty on networks of fMRI brain response

JOHN L. STRICKER,1,2 GREGORY G. BROWN,1,2,3 LESLEY A. WETHERELL,3,4 AND SEAN P.A. DRUMMOND2,3
1VISN 22 MIRECC Program, Veterans Affairs San Diego Healthcare System, San Diego, California
2Psychology Service, Veterans Affairs San Diego Healthcare System, San Diego, California
3Psychiatry Department, University of California San Diego, San Diego, California
4Research Service, Veterans Affairs San Diego Healthcare System, San Diego, California
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Abstract
Previous fMRI research has found altered brain response after total sleep deprivation (TSD), with TSD effects moderated by task difficulty. Specific models of the impact of sleep deprivation and task difficulty on brain response have yet to be developed. Differences in networks of fMRI measured brain response during verbal encoding in sleep deprived and well-rested individuals were examined with structural equation modeling (SEM). During fMRI scanning, 23 healthy volunteers memorized words either easy or difficult to recall, 12 (well-rested) and 36 hours (sleep deprived) after awaking. A priori models that linked specified regions of interest were evaluated, with the focus on the extent to which two left parietal regions interacted with the left inferior frontal gyrus (Model 1) or with the right inferior frontal gyrus (Model 2). Task difficulty, not TSD, determined which model fit the brain response data; Model 2 fit best for hard words before and after TSD, whereas Model 1 fit best for easy words. TSD altered the patterns of interaction within each of the best fitting models; prefrontal interactions with the left inferior parietal lobe were diminished and intra-parietal interactions increased. Sleep deprivation and item difficulty produce different effects on brain networks involved in verbal learning. (JINS, 2006, 12, 1–7.)

Keywords: Echoplanar imaging, Magnetic Resonance Imaging, Brain mapping, Task performance, Verbal learning, Adaptation, Physiological

INTRODUCTION
Increased fMRI brain response can be observed after total sleep deprivation (TSD) (Drummond et al., 2000; Drummond & Brown, 2001), especially when difficult items are studied (Drummond et al., 2004; Drummond et al., 2005). Previously, we argued that the interaction of sleep deprivation with task difficulty supported the prediction of the compensatory recruitment hypothesis, which states that task demands influence the magnitude and location of altered brain activation after TSD (Drummond et al., 2000; Drummond & Brown, 2001). Specifically, more difficult versions of tasks elicited the increased activation after TSD, relative to when subjects were well-rested (WR). These increases manifested as significant activation in brain areas not normally associated with performance of that task and as increased magnitude of response in brain regions that are typically responsible for task performance. In contrast, easier versions of the same tasks showed equivalent activation while WR and after TSD. This conclusion depended on the absence of within-region differences between the WR and TSD conditions. The conclusion drawn from these various studies is the brain will show an increased response to difficult task demands following TSD (relative to WR) but a similar response to easy task demands. An alternative explanation, though, to the idea that isolated brain regions will or will not show increased activation with TSD is that sleep deprivation might affect the interactions among brain regions involved with task performance.

The studies cited earlier suggest an interaction between sleep deprivation and task difficulty, but it is as yet unclear what the unique contributions of these two factors are in producing an increased fMRI response. Sleep deprivation may make complex tasks more difficult to perform, as
reflected in impaired performance on measures of mental arithmetic, logical reasoning, sustained attention, and short-term recognition memory after sleep deprivation (Rogers et al., 2003). Moreover, increasing task complexity has been found to increase fMRI response in well-rested individuals (Drummond, et al., 2003). Thus sleep deprivation might be associated with increased brain activation simply because sleep deprivation makes a task more difficult. If this is the case, it implies that the neural response to increasing difficulty involves the same brain networks as those altered by sleep deprivation.

These assumptions cannot be tested using standard univariate models of functional brain analysis (Frackowiak, et al., 1997) and require an understanding of how different brain areas interact to perform the task (Luria, 1966; McIntosh, 1998, 2004). By examining networks of activation instead of isolated regions of interest (ROI)s, a more complete account of the impact of TSD and task difficulty on brain function can be formulated. In this study, we use structural equation modeling (SEM) to examine how networks of fMRI brain response during a verbal encoding task differ as a function of TSD and task difficulty. SEM is a well documented and verified technique that allows for such a priori model specification along with measures of overall model fit (Kline, 2005; Loehlin, 2004).

To test whether the brain regions interact differently or merely respond differently in isolation following sleep deprivation, and to investigate the impact of task difficulty, we developed two contrasting networks of brain activity during verbal learning.

As a model of WR performance during verbal learning, we hypothesized a network of activation where the left inferior frontal gyrus (LIFG) mediates the left superior parietal lobe (LSPL) and the left inferior parietal lobe (LIPL) as illustrated by Model 1 in Figure 1. In contrast, if the right prefrontal area becomes more active in the verbal learning network during TSD, as shown in previous studies, then it should play a more prominent role in influencing the two left parietal areas, as shown by Model 2 in Figure 1. The structural equation models, which represent these networks, were designed to be recursive in order to ensure greater model stability and parsimony, and thus bidirectional connections were not introduced. In addition to being consistent with previous imaging findings in sleep deprivation (Drummond et al., 2000; Drummond & Brown, 2001; Drummond et al., 2005), these models are consistent with cognitive neuroscience theories (Cabeza & Nyberg, 2000; Clark & Wagner, 2003; Smith & Jonides, 1998). In particular, in well-rested states, the IFG is associated with monitoring and control, whereas the parietal areas are associated with phonological processing and short-term memory store (Cabeza & Nyberg, 2000; Clark & Wagner, 2003; Smith & Jonides, 1998). Moreover, TSD often produces increased activation in the bilateral parietal lobes and inferior frontal gyri, with the parietal regions being associated with better recall performance (Drummond et al., 2000). As mentioned earlier, increased brain response in the inferior frontal and parietal cortices during TSD has been found to be greatest when memorizing difficult words (Drummond et al., 2005). Contrasting a priori networks of brain response allowed us to test several hypotheses: (1) TSD will coherently alter the pattern of regional co-activation rather than produce a less coherent pattern. If TSD results in less coherent patterns of activation (because only single regions are affected and/or TSD reduces the interactivity of these regions), then we would expect poorer model fits with TSD in comparison with the WR condition, regardless of the underlying model; (2) TSD will increase the moderating impact of some brain areas, while lessening the importance of other areas. In particular, the RIFG will modulate parietal lobe activity only after TSD, whereas the modulatory effects of the LIFG will decrease with TSD; (3) Given the role of task difficulty in previous research, it is hypothesized that the effects of task difficulty will be to accentuate the differences produced by TSD (Drummond et al., 2005). Specifically, the pattern observed in hypothesis 2 should produce a better fit after TSD when individuals encoded hard words compared with easy words.

METHODS

Participants

Twenty-three individuals participated in this study (11F; age = 24.2 ± 4.8 years; education = 15.2 ± 1.5 years). The study was approved by the local Institutional Review Board (the UCSD Human Research Protection Program), and it was completed in accordance with the guidelines of the Helsinki Declaration. All subjects provided written informed consent. Subjects were medically healthy, free of current and past psychiatric disorders, had no family history of mood or psychotic disorders, did not use nicotine in any amount, and were no more than moderate caffeine users (<400 mg/day). Polysomnography was used to rule out sleep disorders. Subjects reported habitually sleeping 7 to 9 hours per night between the hours of 22:00 and 08:00.
Networks of brain response

Experimental Periods

After two nights of sleeping in the laboratory on their habitual schedule, subjects were studied with functional magnetic resonance imaging (fMRI) twice, both at the same time of day: once 12 hours after waking from a normal night of sleep in the laboratory and once after 36 hours of no sleep (i.e., TSD). During each fMRI scan, subjects performed a verbal encoding task. Whereas a fixed order of scan session raises the possibility of order effects in the data, we have evaluated this possibility in the past and have found no evidence for such in this task (Drummond et al., 2000; Drummond et al., 2005).

Experimental Task

Stimuli were presented visually on a screen at the foot of the MRI bed that subjects viewed through a mirror fitted to the head coil. The alternating block design task consisted of two visually identical parts. During the entire task, subjects saw nouns presented one at a time, each for 4s followed by 1s of a fixation asterisk. For the baseline blocks, subjects were instructed to press a button on a hand held button box (Current Designs, Philadelphia) to indicate whether the word was printed in all capital or all lowercase letters. They were instructed to not memorize these words. Subjects were instructed to actively memorize the words presented during the memorization blocks, and they knew they would be tested on these words afterwards. After completion of the entire scanning session, subjects were given a free recall and recognition memory test. Unknown to the subjects, half of the memorization blocks contained words that are easy to learn, based on recallability norms, and half contained words that are hard to learn (Christian et al., 1978). A different word list was used for each administration (versions balanced across sessions), with lists matched for recallability, word length, concreteness, and imagery. Previous pilot studies showed that the versions provided similar recall rates in well-rested. A block design was selected for this study to maintain consistency with previous studies. In addition, because the goal was to detect overall differences between groups in different conditions, a block design allowed maximum statistical power (Friston, 1999). However, because of the use of this design, distinctions cannot be made between words that were later successfully encoded and words that were not. Thus, it is not clear to what extent changes in brain response would be driven exclusively by the successful encoding of words. An event related design would more effectively address that issue (Chee, 2003).

fMRI Data Acquisition

Data were acquired with a GE 3T scanner. Functional images consisted of 120 gradient echo. echoplanar, images (EPI) (TR: 2.5s, TE: 35 ms, FOV: 250 mm, 64 × 64 matrix, 3.91 mm × 3.91 mm in-plane resolution) of 32 4 mm axial slices covering the whole brain and measuring the blood oxygenation level dependent (BOLD) signal. The EPI images were aligned with high-resolution anatomical images (FSPGR: 1 mm³ resolution). The task contained 6 memoryzation and 7 baseline blocks. Each block started with directional prompts for 2.5 s and lasted a total of 22.5 s, and contained four nouns. Three images collected at the beginning of each run were omitted from the analysis. The entire task lasted 300 s.

Data Analysis

fMRI data were processed with AFNI software (Cox, 1996). After motion coregistration, individual time-course BOLD signal data were fit to a design matrix using the general linear model (GLM). Parameters estimated from the design matrix represented the constant, linear drift, 6 motion correction parameters, and two reference functions. The reference functions were representations of the task design (baseline vs. easy words and baseline vs. hard words) convolved with an idealized hemodynamic response function (Ward, 2002). The fit of the design matrix to the EPI time series produced an amplitude value for each reference function. The amplitude represented the mean difference in local scanner units between the learning and baseline conditions over the time series weighted by the hemodynamic response function. Data sets were then smoothed with a Gaussian filter of 4.0 mm full-width-half-maximum and transformed to standard atlas coordinates (Talairach & Tournoux, 1988). We used a 3-step procedure to identify the relevant activations for analysis. In the first step, we defined a set of hypothesis-driven search regions (Eyler-Zorrilla et al., 2003) based on the areas we expected to be critical for task performance either well-rested or following sleep deprivation. These search regions are based on our previous reports and were identical to those used in a recent manuscript we published with this task (Drummond et al., 2005). In the second step, we identified significant clusters of activation at the group level for each of the two difficulty types within these search regions. Clusters of activation were identified as areas containing at least 9 contiguous voxels (576 mm³) from areas activated at the p ≤ .05 level from the group analyses. This value produced a False Detection Rate of .05 against the population of detected clusters of any size. These clusters became the relevant functional ROIs used to extract data from each individual subject. Finally, we identified the peak activation within the significant clusters of each ROI for each individual. It is this peak value that subsequently went into the SEM analysis. This process produced a peak value within each of the specified search regions for each individual in each of the 4 conditions: (1) WR Easy: encoding easy words while WR, (2) WR Hard: encoding hard words while WR, (3) TSD Easy: encoding easy words after TSD, and (4) TSD Hard: encoding hard words after TSD.

Covariation matrices were calculated from the peak values and were used as the target data for structural equation models. Mx software was used to perform the structural equation modeling (Neale, 2003). We assessed model fit
with the Root Mean Square Error of Approximation (RMSEA) measure, as well as Akaike’s Information Criterion (AIC) (Browne & Cudeck, 1993). RMSEA does not assume a centralized chi-square distribution and neither AIC nor RMSEA assume the presence of a perfect fitting “true” model. RMSEA indicates overall model fit given the variability in the data, the parsimony of the model, and the number of subjects. It ranges from 0.0 to 1.0, with values below .05 indicating an excellent model fit and >.1 indicating a poor model fit (Browne & Cudeck, 1993). AIC places more value on parsimony and is one of the most commonly used fit statistics in the SEM literature. Smaller values indicate better fits, although the primary interpretation of the AIC index is through model comparison as opposed to absolute values (Burnham & Anderson, 1998).

RESULTS

A General Linear Model analysis of the number of words recalled with sleep status and word difficulty as within subject factors demonstrated a significant effect for both sleep status, $F(1,22)=6.24, p = .02$, and word difficulty, $F(1,22)=90.35, p < .01$, but not an interaction of sleep status and word difficulty, $F(1,22)=.017, p = .937$. After TSD, participants recalled fewer total words compared to when they were well-rested (mean difference = 2.26 words). For word difficulty, three fewer hard words were recalled than easy words, regardless of the sleep condition (mean difference WR = 3.0 words, and TSD = 2.91 words).

Correlations of individual peak values in each of the a priori ROIs revealed significant correlations after TSD between the left inferior frontal gyrus while encoding easy words and recall of easy words ($r = .425, p = .049$), as well as between the right inferior frontal gyrus while encoding hard words and total words recalled ($r = .456, p = .029$). An analysis of the peak values obtained from each individual for each of the a priori ROIs revealed that the majority of these values were significantly correlated across subjects, indicating that good model fits would explain a meaningful amount of variance. The correlations ranged from .164 to .746 with 23 out of 36 correlations significant with $p < .05$ (18 were significant with $p < .01$).

Table 1 shows the results of fitting each covariance matrix to the two models tested, presented separately for easy and hard items. Model 1 fits the easy word condition better than Model 2 for both WR and TSD, whereas Model 2 fits the Hard word condition better than Model 1 for both WR and TSD.

An examination of the relative strengths of the model connections within each item difficulty condition illustrates that TSD influences the pattern of interactions within the network. Because Model 1 and Model 2 share the same number of free parameters, comparisons can be made between strengths of connections within the best model fit for each condition. Examining the impact of removing specific connections and re-running the structural equation analyses evaluates the importance of that connection for overall model fit (Loehlin, 1998). Because the RMSEA is scaled to a standardized range of model fit, and all of the best fitting models start with values of 0.00, the change in RMSEA (delta RMSEA) was used to compare each connection’s contribution to the model’s ability to fit the data. Fig. 2 illustrates the impact of removing each connection on RMSEA for each of the best fitting models within task difficulty. As Figure 2 illustrates, there is a decrease in the relative importance of the connection between the left and right IFG after TSD and a concomitant increase in the importance of the connection from LSPL to LIPL for both easy and hard items. Additionally, the prominence of the interaction between the IFG (left or right) and the inferior parietal lobe is diminished after TSD, regardless of item difficulty. Finally, the right IFG connection with LSPL becomes more prominent after TSD for the hard word model. These findings underscore the conclusion that TSD produces a modulation of connectivity within the network that best fits the WR condition. This modulation occurs when no difference in activation between WR and TSD occur, as in the Easy condition, as well as when TSD alters the magnitude of activation, as in the hard condition.

In order to rule out the possibility that the influence of the RIFG is caused by an indirect effect of the right superior and inferior parietal lobes (which were not included in either a priori model), right inferior and superior lobes were identified and peak voxel values were calculated using the same procedures as for the other ROIs. Exploration of various combinations of models (by starting with a fully connected model and trimming connections if their removal did not increase the error in model fit) revealed that even with the presence of the right parietal areas, the RIFG maintained its importance as a feedback source for the left parietal areas when hard words were learned.
DISCUSSION

Model fit statistics confirmed that TSD coherently altered network connections rather than producing a less coherent network, confirming hypothesis 1. Compatible with hypothesis 2, TSD reduced the importance of inferior frontal to left inferior parietal links in accounting for the covariation among network nodes, whereas it increased the importance of the left superior parietal to left inferior parietal connection. Hypothesis 3 was not confirmed. Difficulty level did

Fig. 2. The reorganization of interactions after sleep deprivation
Panel A: Impact of removing the named connection on the Best Model’s Fit
Panel B: Summary of Sleep Deprivation’s Impact on Model Connections. Dashed lines indicate decreased strength following total sleep deprivation, solid lines indicate increased strength.
not generally potentiate the impact of TSD on the network of connections. Rather, the impact of TSD on network connections differed for easy and hard words, because learning networks differed depending on difficulty level. In particular, variation in item difficulty determined whether parietal areas interacted more with the LIFG or the RIFG while WR. Although the impact of TSD on network connections differed by difficulty level, some similar effects of TSD were seen for easy and hard words. Regardless of difficulty, interhemispheric interaction between the LIFG and RIFG decreased after TSD, and intrahemispheric communication between the LIPL and LSPL increased. Whereas it is not clear if this shift in the pattern of activation may be indicative of a compensatory response to TSD, it demonstrates a coherent change in the pattern of activation in response to TSD. It may also help explain why we previously found the left parietal cortex to be critical for task performance after TSD (Drummond et al., 2000; Drummond et al., 2005). The shift in RIFG interactions from LIPL to LSPL after TSD may indicate a change in encoding strategy, because the LSPL is less integrative than the LIPL (Cabeza & Nyberg, 2000). The SEM results are also consistent with the recall data, which indicated a large effect of word difficulty (associated with a different model fit) and a lesser effect of sleep status on the total number of words recalled (associated with changes in interactions within a good fitting model).

The results described earlier show that TSD and item difficulty differentially influence brain networks involved in verbal learning, at least for the small network of areas selected for analysis. TSD altered the strength of the connections within the best fitting models without altering the overall model fit. Item difficulty appears critical in determining the intrinsic connectivity of the involved networks. TSD appears to modulate the connectivity strength among established network connections, rather than establish new connections to previously uninvolved regions. The study findings support the view that TSD does not elicit activation in new brain areas, so much as it produces a modulation of connectivity within networks used when WR. According to this view, prior studies have found activations in “new” brain regions by altering the strength of connections within the network, thus, activating nodes that are latent when individuals are well rested. More broadly, these results shed an alternative light on imaging studies that interfere with established and contrasting network connections. Moreover, theoretically based a priori models do not capitalize on much on chance as do the exploratory model trimming approaches that are often used in the SEM literature (Horwitz et al., 1999; Horwitz, 2003; Horwitz et al., 2005; MacCallum, 1986). However, the models tested in this study are greatly simplified. Because of concerns about power and noise within the data, the smallest possible number of ROIs and connections were chosen based on previous research that contrasted WR and TSD brain response. In future studies we plan to use a larger number of participants, and gradually develop a more comprehensive model of encoding, including hippocampal and lateral temporal areas. The current study serves as a starting point to test more comprehensively developed a priori models in the future.

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REFERENCES


The Effects of Total Sleep Deprivation on Bayesian Updating*

David L. Dickinson
Dept. of Economics
Appalachian State University

Sean P.A. Drummond
Dept. of Psychiatry
Laboratory for Sleep and Behavioral Neuroscience
University of California—San Diego
Psychology Service
Veterans Affairs San Diego Healthcare System

ABSTRACT

Recent evidence suggests that nearly 25% of U.S. adults (47 million) suffer from some level of sleep deprivation. The impact of this sleep deprivation on the U.S. economy includes direct medical expenses related to sleep deprivation and related disorders, the cost of accidents, and the cost of reduced worker productivity. Sleep research has examined the effects of sleep deprivation on a number of performance measures, but the effects of sleep deprivation on decision-making under uncertainty are largely unknown. In this article, subjects perform a decision task (Grether, 1980) in both a well-rested and experimentally sleep-deprived state. We have two main results: 1) final choice accuracy is unaffected by sleep deprivation, and 2) the estimated decision model used is significantly different when sleep-deprived compared to well-rested. Following sleep deprivation, subjects weigh all sources of information to a lesser degree, but they also do not display the tendency to over-weight new information in forming beliefs. Because the altered decision process still maintains decision accuracy, it suggests that increased accident and error rates attributed to reduced sleep in modern society may result more from a decline in auxiliary functions (e.g., slowed reaction time, reduced motor skills), rather than the inability to process new information.

JEL Key Words: Bayes Rule, Uncertainty, Information, Experiments, Sleep.
JEL Codes: D81, D83, C91

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A large volume of evidence suggests that individuals in industrialized nations are becoming increasingly sleep-deprived. According to a recent poll conducted by the National Sleep Foundation, the average American adult slept less than 7 hours per night in 2005. The nightly average was 7.5 hours in 1975 and 9 hours per night in 1910. This trend towards less and less sleep has significant implications given the known effects of sleep deprivation: decreased motor and cognitive performance, reduced vigilance and reaction time, worsened mood, and reduced ability to think flexibly (Pilcher and Huffcutt, 1996; Harrison and Horne, 1999; Harrison and Horne, 2000). Indeed, even 7 hours of sleep per night leads to significantly diminished cognitive performance relative to 8 or 9 hours (Van Dongen, et al, 2003; Belenky, et al., 2003). Nearly 50 million Americans, close to 25% of all adults, are estimated to suffer from some level of sleep deprivation. Sixty percent of adults surveyed reported driving while drowsy, while 37% reported falling asleep or nodding off at some point while driving.\(^1\) Estimates of the cost of lost U.S. worker productivity caused by sleep deprivation vary, but a conservative estimate—based on a 4% reduction in productivity for sleep-deprived working adults—is over $40 billion dollars annually (Stoller, 1997).

Many occupations promote a culture of sleep deprivation, whether it be the use of shift work in factories or hospitals, or the need to alter sleep schedules to monitor real-time foreign financial market activity. Certain professions that give rise to more significant sleep deprivation as a matter of routine—emergency personnel, medical residents, military personnel, long-haul truck drivers—are also those where impaired functioning can put lives at risk. A study of long-haul truck drivers in Canada and the U.S. (Mitler, et al. 1997) found that they averaged only about 5 hours of sleep per night.

\(^1\) This data is reported by the *National Sleep Foundation*, and can be accessed at [www.sleepfoundation.org](http://www.sleepfoundation.org).
A recent study of first- and second-year medical residency students found that two-thirds reported sleeping an average of six or less hours per night (Baldwin, et al. 2004). A smaller fraction (20%) averaged five hours of sleep a night, and such residents were more likely to report, among other things, having made significant medical errors. Weinger and Ancoli-Israel (2002) concluded that sleep deprivation significantly impairs doctors’ performance, thereby impacting patient safety, in part due to poor decisions made by sleep deprived physicians. Also, sleep deprivation has been considered at least partially responsible for several major historical disasters, including the Space Shuttle Challenger explosion, the Exxon Valdez oil spill, and the Chernobyl Nuclear plant explosion (Coren, 1996). In sum, the impact of sleep deprivation on society as a whole, while difficult to measure precisely, is massive.

This paper reports results from a laboratory study that examines the information processing abilities of subjects in a well-rested versus an experimentally sleep-deprived state. Much of the existing sleep deprivation research examines subject performance on sustained attention, mathematical and/or verbal tasks, such as simple reaction time tasks, arithmetic processing, grammatical reasoning, or verbal learning. Examinations of flexible thinking, strategy updating, and risk assessment are relatively new to sleep research (see references in Harrison and Horne, 2000). There is some evidence that complex or interesting tasks may be less likely to show deficits under total sleep deprivation (e.g., Horne, 1988), but this remains a controversial proposition (Harrison and Horne, 1999; Pilcher and Huffcutt, 1992; Wimmer, et al, 1992).

Our present focus on Bayesian updating as a particular decision model is meant to examine the fundamentals of how information is processed by decision-makers. We
examine differences in subjects’ propensity to incorporate new information as they update prior probabilities to form posterior (subjective) probability estimates. A Bayes rule experiment is administered to subjects both well-rested and after 22-25 hours ($\mu=22.72$, $\sigma=.60$) of total sleep deprivation (TSD). For comparison to existing economics research, we utilize the Bayes rule experiment presented in Grether (1980). His results indicate that subjects tend to overweight new evidence relative to prior odds when forming subjective beliefs. The result, further confirmed in Grether (1992), is largely due to subjects’ tendencies to utilize a ‘representativeness’ heuristic in cases where new sample information looks representative of one population versus another (see, e.g., Kahneman and Tversky, 1972).

The results from our pooled sample (well-rested and sleep-deprived data) are quite similar to those in Grether (1980)—subjects tend to weight new evidence more heavily than the prior odds, which is contrary to the Bayes rule prediction. Notably, our data are consistent with a structural break in the decision model used by subjects following TSD, and the estimated decision model used after TSD is more consistent with the use of Bayes rule than the estimated well-rested decision model. This result may indicate that Bayesian updating is part of a basic decision process that remains intact when other processes become impaired due to sleep deprivation. Interestingly, the outcome measure we analyze reveals no significant difference in final-choice accuracy whether well-rested or following TSD. This indicates that similar decision accuracy is reached by means of distinct decision processes, and neither process is more effective than the other. There is, however, some evidence that decision model error terms have

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2 Grether (1992) indicates that the representativeness heuristic is used when available, and it is available a high proportion of the time in his earlier (1980) design. When not available as often in the (1992) experimental design, overweighting of new evidence is not borne out as a more general result.

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higher variance in the TSD subsample, which implies somewhat less consistent behavior under TSD.

Because information updating is a fundamental component of decision making under uncertainty, this unique examination of Bayesian updating following sleep deprivation is relevant to a large variety of behavioral applications. Our results are also important because they indicate that not all types of decision-making are necessarily impaired following acute TSD. The empirical data on increased accidents/errors due to sleep deprivation may ultimately result from impaired functioning in areas other than one’s ability to process new information.

2. Background

An examination of Bayesian updating under sleep deprivation contributes significantly to both the literatures in economics and sleep. Sleep research indirectly points towards failed information assimilation under sleep deprivation (e.g., increased hesitance and reduced focus among sleep-deprived junior doctors in Goldman et al, 1972). However, direct evidence on decision making under uncertainty and information updating is needed, and Harrison and Horne (2000) recognize the lack of sleep deprivation research on specific decision models. Bayes rule is a fundamental decision model of belief revision and decision-making under uncertainty, and it has application to a variety of contexts. The relevance of this research to economists stems from our desire to understand decision-making behavior, and the evidence indicates that a good portion of decision-makers are, in their typical state, sleep-deprived to some degree. So, any identified differences in behavioral responses relevant to economic decision-making
models highlight the significance of an individual’s sleep-deprived state in behavioral analysis. Such differences also identify a previously uncontrolled confound in experimental data sets (for example, student subject experiments during exam periods may include relatively more sleep-deprived subjects).

Only a small amount of economics research has examined sleep. Biddle and Hammermesh (1990) incorporate labor productivity effects of sleep in a theoretical model of the allocation of time. Their empirical results from a variety of sources lead them to conclude that increased labor market time reduces sleep, as opposed to leisure activities. Their estimates from a system of demand equations indicate that higher wages reduce sleep—more so for men than women. This is consistent with the aggregate evidence on sleep reduction in many industrialized countries, and it implies that sleep deprivation will be an inevitable byproduct of wage growth in a society.

Kamstra et al. (2000) examine the effects of daylight saving time changes on financial market returns. Interestingly, stock market returns drop both after losing an hour (Spring) and gaining an hour (Fall) of sleep. Reduced performance even after gaining an hour of sleep can be attributed to what sleep researchers call ‘desynchrony’, or being out-of-sync with one’s internal (biological) circadian rhythm. Somewhat relatedly, Saunders (1993) concludes that mood swings due to weather fluctuations have a significant impact on stock prices. Because sleep deprivation has been found to worsen mood even more than cognitive or motor performance (Pilcher and Huffcutt, 1996), some of the effects of sleep deprivation in our economy may be difficult to measure. As a whole, sleep is largely unexplored by economists, and we believe that this paper is a
significant first step towards understanding the effects of sleep reduction on fundamental decision-making processes.

Sleep deprivation can be either partial or total, where total sleep-deprivation implies no sleep at all during a given day(s) (i.e., one or more 24 hour periods). Intuition might suggest that total sleep deprivation impairs functioning more than partial sleep deprivation. If this were true then one might not feel as concerned about the average partially sleep deprived adult—a college student studying all night for an exam would be the exception. However, existing research indicates that there are just as many reasons to be concerned about the effects of partial sleep deprivation. Van Dongen et al. (2003) found that chronic partial sleep deprivation of 4 or 6 hours per night for as few as six consecutive nights resulted in significant deficits on cognitive performance. In fact, the deficits were equivalent to those from up to two nights of total sleep deprivation experienced by a separate treatment group. In other words, chronic partial sleep deprivation can cause performance deficits equivalent to those from 1-2 nights of zero sleep. And yet, partially sleep deprived subjects did not (subjectively) report feeling as sleepy as TSD subjects. Pilcher and Huffcutt (1996) also find that the average partial sleep deprivation study included in their meta-analysis reported evidence of significant performance and mood effects, and they note that these partial sleep deprivation effects have perhaps been underestimated in some narrative reviews of the sleep literature.  

Even when sleep deprivation might not affect some behavioral outcome measures, there is still much to understand about how underlying decision processes might be

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3 In this paper, we focus on the effects of TSD on information processing, which are relatively understudied compared to cognitive tasks of various sorts. There is another family of effects of sleep deprivation, which includes decreased glucose metabolism, increased risk of obesity, and decreased release of growth hormone, among others.
altered. Drummond et al. (2000) is an intriguing study that shows how versatile the brain can be under adversity. In their study, recognition memory on a verbal learning task showed no significant change as a result of a TSD treatment, though there was evidence that additional brain regions became activated following sleep deprivation. The subjects’ parietal lobes, especially in the left hemisphere, came ‘on-line’ after total sleep deprivation. Because the parietal lobes are related to performance, their activation after TSD compensated for any decreased performance resulting from deficits in other brain regions. Others have reported similar increases in brain activation and resultant intact performance during TSD on a variety of tasks (Drummond et al., 2001, 2004, 2005; Portas et al, 1998; Chee and Choo, 2004). Hsu et al. (2005) examine decision-making under uncertainty in a neuoeconomics experiment, and they suggest a multi-regional neural system for evaluating uncertainty.

For the present paper we only examine behavioral outcomes (not neural outcomes). The evidence we find in support of distinct decision-weights across sleep-states may, however, be a clue indicating neural activation differences in information-updating environments. For example, the ventrolateral prefrontal cortex has been implicated in the neural process of integrating new contingencies (Paulus, et al, 2004). Our finding that subjects decrease the decision weight placed on new evidence following TSD might indicate decreased activation of the ventrolateral prefrontal cortex. Studies of the Bayes rule decision task we use are absent in the neuro-imaging literature, but research on other tasks suggests that compensatory activation may occur in the parietal lobes following TSD, thus allowing performance to maintain intact (e.g., Drummond et al., 2000, 2001). Together, these results indicate that our understanding of decision-
making under sleep deprivation is incomplete at best, and more exploration is needed even in cases where individuals apparently retain functional ability. An analysis of our behavioral data following TSD is an important first step in this direction.

3) The Experiments

As noted, the experiments replicate the Grether (1980) design for a hand-run Bayes rule decision task, which we administer to one or two subjects at a time. Two bingo cages are each filled with six colored balls: Cage A is filled with four green and two red balls, and Cage B is filled with three red and three green balls. Six draws, with replacement, are to be made from one of the cages. Each subject was informed of a ‘prior’ probability of using Cage A in terms of a die roll. For example, a 1/3 prior odds of Cage A was implemented by informing the subject that Cage A would be used if the die roll was 1-2 (3-6 implied use of Cage B). Subjects did not see the actual die roll, but its result tells the experimenter from which Cage to make the six draws from behind an opaque divider. The subject was shown each draw from the bingo cage, and after six draws was asked to indicate whether the balls were drawn from Cage A or B. A correct cage response resulted in payment of $12, whereas an incorrect response paid $2.

The procedure—choose the cage, draw a sample of six balls, subject indicates cage used—was repeated six times, and subjects were informed that only one of these times would count for payment as determined by a random draw at the end of the experiment. The design was balanced across prior A odds of 1/3, 1/2, and 2/3.\(^4\) This creates a reasonably high proportion of samples, on average, that yield three or four green balls out of six, which are samples ‘representative’ of Cage B or A, respectively. This

\(^4\) One implementation accidentally utilized one instance each of the prior odds of 1/6 and 5/6.
allows for an examination of subjects’ propensity to utilize a ‘representativeness’ heuristic, or rule-of-thumb, decision process in making their cage decision. Note that because compensation is higher when correctly indicating the cage, it is incentive compatible to indicate Cage A only if subjects perceive the (posterior) probability of Cage A to be greater than 50%.

If subjects use Bayes rule in their cage choice, they will form a posterior probability that Cage A is used from the particular sample of green/red balls drawn--

\[
P(Cage\ A\mid\text{# green balls}) = \frac{P_A \cdot P(\text{# green balls}\mid Cage\ A)}{P_A \cdot P(\text{# green balls}\mid Cage\ A) + P_B \cdot P(\text{# green balls}\mid Cage\ B)},
\]

where \(P_i\) is the prior odds of the cage \(i\) being used. That is, the new sample information is used to update the prior probability of Cage A. Table 1 shows the Bayesian updated posterior odds of Cage A in this Grether (1980) design. If subjects use a representativeness heuristic to make their choice of which cage is used, then a sample draw of three or four green balls out of six will induce a choice of Cage B or A, respectively, simply because the sample drawn looks like the population of one of the cages. One can see from Table 1 that the use of the representativeness heuristic can lead to an incorrect cage choice. For example, the posterior probabilities indicate that Cage A is more likely when \(P_A=2/3\) and three green balls are drawn, but this sample looks like the Cage B population. Similarly, when \(P_A=1/3\) and four green balls are drawn, Bayesian updating would lead one to indicate that Cage B was used—the posterior probability of Cage A is less than 1/2. The design is balanced so that, on average, the proportion of representative samples should not bias accuracy in favor of (or against) Bayesian choices.
A total of 24 subjects were administered the Bayes rules experiment. These subjects participated in a total sleep deprivation study, which involved 6 consecutive nights and days in the Laboratory for Sleep and Chronobiology at the University of California-San Diego. Subjects were compensated several hundred dollars for the entire stay at the lab, but it was made clear to the subjects that these experiments afforded the opportunity to earn additional payments that were unrelated to their fixed compensation. Lab staff generally indicated that the subjects were more engaged in these Bayes rule experiments than in other cognitive task experiments in which they participated during their lab stay, and so the extra compensation appeared salient to the subjects. Subjects were tested on various cognitive dimensions during their entire lab stay, with testing occurring approximately every two hours. This basic Bayes rule experiment was performed twice by each subject (so, they had the opportunity to earn $12 twice); once in a well-rested state, and once after 22-24 hours of total sleep deprivation. Each administration of the Bayes rule experiment lasted approximately thirty minutes.

Screening criteria for this study only allowed subjects who were right-handed, healthy, and considered ‘normal’ sleepers—those who had a consistent sleep-wake schedules that included 7-9 hours in bed each night. Subjects are indirectly monitored for one week prior to reporting to the sleep lab by keeping a sleep journal and wearing an actigraph. Because we motivated the relevance of this research by indicating how

---

5 Though the sample size is small, multiple subject trials create a panel of N=144 well-rested and N=144 TSD observations. A small number of total subjects is quite common in sleep-deprivation studies, because of the screening criteria, the requirement that subjects stay in the sleep lab several days, and the total compensation per subject for a TSD experiment (often several hundred dollars per subject).

6 The actigraph measures wrist movement as a proxy of gross motor activity. This movement, in turn, is used to determine sleep and wake. These data verify that subjects are engaged in normal sleep patterns prior to their lab stay and are not partially sleep deprived at the beginning of the experiment. The complete list of experimental inclusion/exclusion criteria is fairly standard for sleep deprivation research, and they are available on request.
common it is to not be a normal sleeper, one may question the external validity of using only normal sleepers. As experimentalists, however, we face the usual trade-off of internal control versus external validity in conducting a sleep deprivation study. Only by using otherwise normal sleepers can we be confident of having removed other confounds that may limit our ability to attribute treatment affects to sleep deprivation itself. During sleep deprivation, subjects were not allowed any sleep, not allowed stimulants of any sort, and they were under constant supervision by lab staff to ensure no sleep during this time. Figure 1 describes the basic timeline of the subjects’ lab stay relative to their participation in these decision experiments.

In a more recent paper, Grether (1992) notes that there are limits to what can be gleaned from the data using his simpler 1980 design. Because the design favors generating samples that are representative of Cage A or B, we are somewhat limited in our ability to generalize towards instances in which new information is not necessarily representative. On the other hand, we chose the more simple design in order to present subjects the most straightforward decision task that involved prior and new-sample information. As stated above, this design also provides an efficient evaluation of the use of a representative heuristic compared to a Bayes rule in subjects’ decision making. The dichotomous choice of Cage A or B does not allow us to infer strength of belief (i.e., 55% versus 95% certain that the balls came from Cage A), as does Grether (1992) in a modified design. However, given the known debilitating effects of sleep deprivation on vigilance, we felt this was a reasonable trade-off in design choice in order to be more assured that subjects understood the decision task, even after total sleep deprivation.
The particular placement of our Bayes rule task during the subjects’ lab stay implies that all subjects complete their second Bayes rule decision task in their sleep deprived state. As such, one might be concerned that subject learning may be generating some of the data. To explore this possibility, the Bayes rule experiment was also administered to an additional twelve control subjects (N=144 total observations). These control subjects performed the Bayes rule decision task twice, at the same 22-24 hour interval, but the control subjects were well-rested in both instances. Decision model estimates for these control subjects (see Appendix) find no significant difference in the weight placed on the evidence during the second Bayes rule experiment—contrary to the main finding in the TSD data.

In other words, we find no evidence that the differences in decision-making we report in the next section are due to subject learning across the two administrations of the experiment. In addition, subject learning would imply that choice accuracy should be higher the second Bayes rule experiment, but it is not. Or, learning might imply that a particular empirical model should better fit the data as choices converge to a particular set of model parameters—Grether (1980) finds this among experienced subjects, for example. Our results also show that this is not the case. We are therefore confident in attributing the second trial effects to the sleep deprivation treatment.

4) Results

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7 Due to an un-planned deviation from the sleep lab protocol for these experiments, one subject was administered the Bayes rule task under the TSD treatment first, in which case the coding of the TSD dummy variable distinguishes this one subject from the others. Ideally, the ordering of the TSD and well-rested administration would be counter-balanced but, as described above, the surrounding evidence does not indicate that subject learning is generating the TSD treatment effects.
Our subjects ranged from 18 and 39 years of age ($\mu=23.83$, $\sigma=5.37$), and each gave voluntary consent for the total sleep deprivation study. Because each Bayes rule experiment involves 6 trials of the cage choice task, the total number of observations generated by our 24 subjects is $N=288$ ($N=144$ in the well-rested state and $N=144$ in the sleep deprived state). The econometric estimations reported in this section account for the potential non-independence of decisions of a given subject across different trials as a subject-specific random effect, but our results are robust to error-term specification.

Table 1 shows the posterior probabilities of Cage A, which imply posterior odds of either Cage A or B being more likely. For example, the posterior probability of Cage A of .584 indicates a posterior odds of Cage A of approximately 1.40:1. Certain prior odds and sample draws imply a relatively easier choice for the subject in the sense that the posterior odds of the more likely cage are quite high (e.g., if $P_A=1/3$ and only one green ball is drawn, the posterior odds of the more likely cage (Cage B in this case) are about 11:1. The bold cells in Table 1 highlight the sample possibilities for Cage A that lead to the most difficult choices among all possibilities. These highlighted cells represent all instances when posterior odds of the more likely choice are about 1.40:1 (some in favor of Cage A, some in favor of Cage B). Grether (1980) initially restricts attention to this subsample of data in order to compare choices of equal difficulty that include cases where the representativeness heuristic favors the right choice, cases where it favors the wrong choice, and cases where it provides no direction on cage choice.

Table 2 shows the summary data for this subsample of cases of relatively difficult subject choices. Interestingly, a breakdown of the TSD versus well-rested data indicates that, after TSD, subjects get a significantly higher proportion of responses correct when
the representativeness heuristic favors the Bayesian updated cage choice (p=.10). When well-rested, a higher proportion of difficult choices are correct when representativeness is not available or at odds with the Bayesian updated choice, although these differences are not significant. This subset of the data also shows evidence consistent with some of the sleep deprivation literature, which has found that performance (i.e., accuracy) does not necessarily decline under TSD when the task is interesting and/or financially motivated (see Harrison and Horne, 2000). However, a simple look at the percentage of correct choices in Table 2 examines only a subsample of less than half of the total data. Furthermore, a model of the posterior probability estimates is necessary in order to identify any general difference in the decision model used by the subjects. Such a difference is implied if subjects apply compensatory effort following TSD.

A more complete analysis of subject choice is shown in Table 3. Here, following Grether (1980) for comparison, we estimate the following decision model:

\[
Y^*_it = \alpha + \beta_1 \ln LR(A)_t + \beta_2 \ln \left( \frac{P_A}{1-P_A} \right)_t + \mu_i + \epsilon_{it}
\]

where \( Y^*_it \) is the subject \( i \)'s subjective log odds in favor of Cage A in trial \( t \), \( LR(A)_t \) is the likelihood ratio for Cage A, and \( P_A/1-P_A \) is the prior odds ratio for Cage A. The dichotomous variable \( Y_it \) is observed equal to 1 if \( Y^*_it > 0 \), and so we estimate (1) using a random effects probit estimation. Grether (1980) estimates logit results for this model, and does not account for subject-specific random effects, and so our econometric

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\( ^8 \) We use a binomial test of the null hypothesis that the proportion of correct choices in TSD subsample is equal to the proportion of correct choices in the WR subsample. We avoid testing this hypothesis in case C, when the representativeness heuristic is unavailable, due to extremely low number of cases (N=2) in the WR data.
specifications are similar but not identical. A Bayes rule hypothesis amounts to testing jointly whether $\alpha=0$, $\beta_1=\beta_2>0$, while the representativeness heuristic would be supported if $\beta_1>\beta_2\geq0$. In other words, a Bayesian subject will weight the evidence and the prior odds equally, while a subject who uses the representativeness heuristic would place more weight on the evidence than the prior odds of cage A. The basic findings of Grether (1980), who estimates a version of (1) as a logit model, support the representativeness heuristic hypothesis. That is, $\beta_1>\beta_2\geq0$ for most of his subject groups, indicating that subjects overweight the evidence (i.e., the likelihood ratio) relative to the prior odds.

Table 3 shows our random effects probit estimation of model (1) for our subjects, though our results are robust to estimation of a fixed effects model as well.9 A test for structural change is performed on the data to test whether or not the same model parameters ($\alpha$, $\beta_1$, and $\beta_2$) apply to the well-rested and TSD data. Using the likelihood ratio test on the restricted model of pooled data and the unrestricted models of the separate TSD=1 and TSD=0 subsamples, we reject the null hypothesis that a single set of model parameters applies to both sets of data (the chi-squared statistic=13.36—significant at the $p=.01$ level for the test of three restrictions). Thus, the results indicate a structural change in the parameter estimates following TSD, and so we next turn our focus to the model estimates for the separate well-rested and sleep-deprived subsamples.

As noted earlier, results from additional control subjects do not support the hypothesis

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9 For comparison to Grether’s (1980) logit estimations, we also perform a logit estimation of the model similar to (1) above, but without the random effects error-term specification. The pooled results that Grether reports for his financially motivated subjects yield the estimated model $Y_{it} = -.11 + 2.25 \ln LR(A)_{it} + 1.82 P_A(1-P_A)_{it}$, where $\alpha$, $\beta_1$, and $\beta_2$ are statistically significant. In estimating the same logit model for our pooled data, the results are $Y_{it} = .04 + 2.26 \ln LR(A)_{it} + 1.95 P_A(1-P_A)_{it}$ with $\beta_1$ and $\beta_2$ being statistically significant ($p=.00$). So, our results are quite comparable to those reported in Grether (1980), and logit estimations of any of the models in this section are consistent with the results we find in the probit estimations that we report. The results we find are also similar for a fixed effects specification (logit and/or fixed effects estimation results available from the authors on request).
that the differences in the well-rested and TSD data are due to subject learning. The supporting evidence from these control subjects is given in detail in the Appendix.

One difference that stands out in Table 3 is that well-rested subjects place more weight on the evidence than the prior odds. This difference is statistically significant using the chi-squared test for the restriction that $\beta_1 = \beta_2$ ($p=.06$). When subjects are well-rested, the estimated decision model replicates a key result from Grether (1980) using the same basic experimental design. When sleep-deprived, however, there is no significant difference in the weight the subjects place on the prior odds versus the sample evidence ($p=.91$). Sleep deprivation reduces the weight the decision-maker places on the evidence relative to the prior odds. Ironically, the decision model under sleep deprivation is consistent with the Bayes rule hypothesis, because sleep deprivation apparently eliminates the over-weighting that well-rested subjects tend to place on the evidence. In all cases, the models do a reasonably good job of predicting the Cage A and Cage B choices of the subjects, correctly predicting their choice between 83% and 85% of the time.  

In additional to the coefficient estimates, the estimated marginal effects are shown in Table 3 for interpretability. Consider the marginal effect on the log odds term, $\ln\left(\frac{P_A}{1-P_A}\right)$. With our particular experimental parameterization, this term increases by about one when comparing $P_A=1/3$ to $P_A=2/3$. So, the marginal effects of .54 and .34 for...
the well-rested and TSD data, respectively, imply that this increase in prior odds makes subjects 54 percentage points more likely to choose Cage A when well-rested, but only 34 percentage points more likely to choose Cage A when sleep-deprived. This difference between marginal effects on the log odds terms may not be statistically significant, however. Consider an alternative formulation for the pooled data set with a dummy variable for TSD=1, along with interaction terms

\[
Y_{it}^* = \alpha + \beta_1 \ln LR(A) + \beta_2 \ln \left( \frac{P_A}{1-P_A} \right) + \beta_3 \ln \left( \frac{P_A}{1-P_A} \right)^* TSD_{it} + \beta_4 \ln LR(A)^* TSD_{it} + \beta_5 \ln \left( \frac{P_A}{1-P_A} \right)^* TSD_{it} + \mu_i + \epsilon_{it}
\]

We estimate this random effects probit specification to allow a more direct parameter estimate comparisons. The results are:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$\alpha$</th>
<th>$\beta_1$</th>
<th>$\beta_2$</th>
<th>$\beta_3$</th>
<th>$\beta_4$</th>
<th>$\beta_5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marginal effect</td>
<td>.07</td>
<td>.91</td>
<td>.58</td>
<td>-.09</td>
<td>-.56</td>
<td>-.24</td>
</tr>
<tr>
<td>p-value (two-tailed test)</td>
<td>.64</td>
<td>.00***</td>
<td>.00***</td>
<td>.61</td>
<td>.00***</td>
<td>.23</td>
</tr>
</tbody>
</table>

These estimates are consistent with Table 3 results in showing that the tendency to significantly overweight the evidence ($\beta_1 > \beta_2$) is mitigated when the subject is sleep deprived ($\beta_4 < 0$). The coefficient on $\beta_5 < 0$ is in the direction indicating that sleep deprivation significantly reduces the weight one places on the prior odds, but the estimate is not statistically significant.\(^{11}\)

\(^{11}\) For a similarly estimated logit model, $\beta_5$ significance is at $p=.12$. We also examine the relative difficulty of the different choices subjects would make, as proxied by the Bayesian posterior-odds of the more likely choice—higher odds represent an easier choice. As expected, we find that more difficult choices reduce the likelihood that subjects pick the correct cage. However, the TSD treatment does not significantly affect subject choice-accuracy, neither in general—noted earlier—nor for varying difficulty levels of choice, relative to when subjects are well-rested. These results are available from the authors on request.
The marginal effect on the evidence, $\ln LR(A)$, term in Table 3 represents the marginal change to the probability of choosing cage A for a one-unit change in the log-likelihood ratio for Cage A. For our design, a sample of two green and four red balls, for example, generates a likelihood ratio of -1.05, while a sample of three green and three red balls generates $\ln LR(A) = -.353$, which is an increase in $\ln LR(A)$ of about .70. The estimated marginal effect for well-rested subjects implies that this change in $\ln LR(A)$ from drawing one additional green ball would make subjects 57 percentage points more likely to choose Cage A. For sleep-deprived subjects the comparative marginal effect is only about 25 percentage points. Of course, this does not take into account the fact that 'representative' samples may affect decisions independent of their effect on the likelihood ratio, but it is clear that these effects are behaviorally, as well as statistically, significant. The different sample draws in our experiment created a range of likelihood ratios from $\ln LRA(A) = -2.50$ for the case where six red balls were drawn, to $\ln LRA(A) = 1.73$ for the case where six green balls were drawn, though the extreme draws were rare.

These differences in the parameter estimates for the decision models when comparing subjects well-rested versus sleep-deprived are significant given that they indicate that TSD causes subjects to place a decreased decision-weight on new evidence and on prior odds. The estimated effect is significant in the case of the likelihood ratio (i.e., the evidence), and the effect is robust to model specification (compare sub-sample estimates in Table 3 with estimates of model (2)). We also estimate that TSD reduces the decision-weight that subjects place on the prior odds, though the effect is not as large in magnitude and did not reach statistical significance.
It is intriguing, however, that the accuracy of the subjects’ choices is no worse when sleep-deprived than when well-rested, on average. For all N=144 observations of both well-rested and TSD data, subjects indicated the correct cage 67-68% of the time.\textsuperscript{12} Our model estimates indicate that less weight is placed on both prior odds and new information following TSD. To the extent that weighting both sources of information increases accuracy, TSD should therefore reduce choice accuracy. However, TSD also eliminates the significant overweighting of the new information, and this should increase choice accuracy. By removing a tendency to perhaps over-think the problem, TSD appears to provide the necessary compensation for its own harmful decision effects.

For our control subjects, we find that choice accuracy drops for the second administration of the task (75% to 56% accuracy). This is consistent with the hypothesis that the maintained choice accuracy following TSD results from compensatory effort of some sort. Research on sleep deprivation has found that the underlying cognitive process may be quite different even though task performance is unaffected (Drummond et al., 2000). The different parameter estimates of our decision model are likely an important first clue to the type of cognitive process change that results from TSD.

An examination of the residuals from estimating (1) indicate that the TSD sample yields somewhat higher-variance residuals, though the difference is not statistically significant (two-sample F-test for variance, p=.20). This may suggest that choices following TSD are not as convergent upon the decision model in (1) as when well-rested. Though our residuals-variance result is statistically insignificant, it is similar to Grether’s

\textsuperscript{12} Choices and accuracy are not consistent with random decisions. In the well-rested subsample, the actual Cage A frequency is 54.2%, and subjects chose Cage A 52.8% of the time (actual accuracy was 68.1%). In the TSD subsample, Cage A frequency was 43.8%, and Cage A choice occurred 46.5% of the time (67.4% accuracy).
(1980) finding of less consistent behavior for inexperienced subjects. Our lack of significance may be due to our limited sample size, but the result is consistent with results in the sleep literature that indicate increased variability and statistical variance under TSD.

It is also worth noting that our result of unaffected choice accuracy in the Bayes rule experiment following sleep deprivation only implies that subjects are equally accurate in assessing the likelihood of being in state A versus state B. This does not imply that a TSD subject is as adept at dealing with any further ramifications of being in one state versus the other. This latter consideration will also be a function of TSD effects on factors like vigilance and reaction time. Furthermore, because the Bayes rule experiment does not allow subjects to sort themselves out of the uncertain choice environment, it is important to complement these research findings with an examination of preferences for risk. Such an examination is the topic of some of our related research.

5. Conclusions

The topic of sleep deprivation is virtually unexplored in research on economic decision models. Because of the evidence indicating that, as a society, we are more sleep deprived at present than in any previous generation, the implications this has on decision-making under uncertainty across many environments are worth exploring. Not only is the impact of sleep-deprivation significant to an economy (e.g., lost worker productivity), but any adverse effects of sleep-deprivation take on increased significance in certain susceptible labor markets when one considers the public health/safety ramifications (e.g., medical residency, long-haul truck driving, the military). Because recent sleep research
indicates that performance of selected tasks may be just as affected under chronic partial
sleep deprivation as under total sleep deprivation (Van Dongen et al., 2003), the effects
of sleep deprivation on decision-making are not likely to be limited to only the short-term
totally sleep deprived individual.

This paper examines the effects of sleep deprivation on a particular type of
decision-making that is of interest to decision scientists, in general, and is unexplored by
sleep researchers. We administer a Bayes rule decision experiment to subjects in
experimentally controlled well-rested and sleep-deprived states. Because the general
population does not exactly fit either of these experimentally induced states, the results
can be viewed as indicative of the decision processes of a given individual when
approaching either the well-rested or TSD state. This decision experiment provides a
fundamental look at how subjects process and filter information in uncertain choice
environments. That is, a Bayesian subject is assumed to update a prior belief with new
information on a situation in order to form a posterior belief of event occurrence. So, the
experiment examines a basic decision model that may serve as a building block for many
more complicated decision environments.

We find that that, following sleep deprivation, subjects no longer overweight new
information in forming subjective probability estimates\(^{13}\), which ironically makes their
behavior more consistent with Bayes rule than when subjects are well-rested. There is
also some indication that, following TSD, subjects reduce the decision weight placed on
prior odds (i.e., prior information), although this is somewhat less conclusive. In terms of
the experimental outcome measure, we find that choice accuracy is statistically

\(^{13}\) Grether (1980) finds this overweighting of the evidence among a typical sample of student subjects in his
design that we replicate.
equivalent when well-rested versus sleep-deprived. Together, these results indicate that sleep deprivation may reduce the natural tendency to over-think the problem, thus mitigating the negative decision effects that one might typically associate with sleep deprivation.

For the experimental economist, these results indicate that there may be an important confound in laboratory data for certain types of experiments. For example, neuro-economists who compete with other neuro-scientists for the use of scanning equipment may conduct experiments at abnormally late evening hours when subjects would be especially tired. Another example is if experiments are conducted during exam week, when student subjects might be function on less sleep than normal. Sleep deprivation may be an unidentified confound in the behavioral (and neural) data generated in such circumstances.

Our results may suggest that Bayes rule is a fundamental decision process that remains intact under adverse conditions. The result is also significant in today’s modern sleep-deprived society. Though there is ample documentation of the detrimental effects of TSD on cognitive and motor skills, and certain decision tasks, the present results (showing intact decision performance through an adapted decision model) suggest that not all decision-making is negatively affected by TSD. This is an important finding because it suggests that increased accident and error rates attributed to sleep deprivation may have more to do with auxiliary function impairment (e.g., reduced vigilance, reaction times, or short-term memory) than the ability to process new information.

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14 If students, on average, are more sleep deprived than the general population as survey data suggests, then the data from any experiments using student subjects will contain sleep deprivation related confounds.
Our experiment involves an unavoidable risky decision environment. Some of our related research shows evidence that sleep-deprived subjects are less risk-averse for gambles over monetary gains. As such, further research is needed to examine potentially interesting secondary effects of sleep deprivation. Namely, a TSD individual may be less likely to avoid a risky decision environment, when the opportunity to sort oneself out of the decision exists. Sleep deprivation may therefore lead individuals to choose more risky decision environments, on average. Though we find error rates to be unaffected by TSD, the cost of each error may be higher in a riskier scenario. This has interesting implications for, among others, military personnel choosing to engage or not engage in a riskier outcome scenario, or a physician choosing between two courses of surgical action.

Because we find that subject decision accuracy in the Bayes rule experiment is unaffected by TSD, the finding of significant differences in estimated decision models for subjects whether well-rested or sleep-deprived merits further exploration. Such results are likely an important first step towards understanding how the brain processes information and how it reacts to adversity. Some emerging neuroeconomics research suggests that certain brain regions form a neural system for evaluating uncertain decision environments (Hsu et al, 2005). Other neuroimaging studies support the hypothesis of compensatory brain activation (e.g., Drummond et al., 2000, 2001, 2004, 2005; Portas et al, 1998; Chee and Choo, 2004). Our findings may be an initial indication of compensatory neural activity following TSD that we intend to explore further.

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15 The hypothesis of compensatory activation following TSD is supported not only by existing sleep research, but also by our finding that choice accuracy in our well-rested control subjects is actually lower during the second administration of the experiment, though subjects are still well-rested.
Table 1: Posterior probabilities of Cage A

<table>
<thead>
<tr>
<th>Prior probability of Cage A</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/3</td>
<td>.149</td>
<td>.260</td>
<td><strong>.413</strong></td>
<td><strong>.584</strong></td>
<td>.737</td>
<td>.849</td>
<td>.918</td>
</tr>
<tr>
<td>1/2</td>
<td>.081</td>
<td>.149</td>
<td>.260</td>
<td><strong>.413</strong></td>
<td><strong>.584</strong></td>
<td>.737</td>
<td>.849</td>
</tr>
<tr>
<td>1/3</td>
<td>.042</td>
<td>.081</td>
<td>.149</td>
<td>.260</td>
<td><strong>.413</strong></td>
<td><strong>.584</strong></td>
<td>.737</td>
</tr>
</tbody>
</table>

Table replicated from Grether (1980) Table 1. Bold cells represent approximately equal posterior odds of the more likely Cage (i.e., choices of approximately equal difficulty for subjects).

Table 2

Proportion correct by sample type when posterior odds are approximately 1.40:1 (subsample of data: \(N_{\text{well-rested}}=60, N_{\text{TSD}}=62\))

<table>
<thead>
<tr>
<th></th>
<th>Well-rested</th>
<th>Sleep Deprived (TSD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A&lt;sup&gt;a&lt;/sup&gt;</td>
<td>B&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>.52 (N=27)</td>
<td>.58 (N=31)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Weighted average=.57</th>
<th>Weighted average=.57</th>
</tr>
</thead>
</table>

a. Representativeness heuristic favors Bayesian updated cage choice  
b. Representativeness heuristic does not favor the Bayesian updated cage choice  
c. Representativeness heuristic not available.
Table 3: Probit estimates of $Y_{it}^*$ model  
(random effects specification. p-values given in parenthesis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pooled (N=288)</th>
<th>Well-rested (N=144)</th>
<th>Sleep-deprived (N=144)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coeff. marg. effect</td>
<td>Coeff. marg. effect</td>
<td>Coeff. marg. effect</td>
</tr>
<tr>
<td>Constant</td>
<td>.03 (.83) .01 (.83)</td>
<td>.13 (.42) .05 (.42)</td>
<td>-.08 (.68) -.03 (.68)</td>
</tr>
<tr>
<td>lnLR(A)</td>
<td>1.27 (.00)*** .48 (.00)***</td>
<td>2.20 (.00)*** .81 (.00)***</td>
<td>1.01 (.00)*** .36 (.00)***</td>
</tr>
<tr>
<td>ln($\frac{P_A}{1-P_A}$)</td>
<td>1.10 (.00)*** .42 (.00)***</td>
<td>1.46 (.00)*** .54 (.00)***</td>
<td>.97 (.00)*** .34 (.00)***</td>
</tr>
<tr>
<td>% correctly predicted</td>
<td>84.38%</td>
<td>85.42%</td>
<td>83.33%</td>
</tr>
</tbody>
</table>
FIGURE 1
A week in the sleep lab: time-line

Note: Some subjects stayed in the lab one less day and participated in a one-night TSD study. Our examination of TSD effects after one night of TSD allows us to combined subjects from different sleep studies, whether or not they participated in a one or two night TSD lab stay.
REFERENCES


Appendix: Control Subject Data

The experimental protocol was administered to an additional twelve subjects, who were well-rested for both the first and second administration of the Bayes rule experiment—well-rested was verified using similar measures as for the sleep deprivation subjects, and average subject age was similar to non-control subjects ($\mu=24.12$ years old, $\sigma=4.278$). The results of estimation equation (1) from the text for the sample of $N=144$ Bayes rule decisions are shown in Table A1 below.

Table A1: Probit estimates of $Y^*_R$ model for CONTROL SUBJECTS
(random effects specification. p-values given in parenthesis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pooled (N=144)</th>
<th>marg. effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>0.02 (.88)</td>
<td>0.01 (.88)</td>
</tr>
<tr>
<td>$\ln LR(A)$</td>
<td>1.62 (.00)***</td>
<td>0.63 (.00)**</td>
</tr>
<tr>
<td>$\ln \left( \frac{P_A}{1-P_A} \right)$</td>
<td>1.47 (.00)***</td>
<td>0.58 (.00)***</td>
</tr>
</tbody>
</table>

As can be seen, results are similar to those from the main data set, except that the estimated weights on evidence and prior odds are somewhat higher. Estimation up to an unknown scale parameter, however, prohibits a direct comparison across models. A test for structural change in the data across the first- and second-administration fails to reject the null hypothesis that the same parameter estimates apply to both the subsamples of first- and second-administration of the experiment (the Likelihood Ratio statistic is 1.772 compared with the 90% critical value of 6.25 for the $X^2$ statistic for $n=3$ restrictions). This constrasts with the results from the well-rested and TSD subsamples of the main data. Control subjects who are not sleep-deprived for the second administration of the task fail to display a significant difference in the estimated decision model across the two administrations of the task. In other words, the differences found in the main data appear to be a result of the sleep deprivation treatment as opposed to learning from first to second administration of the experiment.

These results are robust to alternative examinations of the control subject data as well. For example, we might also estimate a model similar to (2) in the text. That is, the pooled control-subject data is analyzed with dummy variables for second-administration of the experiment, with interaction terms that allow for the second-administration effects to potentially differ with respect to decision weights on evidence and prior odds. Thus, we estimate
\[ Y_{it}^* = \alpha + \beta_1 \ln LR(A) + \beta_2 \ln \left( \frac{P_A}{1 - P_A} \right)_{it} + \beta_3 * 2\text{ndAdmin}_{it} + \]

\[ \beta_4 (\ln LR(A) * 2\text{ndAdmin}_{it}) + \beta_5 \left[ \ln \left( \frac{P_A}{1 - P_A} \right)_{it} * 2\text{ndAdmin}_{it} \right] + \mu_i + \varepsilon_{it} \]

(1A)

The results are:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(\alpha)</th>
<th>(\beta_1)</th>
<th>(\beta_2)</th>
<th>(\beta_3)</th>
<th>(\beta_4)</th>
<th>(\beta_5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marginal effect</td>
<td>-0.004</td>
<td>0.55</td>
<td>0.60</td>
<td>-0.30</td>
<td>0.27</td>
<td>0.01</td>
</tr>
<tr>
<td>p-value (two-tailed test)</td>
<td>0.96</td>
<td>0.00***</td>
<td>0.00***</td>
<td>0.30</td>
<td>0.22</td>
<td>0.97</td>
</tr>
</tbody>
</table>

The only significant variables are the prior odds and the evidence (we fail to reject the null hypothesis that \(\beta_1=\beta_2\), \(p=0.75\)). The second administration of the Bayes rule task does not significantly affect the likelihood of choosing Cage A. The results are also unchanged if one considers a model of the entire pooled data set (main data and control subject data), with dummy variables for TSD, 2nd administration of the task for control subjects, and interaction terms. The only significant variables remain the \(\ln LR(A)\), \(\ln \left( \frac{P_A}{1 - P_A} \right)\), and the interaction of TSD and \(\ln LR(A)\).

In short, the data indicate that there are no significant differences in the control subjects’ decision model from one day to the next. It is also noteworthy that the control subjects were correct in their cage choice 76% of the time during the first administration of the experiment, but only 61% of the time in the second administration. Recall that the main data show maintained accuracy levels when comparing subjects well-rested versus sleep-deprived. This evidence is in support of our conclusions that the sleep deprivation treatment, not learning, is generating the behavioral differences we estimate in the main text. The data are also consistent with the hypothesis that there is compensatory effort engaged following sleep deprivation that helps maintain choice accuracy, though the mechanism involved cannot be fully explored in the current data.
RECOVERY OF BEHAVIORAL PERFORMANCE FOLLOWING 64 HOURS OF TOTAL SLEEP DEPRIVATION
Salamat JS, Chen T, McKenna BS, Orff HJ, Drummond S
(1) Research Services, VA San Diego Healthcare System, San Diego, CA, USA, (2) Joint Doctoral Program in Clinical Psychology, SDSD/UCSD, San Diego, CA, USA, (3) Psychology, VA San Diego Healthcare System, San Diego, CA, USA, (4) Department of Psychiatry, University of California, San Diego, San Diego, CA, USA

Introduction: Individuals typically show some behavioral impairment during total sleep deprivation (TSD). Less clear is how long it takes to recover behavioral performance after a given length of TSD. We examined the effects of 64 continuous hours of TSD and recovery sleep on performance on three tasks.

Methods: Forty healthy subjects (22M, age=24.0 ± 4.9yrs., edu=15.3 ± 1.7yrs) were studied for five days in the lab and underwent five conditions: baseline sleep (BSL), two days and nights TSD (TSD1, TSD2), and two full nights of recovery sleep (REC1, REC2). An arithmetic working memory (Math) task, verbal learning task (VL), and the PVT were administered the same times each day at two (AM) and twelve (PM) hours post BSL wake-up time.

Results: Performance showed a main effect of condition on all tasks (all p<.001), deteriorating steadily from BSL through TSD. Only VL showed an interaction between time of day and condition, with impairment (words recalled) being greater for AM than PM testing during TSD. Performance on both Math (accuracy) and VL PM (but not AM) recovered to BSL levels during REC1 (p>.09). Both VL AM and PM recovered, and actually showed improvements over BSL, by REC2. In contrast, PVT performance (lapses and speed of slowest 10% responses) did not recover to BSL after either REC1 or REC2 (all p<.05).

Conclusion: Time of day only affected VL performance, with AM testing showing more deterioration and slower recovery than PM testing. While complete recovery to BSL performance levels was seen on Math (after REC1) and VL (after REC2), PVT performance never returned to BSL, even after two full nights of recovery sleep. These results suggest performance on tasks measuring different cognitive domains recovers at significantly different rates following 64 hours TSD.

Support (optional): 1. US Army DAMD17-02-1-0201 2. UCSD GCRC M01 RR00827
RISK TOLERANCE AND DECISION MAKING DURING TOTAL SLEEP DEPRIVATION

Drummond SP,1,2,4 Dickinson DL,3 Orff HJ,4,5 McKenna BS,3
(1) Psychiatry, University of California San Diego, San Diego, CA, USA, (2) Psychology, Veterans Affairs San Diego Healthcare System, San Diego, CA, USA, (3) Economics, Appalachian State University, Boone, NC, USA, (4) SDSU/UCSD Joint Doctoral Program, San Diego, CA, USA, (5) Research, Veterans Affairs San Diego Healthcare System, San Diego, CA, USA

Introduction: Sleep deprivation appears to impair decision making. However, many studies have used complex multimodal decision tasks. Thus, they cannot identify which aspect(s) of decision making is impaired. We examined the effects of one night sleep deprivation on risk tolerance in decision making.

Methods: Subjects (n=20, 7F, age=23.1 ±4.6 edu=14.9 ±1.7) performed a lottery choice task both well-rested (WR) and after 22-23 hours total sleep deprivation (TSD). Subjects made a series of choices, each one between a safer and a riskier gamble involving either gains or losses of money (but never both) with known probabilities. At the end of the study, gambles were randomly played out and subjects were paid based on the outcomes. We analyzed the proportion of risky choices across the four conditions.

Results: The proportion of riskier choices made (i.e., preference for risk) was: WR gains =.25, TSD gains =.41, WR losses =.81, TSD losses =.70. The 2x2 ANOVA (night vs gain/loss) showed a significant interaction [F(1,19)=9.35, p=.006]. Risk tolerance for gains increased with TSD, while risk tolerance for losses decreased.

Conclusion: WR subjects responded as predicted by Prospect Theory. For gambles with known odds, they showed risk aversion for gains and risk seeking for losses. Following TSD, subjects became less risk averse for gains and less risk seeking for losses. These data suggest that, overall, individuals become less sensitive to risk with TSD. With TSD, subjects moved towards a risk-neutral position, meaning that risk may have played a smaller role in their decisions. Relative to their risk preferences when well-rested, during TSD, individuals become less conservative (take greater risk) when they stand to gain, but more conservative (take less risk) if they stand to lose. These data hold major implications for settings where safety and lives are at stake, as well as for fiscal settings.

Support (optional): DAMD17-02-1-0201; National Academy of Sciences; UCSD GCRC M01 RR0082; ONR Stress Physiology Program Work Order N00014-04-AF-00002
CEREBRAL ACTIVATION DURING 60 HOURS TOTAL SLEEP DEPRIVATION: COMPENSATORY FAILURE ON THE SECOND NIGHT

Drummond SP,1,2 Wetherell LA,1,3

(1) Psychiatry, University of California San Diego, San Diego, CA, USA, (2) Psychology, Veterans Affairs San Diego Healthcare System, San Diego, CA, USA, (3) Research, Veterans Affairs San Diego Healthcare System, San Diego, CA, USA

Introduction: We have previously reported 36 hours total sleep deprivation (TSD) increases brain activation as measured with functional MRI (FMRI) during a verbal learning task. It remains unclear, though, for how many hours of TSD the brain can continue to compensate. Here, we examine this question by measuring brain activation with FMRI throughout 60 hours TSD. We hypothesized the brain would show compensatory recruitment during the first TSD night, but be unable to compensate for a second night of TSD, thus showing decreased activation relative to baseline.

Methods: 26 subjects (13F, age=26.6 ±5.4; edu=15.2 ±1.7) participated in a 6 night/day protocol, including two consecutive nights each of the following: baseline sleep, TSD, and recovery sleep. These analyses focus on a verbal learning task performed during FMRI 12 hours after waking from normal sleep (NORM), and at the same time of day after each TSD night (TSD1: 36hrs, TSD2: 60hrs). Due to our specific hypothesis, we analyzed the data for a negative quadratic trend: increased activation from NORM to TSD1 and decreased activation from TSD1 to TSD2. Whole brain alpha = .05.

Results: Several brain regions showed the expected negative quadratic change across days, including: bilateral inferior frontal gyrus (left BA45/47, right BA44/45), left inferior (BA40/2) and superior (BA7) parietal lobes, bilateral temporal lobes (left BA39/22, right BA21, right BA22), and several motor-related regions.

Conclusion: While the brain can recruit additional resources during task performance after one night TSD, a second TSD night appears to overwhelm the brain’s capacity to compensate. These data show there is a failure of the compensatory recruitment response during TSD2 in the same regions previously reported to show increased activation after one night TSD. These findings suggest a functional limit to the brain’s ability to compensate for TSD and hold implications for operational settings where TSD extends beyond 36 hours.

Support (optional): US Army DAMD17-02-1-0201 UCSD GCRC M01 RR00827
SLEEP DEPRIVATION AND BRAIN CONNECTIVITY: THE IMPACT OF SLEEP DEPRIVATION AND TASK DIFFICULTY ON NETWORKS OF FMRI BRAIN RESPONSE

Stricker JL, Brown GG, Wetherell LA, Drummond SP.


Introduction: Previous research has found both increased & decreased regional brain responses after total sleep deprivation (TSD) and that task difficulty influences these changes. An alternative strategy is to consider not just discrete regional changes with TSD, but changes in how brain regions interact with one another. Here, we apply structural equation modeling (SEM) to functional MRI (FMRI) data in order to examine differences in networks of brain response during verbal encoding in sleep deprived and well-rested (WR) individuals.

Methods: Normal controls (n=23, 10F, age=24.0 ±4.8yrs) memorized words either easy or hard to recall during FMRI after being well rested (WR) and after 36 hours without sleep (TSD). Based upon our previous work, regions of interest were defined prior to data analyses: left and right inferior frontal gyrus, (LIFG & RIFG) left inferior parietal lobe (LIPL) and left superior parietal lobe (LSPL). Using SEM, we evaluated two a priori models specifying different patterns of interactions among these regions. Model 1 specified a strong interaction between LIFG and the two parietal regions while Model 2 specified strong RIFG to parietal interactions.

Results: Task difficulty, not TSD, determined which model fit the data. For easy words, Model 1 produced excellent fits both nights, while Model 2 best fit hard words. TSD, however, produced significant changes in the interactions among brain regions. For both easy and hard words, TSD reduced the strength of LIFG-RIFG and IFG-LIPL interactions and increased the strength of the LIPL-LSPL interaction. For hard words only, the RIFG-LSPL interaction became stronger with TSD.

Conclusion: While TSD did not affect which model best fit the data, it did strikingly alter the patterns of interaction among brain regions during task performance: interhemispheric prefrontal interactions were diminished and intrahemispheric parietal interactions increased. These results demonstrate that examining the interactions among brain regions can reveal new findings and a more detailed picture of the effects of TSD on brain function.

POWER SPECTRAL PROFILES OF SLEEP FOLLOWING 64-HOUR TSD

Orff HJ,1,2 Wong RT,3 Schlosser AM,4,3 Wetherell LA,5,3 Drummond S,2,1

Introduction: Total sleep deprivation (TSD) alters the macroarchitecture of sleep during recovery. Compared to baseline, sleep is more consolidated and homeostatic competition between slow wave and REM sleep results in significant changes in relative sleep stage distribution during recovery. Here we examined changes in sleep microarchitecture by comparing the spectral components of sleep on baseline and for two consecutive nights of recovery sleep following 64-hours of TSD.

Methods: 30 subjects (24.3±4.7 yo, 15F) participated in this study. The protocol involved one night baseline sleep, 64hrs TSD and 2 nights recovery sleep (REC1, REC2). 14 spectral windows were evaluated: 0-.3hz, .3-.5hz, .5-2hz, 2-4hz, 4-7.5hz, 7.5-10hz, 10-12hz, 12-14hz, 14-16hz, 16-25hz, 25-35hz, 35-45hz, 45-100hz, 100+hz. Relative power for whole night NREM and REM sleep was calculated. Data analyses utilized repeated measures ANOVAs with planned contrasts.

Results: For NREM sleep, significant main effects of power across nights (p<.05) were observed in all frequencies (0-25hz) with the exception of the 0-.3hz. Power in .3-.5hz was observed to decrease across the nights. Power in the .5-4hz range increased on REC1 and decreased in REC2. Power in the 4-25hz range decreased on REC1 and returned to baseline levels on REC2. No significant main effects were noted in frequencies >25hz. For REM sleep, significant main effects of night (p<.05) were noted for all frequencies except .3-.5hz, 12-14hz, and >45hz. In the slower frequencies (<7.5hz) power increased on REC1 and decreased on REC2, with the opposite pattern observed for frequencies between 7.5-45hz.

Conclusion: These data provide information on changes in sleep microarchitecture that are associated with TSD. Delta changes in NREM sleep paralleled slow wave sleep changes previously reported during recovery sleep. Interestingly, theta changes in REM did not parallel REM% changes previously reported, although most high frequencies did. This suggests that REM rebound may be characterized by higher frequency activity than normal REM sleep.

Support (optional): UCSD GCRC M01 RR00827 US Army DAMD17-02-1-0201
SEARCHING FOR A MARKER OF REM PROPENSITY IN HUMANS

Wong R, Wetherell L, Schlosser A, Orff HJ, Drummond S;
(1) Department of Psychiatry, University of California, San Diego, San Diego, CA, USA, (2) Psychology Service, Veterans Affairs San Diego Healthcare System, San Diego, CA, USA, (3) Research Service, Veterans Affairs San Diego Healthcare System, San Diego, CA, USA, (4) General Clinical Research Center, University of California, San Diego, San Diego, CA, USA, (5) Joint Doctoral Program in Clinical Psychology, San Diego State University/University of California, San Diego, San Diego, CA, USA

Introduction: Delta activity during sleep and Theta activity while awake increase proportionately with the homeostatic drive for sleep, and are understood to be markers for sleep propensity. There is no accepted EEG marker for REM propensity in humans, although REM Theta has been correlated with REM density (REMd) in animals. Alpha is thought to be negatively correlated with REM measures. Here we examined whether Power Spectral Analysis (PSA) of the EEG during REM could clarify whether Theta can serve as a marker of REM propensity or intensity.

Methods: 30 subjects (age=24.3±4.7, 15F) participated in a 6 consecutive night study in the sleep lab: Screen (SCR), Baseline (BL), TSD (DEP1 & DEP2), and Recovery (REC1 & REC2). PSA and hierarchical regression were used to examine the relationship between relative power in three frequency bins [Theta (4-7.5Hz), Delta (.5-4Hz), and Alpha (7.5-10Hz)] during REM and two measures of REM propensity (REM% and REMd).

Results: Theta accounted for a significant amount of the variance in REM% during BL, REC1 and REC2 (p<.002). While Alpha contributed to variance explained during REC1 (p<.01), Delta did not add to variance accounted for on any night. Spectral power in all 3 bands was much less related to REMd, with the only significant relationships being Theta for REC1 (p<.004) and Alpha for BL (p<.04). Alpha was not negatively correlated with REM measures.

Conclusion: Theta power appears more related to REM% than to REMd. While Theta seems to be a reliable marker for the amount of REM sleep on a given night, it only accounted for about 34% of the variance. Furthermore, it did not index REMd well, nor the changes in REMd seen with TSD and Recovery. Theta power did not seem to be as good a marker for REM sleep as Delta power is for SWS.

Support (optional): UCSD GCRC M01RR00827 US Army DAMD17-02-1-02-01