AFFECTIVE CONSEQUENCES OF SLEEP DEPRIVATION

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A DISSERTATION

in

Psychology

Presented to the Faculties of the University of Pennsylvania

in Partial Fulfillment of the Requirements

for the Degree of Doctor of Philosophy

2010

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ABSTRACT

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Surprisingly little is known about the effects of sleep deprivation on affective processes. Although clinical evidence and introspection suggest that emotional function is sensitive to sleep loss, there are only three published studies that have experimentally manipulated both stress and emotion in a single experiment, the earliest of which was published in 2007. This dissertation presents findings from three studies that were designed to improve our understanding of the influence of sleep loss on affective functioning in healthy adults. Study 1 (Sleep and Mood) measured the effects of sleep loss on affect in the absence of specific probes. Three facets of mood (Fatigue, Vigor and Confusion) were found to be sensitive to sleep restriction, increasing in a dose-response manner with extended wakefulness and covarying with a well validated behavioral assay of alertness (the PVT reaction time task). Three other facets of mood (Depression, Anxiety, and Anger) were not sensitive to sleep restriction and did not covary with objective alertness. Study 2 (Sleep and Emotion) found that sleep deprivation decreased facial expressiveness in response to positive and negative emotion probes. There was also a trend toward decreased intensity of positive and negative subjective emotional reactions for sleep deprived subjects as well. Study 3 (Sleep and Stress) found that sleep deprived subjects reported a more negative subjective response than control subjects to a mild

stressor, but not to a more intense stressor. When taken together, these studies offer a more nuanced account of the relationship between sleep deprivation and affective functioning. This dissertation ends with a discussion of the implications of these findings for both healthy and clinical populations and proposes future direction for research on sleep and emotion.

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INTRODUCTION

The overarching goal of the work presented here was to improve our understanding of the ways in which sleep deprivation influences affective processes. The subject of emotional changes with sleep loss is important in several areas, both applied and theoretical. Recent epidemiological studies have demonstrated that large sectors of society obtain inadequate sleep (National Sleep Foundation, 2006). Although the cognitive consequences of such schedules have been well studied, very little is known about the emotional consequences. Reports of such effects commonly appear in the popular and even some academic journals, but these are based on opinion, anecdote, or at best indirect evidence from uncontrolled settings. It is therefore important to gather objective data from controlled experiments to better inform both the public and the scientific community about the emotional sequelae of inadequate sleep.

Clinically, it is well established that people suffering from psychiatric and medical disorders often achieve suboptimal sleep (Benca et al., 1992). The association is so strong that disrupted sleep is even in the diagnostic criteria for some of the most common mental health problems, including Major Depression and Generalized Anxiety Disorder (American Psychiatric Association, 2000). Understanding the role of sleep in emotional functioning would help dissociate true symptoms of psychiatric disturbance from secondary symptoms caused by sleep disturbances. Such dissociation is important for developing new treatments and for deciding if someone with a medical condition, such as sleep apnea, should also be given a psychiatric diagnosis. At present, such decisions are based on clinical judgment and vary widely among practitioners.

Finally, understanding links between sleep and emotion would improve our theoretical understanding of the functions of sleep. There is compelling evidence that sleep plays an important role in many biological processes, including energy regulation, immune system function, and neurocognitive abilities such as vigilant attention and inhibitory control (Banks & Dinges, 2007; Durmer & Dinges, 2005; Lim & Dinges, 2008; Simpson & Dinges, 2007). Although few doubt that sleep is required for proper emotional functioning as well, the nature of affective changes is almost entirely unknown. The studies presented here represent an initial attempt to document the effects of sleep loss on fundamental aspects of human affect, including mood, emotion, and stress. Only a handful of studies combining controlled manipulations of sleep and affect have been conducted to date, making the findings presented here some of the first in a new field of inquiry.

The studies included in this dissertation were written for a general psychological audience, but a brief review of affective science and sleep research is still warranted, given that very few researchers have expertise in both fields. After a focused review of the concepts that are most important for evaluating the studies presented here, the specific hypotheses that motivated the experiments will be introduced.

Key Concepts from Affective Science

The scientific study of emotion has been challenged by conceptual problems, philosophical disagreement, and competing theories about the boundaries of the field. To avoid discussions about whether or not a given phenomenon was “really” emotion, many researchers have embraced the term “affect” as an intentionally broad construct that

includes emotion, feelings, mood, attitudes, affective style, and temperament. Researchers in this tradition tend to err on the side of inclusivity rather than specificity and although this comes at a price, it is the approach adopted here. All affective phenomena share certain prototypical features, including hedonic value, motivation, and the conscious experience of a feeling. The studies presented here focused on the manipulation and measurement of three key affective constructs: mood, emotion, and stress. Although they share the key features mentioned above, these three constructs have important differences in their temporal profiles, physiological correlates, and required conditions for elicitation.

Definitions

The term *mood* typically refers to a diffuse affective state that is often of low intensity and long duration. Moods are not usually associated with the patterned expressive signs and can occur without a clear cause (Scherer & Peper, 2001). Prototypical mood states include cheerful, gloomy, irritable, listless, depressed, etc. Their lack of objective correlates requires that they be measured by self-report.

In contrast to mood states, *emotions* are generally understood to be relatively brief episodes that organize behavior and physiology around attaining goals or avoiding harm (Gross, 1998). Unlike mood states, they have several associated features including, and action tendencies (meaning a state of preparedness to engage in a specific behavior, such as fighting, (Frijda, 1986), physiological changes detectable in heart rate and skin conductance (Levenson, 1992), and facial displays (Ekman, 1992; Ekman & Oster, 1979).

Technological advances have allowed researchers to extensively investigate neural correlates of emotion. Although there is not universal consensus about the neural correlates of emotion, certain key brain regions have consistently been implicated, including the amygdala, hippocampus, insula, anterior cingulated, and several sectors of the prefrontal cortex (Davidson, 2004). Although the studies presented below did not measure neural activity, current thinking about interactions between sleep and emotion rely heavily on neuroimaging research.

The most important behavioral correlate of emotion for our purposes here is facial expression. Several decades ago, researchers showed that some expressions of emotion can be understood cross-culturally, suggesting that they have a fundamental biological foundation that can be dissociated from culture. In addition to offering an objective correlate of subjective feeling states, facial displays are crucial for coordinating social interactions (Keltner et al., 2003), giving them a unique status of both scientifically viable for measurement and practically important in real-world settings.

Stress can be defined as a physical or psychological threat to well-being (Gunnar & Quevedo, 2007; McEwen & Seeman, 2003) and can result in physiological responses that increase survival. A major component of the stress response involves the hypothalamic-pituitary-adrenal (HPA) axis and includes cortisol secretion that can be measured in blood and saliva. Cortisol is of particular interest not only because it is relatively easy to collect and assay, but also because it has neurotoxic effects with chronic exposure (McEwen, 1998). In Study 3 (Sleep and Stress) we measured salivary cortisol as the primary physiological outcome to determine if sleep loss produced differences in resting cortisol concentrations or in peak responses to the stressors.

In addition to the physiological responses, stressors are associated with a general elevation in negative affect. In contrast to emotion probes that can be carefully selected to produce a relatively pure, discrete emotion, stress induction procedures have been shown to elicit facial displays of anger, sadness, and fear at different relative intensities depending on the person. Despite the disadvantage of less experimental control, stress is both a more potent method for inducing affect than most emotion elicitation procedures, and it is more relevant to negative events encountered in the real world. In the study of stress and sleep deprivation presented here, we therefore administered a comprehensive mood questionnaire after each stress induction procedure to determine how subjects responded to the stressor before and after sleep deprivation.

Sleep Research Overview

In contrast to the constructs in affective science, sleep has a widely agreed upon definition that integrates behavior and biology. *Sleep* is a reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment (Carskadon & Dement, 2005) with characteristic cortical activity that can be measured by EEG (Steriade, 2005). Animal studies have established that sleep is a biological necessity by demonstrating that severe sleep deprivation results in death, even when the methods for maintaining wakefulness are mild (Rechtschaffen et al., 1983). Nevertheless, efforts to clearly identify a biological function of sleep has been surprisingly difficult. It now seems most likely, that sleep and circadian rhythmicity is involved in many biological systems including metabolism (Knutson et al., 2007), and immune system function (Dickstein &

Moldofsky, 1999). In the studies presented here, we attempted to understand the role sleep plays in affective systems through relatively short term sleep deprivation.

Two process model of sleep

Extensive evidence has demonstrated that predicting and mathematically modeling sleep behaviors and deficits requires at least two processes (Borbély, 1982). The homeostatic process can be thought of as sleep pressure that builds with wakefulness and dissipates with sleep. The circadian system represents a daily oscillatory fluctuation in levels of alertness. Under healthy sleep conditions, the two processes interact to produce stable levels of alertness during the day and consolidated sleep at night. When the two systems are properly aligned, the sleep pressure that builds through the day is opposed by the circadian system throughout the day, preventing sleep onset and neurobehavioral impairments due to sleepiness. At night, when sleep pressure is highest, the circadian system begins to decrease it's alerting effect and sleep is initiated. Throughout the night, sleep pressure dissipates at about the same rate as the circadian propensity for wakefulness decreases, thus preventing sustained awakenings during the night.

There are several ways to misalign these two processes, the most relevant here is through sleep deprivation. When sleep time is restricted, the circadian system continues to oscillate, leading to instability throughout the day. Figure 1 shows the interaction of both processes over 88 hours of continuous wakefulness. In Study 1 (Sleep and Mood) we took advantage of this variability in calculating coherence between objective performance and subjective changes in mood. The circadian influence on reaction times

prevents inflated estimates of coherence due to a steady linear increase in both variables. In Study 2 (Sleep and Emotion) and Study 3 (Sleep and Stress) variability due to circadian influences was minimized by inducing affect at the same time each day.

Methods of sleep deprivation

The most common method of sleep deprivation, called *total acute sleep deprivation*, involves maintaining wakefulness with no opportunity to sleep until the experimental restriction phase has been completed. This method is cost-effective, quickly producing high levels of sleep pressure. Its primary limitation is limited generalizability. A night of total sleep deprivation is rare in real-world settings. Findings using this paradigm are therefore most useful for answering important theoretical questions about neural and behavioral functioning without sleep. Study 2 (Sleep and Emotion) and Study 3 (Sleep and Stress) were conducted using total acute sleep deprivation.

An alternative to total acute sleep deprivation is *chronic partial sleep restriction*. In this paradigm, sleep opportunity is restricted, typically to about 4 hours per night, for several consecutive nights. Two seminal studies independently established that under controlled conditions, cumulative effects can be seen when sleep is reduced to less than 7 hours per night for 4 or more nights (Belenky et al., 2003; Van Dongen et al., 2003). Individual differences are large however, with a substantial subgroup showing no deficits from partial sleep restriction (Banks & Dinges, 2007). This approach has superior ecological validity to total acute sleep deprivation, but costs are extremely high and subject recruitment can be more difficult given the long periods of time required to

participate in such studies. Study 1 (Sleep and Mood) utilized a chronic sleep restriction paradigm with the largest sample currently available in the world (N=148).

Consequences of sleep deprivation

Over one hundred years of research have established several robust cognitive and performance deficits associated with sleep loss (see (Durmer & Dinges, 2005) for a comprehensive review). The most important cognitive systems that are sensitive to sleep loss for our purposes include vigilant attention and executive functions. Vigilant attention is typically measured by reaction time performance on the Psychomotor Vigilance Task (PVT), a simple reaction time task developed by Dinges and Powell (Dinges & Powell, 1985) that is described in detail in a recent review by Lim & Dinges (Lim & Dinges, 2008). The PVT is the dominant assay of vigilant attention used in sleep deprivation experiments and is sensitive to homeostatic and circadian processes (see **Figure 1** for an example of PVT outcome data).

More recently, experiments demonstrated that higher order tasks involving executive functions are also sensitive to sleep deprivation. *Executive functions* are defined as the ability to plan and coordinate a willful action in the face of alternatives, to monitor and update action as necessary and suppress distracting material by focusing attention on the task at hand (Miller & Cohen, 2001). Such tasks are thought to rely primarily on the prefrontal cortex, leading sleep researchers to hypothesize that this brain region is particularly sensitive to sleep deprivation (Durmer & Dinges, 2005; Horne, 1993). As mentioned earlier, the prefrontal cortex is highly involved in neural systems of emotion and thought to serve as a moderator of emotion rather than a mediator

(Davidson, 2004). This overlap with emotion circuitry has led to the hypothesis that sleep loss causes deficits in emotion regulation (Dahl & Lewin, 2002) and has received support from neuroimaging studies of inhibitory control (Chuah et al., 2006) and a very recent study of sleep deprivation and emotion (Yoo et al., 2007).

The current studies

The following three studies were designed based on the findings reviewed above.[1] Study 1 (Sleep and Mood) reports changes in affect in the absence of emotionally provocative probes or stimuli. Study 2 (Sleep and Emotion) reports the effects of sleep deprivation on behavioral and subjective responses to probes of discrete emotions (amusement and sadness). Study 3 reports the effects of sleep deprivation on subjective and physiological responses to an experimental stress induction procedure. In addition to the discussion of findings after each study, a comprehensive discussion that integrates findings from all three studies is included as the final chapter of the dissertation. Together, these three studies offer the most comprehensive experimental investigation of sleep and affect ever conducted.

[1] Except for a few studies we were unaware of until their very recent publication, including Yoo et al. (2007).

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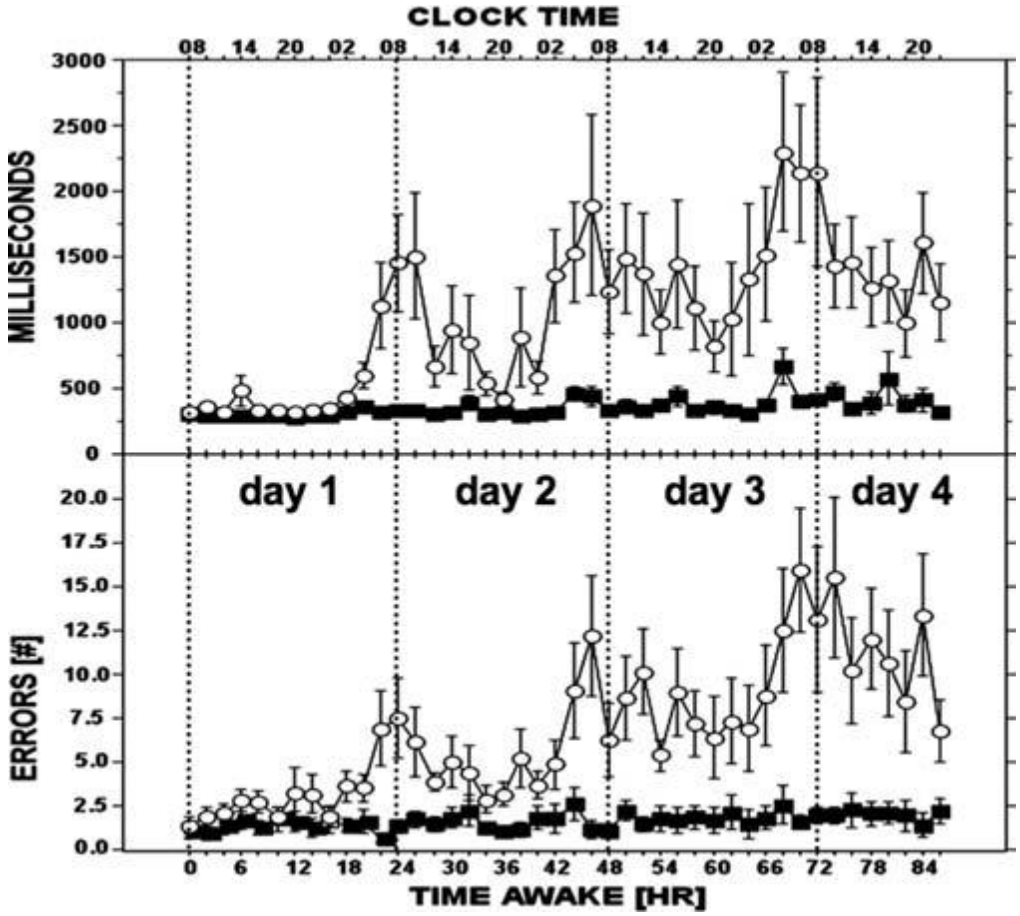

Figure 1. Figure shows interaction of homeostatic and circadian processes on reaction time and false start errors over 84 hours of wakefulness. The homeostatic sleep drive is responsible for the overall increase in reaction time and errors and the circadian system is responsible for their daily fluctuations. Figure taken from Lim and Dinges (2008).

Running Head: **SLEEP RESTRICTION AND MOOD**

Word count = 3,048

Changes in Mood and Reaction Time Associated with Sleep Restriction: Findings from a Large Sample Using a Novel Statistical Method

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Abstract

Chronic sleep restriction is known to have deleterious effects on mood and vigilant attention, but it is not known which aspects of mood are most sensitive to sleep restriction or how strongly related they are to deficits in objective performance. We investigated these issues using a large sample (N=148) of healthy adults studied across seven consecutive days in a controlled laboratory environment. Subjects completed a performance battery every 2 hours during wakefulness that included a reaction time task and a comprehensive mood measure. Fatigue and confusion increased cumulatively over the study and were significantly different from the responses of a small control group (n=9) while depression, anger, and anxiety did not show a clear dose-response relationship to sleep loss and were not significantly different between sleep restricted and control subjects. A novel statistical approach demonstrated strong relationships between subjective mood changes and reaction time within individuals. Traditional statistics failed to detect this relationship at a group level. Our results indicate that sleep restriction is associated with specific mood changes and is not sufficient to elevate mood states commonly associated with psychiatric conditions. Those mood states that are sensitive to sleep restriction are closely linked to neurobehavioral deficits in alertness, but the relationship is masked by individual differences in self-report styles when group-level statistics are used.

Changes in Mood and Reaction Time Associated with Sleep Restriction: Findings from a Large Sample Using a Novel Statistical Method

Introduction

Inadequate sleep is a common consequence of modern lifestyle demands (National Sleep Foundation, 2006) as well as medical and psychiatric problems (Benca et al., 1992; Parish, 2009). Laboratory studies of sleep deprivation are intended to illuminate the possible consequences of inadequate sleep, but often use total sleep deprivation paradigms that include extended periods of wakefulness that do not closely mimic real world sleep. An alternative experimental approach, chronic sleep restriction, reduces sleep over several consecutive nights to levels that more closely match real world behavior.

Studies using a chronic sleep restriction approach have consistently demonstrated cumulative deleterious effects on cognitive performance over several consecutive days (Belenky et al., 2003; Dinges et al., 1997; Van Dongen et al., 2003). This evidence has been used to inform public policy about levels of sleep necessary for operating motor vehicles or safely performing other tasks.

The effects of chronic sleep restriction on affect have received less attention, but there is substantial evidence that mood is also sensitive to inadequate sleep. Several studies have reported that overall mood becomes more negative over the course of sleep restriction (Belenky et al., 2003; Van Dongen et al., 2003) but have not specified which aspects of mood are most sensitive to sleep loss. The first study to show cumulative mood

changes over chronic sleep restriction reported significant changes on all mood scales except depression (Dinges et al., 1997). The most comprehensive study of mood changes during sleep restriction conducted to date (Haack & Mullington, 2005) reported significant changes on all mood scales measured, but there were larger effects on energy level and sociability than on anger and gloominess. These studies suggest that sleep restriction has fairly broad effects on mood, but additional research with larger samples would be useful in more accurately predicting the effect sizes of different subcomponents of mood.

Although there is little doubt that mood is sensitive to sleep restriction, it is not clear how closely linked these subjective changes are to objective measures of behavioral alertness. No studies to date have reported relationships between these two domains. Previous research has established large individual differences in the cognitive effects of sleep loss (Banks & Dinges, 2007), but it is still an open question whether or not these people are also better able to cope with the subjective effects of sleep loss.

The following study was conducted on 148 healthy adult volunteers, the largest dataset of chronic sleep restriction that is currently available. Analyses were conducted to first determine which aspects of mood are sensitive to chronic sleep restriction and then to evaluate the strength of the relationship between changes in mood and changes in reaction time. While previous studies have attempted this goal using correlations, we employed a time-series design to measure coherence between these two parameters within each individual. This approach removes noise due to individual differences in self-report styles that may mask the true association.

Methods

Subjects

Subjects were 148 healthy adult volunteers in an 11 day and 11 night laboratory-based protocol, approved by the Institutional Review Board of the University of Pennsylvania. The sample included 75 men and 73 women (mean age = 30.5 +/- 7.0 years) who reflected the diversity of the metropolitan area from which the sample was drawn. Fifty-six were Caucasian, 84 African-American, and 8 subjects reported other ethnicities. All subjects provided informed consent and were compensated for their participation. In order to participate in the experiments, volunteers had to meet the following inclusion/exclusion criteria: age between 22 and 45, have normal sleep wake schedules for the past 60 days, be free from psychiatric disorders (including drug and alcohol abuse), avoid smoking, and be free of debilitating medical conditions. After entry into the study, subjects were removed if they became physically ill, refused to cooperate with procedures, or requested to end their participation. Twelve subjects were removed from the study.

Subjects were pre-screened to ensure they had no medical, psychiatric, or sleep-related disorders and were drug-free. This was determined by history, physical examination and psychological questionnaires, and by clinical blood and urine laboratory tests and toxicological screening. Subjects reported working neither regular night nor rotating shift work within the past 2 years. They also reported not having traveled across time zones in the 3 months before the experiments.

Study Design

Sleep Restriction. Subjects completed all testing in the Sleep and Chronobiology Laboratory of the Hospital of University of Pennsylvania, under controlled conditions and with strict schedules for time in bed. The experiment involved two baseline days with 10 hours of sleep opportunity (from 10:00 p.m. to 8:00 a.m.) followed by five nights of 4 hours of sleep opportunity (from 4:00 a.m. to 8:00 a.m.). Subjects then completed four additional days and nights in the laboratory (data not reported here). All subjects were given opportunity for recovery sleep prior to discharge.

At all scheduled wake times, subjects were kept awake in the laboratory under continuous behavioral monitoring, and they completed cognitive testing followed by a mood questionnaire every 2 hours (procedures described below). Between test bouts they were allowed to read, watch movies, and interact with laboratory staff to help them stay awake, but no vigorous activities were permitted. Light was maintained at very dim levels (below 30 lux) and no daylight entered the facility. During scheduled sleep times, all lights were turned off and subjects were monitored by closed-circuit infrared cameras. During the protocol, access caffeine and alcohol was strictly prohibited.

Neurobehavioral Performance

Subjects completed a 20 minute battery of cognitive tests every 2 hours during wakefulness. The primary outcome from this test battery was the Psychomotor Vigilance Task (PVT; Dinges & Powell, 1985), a simple reaction time task that has been

extensively validated in chronic sleep restriction and acute sleep deprivation studies (Doran, Van Dongen & Dinges, 2001). Our analyses involved two metrics from the PVT, average reaction time and lapses (reaction times greater than 500 ms). Other tasks included a computerized digit symbol substitution task and a serial addition/subtraction task (data not reported here, see Van Dongen et al., 2003 for description of tasks).

Subjective Measures

The Profile of Mood States (POMS; McNair & Heuchert, 2005) was administered by computer immediately after each cognitive test battery. The POMS is a 65 item self-report inventory that asks participants to respond to words or brief phrases from 1 (Not at All) to 5 (Extremely) based on how they are currently feeling. This mood measure includes a composite scale, Total Mood Disturbance (TMD) and 6 subscales: Fatigue, Confusion, Anxiety, Anger, Depression and Vigor (see **Appendix A** for individual items that contribute to each subscale).

The Stanford Sleepiness Scale (SSS; Hoddes et al., 1973) was administered by computer before and after each cognitive test battery. The SSS is a single-item scale ranging from 1 (Feeling wide awake) to 7 (Sleep onset soon, having dream-like thoughts).

Statistical Approach

We had two overarching goals for our analyses: 1) to determine which aspects of mood were sensitive to sleep restriction and 2) to examine the relative strengths of the

relationships between aspects of mood that were sensitive to sleep loss and objective measures of behavioral alertness.

Mood changes during sleep restriction. The first goal was accomplished by comparing mood at baseline with mood after five nights of sleep restriction. Daily averages of responses to the Profile of Mood States were calculated based on seven testing bouts completed between 8:00 a.m. and 8:00 p.m. The primary analyses were performed using repeated measures ANOVA, first on the composite mood scale, Total Mood Disturbance, followed by each of the mood subscales. Mood variables were treated as a repeated measure and experimental condition (restriction or control) was treated as a between subjects factor. Significant interactions of mood by condition were interpreted as evidence that there was a significant effect of sleep restriction on that mood variable.

In addition to inferential statistics, efforts were made to accurately describe the size and direction of the effect. Cohen *d* effect sizes (Cohen, 1988) were computed within subjects using the pooled standard deviations from each day rather than the paired t-test value in order to give a more conservative estimate of the effect size (Dunlop et al., 1996).

Coherence between mood and behavioral alertness. The second overarching aim of the study, to determine how closely each aspect of mood tracked reaction on the PVT, was addressed using "coherence" statistics developed by Maislin and colleagues (Dinges et al., 1998). Rather than using group values, a Pearson correlation was calculated separately for each subject based on mean reaction time on the PVT and self reported

mood on the POMS at each test bout.[1] Test bouts from the second day of baseline testing through the fifth day of sleep restriction were used for these analyses. The first baseline day was not included in order to avoid exaggerated coherence estimates due to measurement before sleepiness was induced. Each correlation was therefore based on 42 discrete performance bouts collected over six consecutive laboratory days on each subject. The resulting coherence values were summarized to determine average coherence for groups of subjects.[2] In order to test the utility of this statistical approach, a simple group-level correlation between mood and reaction time was also calculated using daily averages of mood and reaction times.

Results

Changes in Mood

The sleep restricted group showed a cumulative increase in the composite mood scale, Total Mood Disturbance, across days while the control group did not show this pattern of mood change (see **Figure 1, Panel A**). Repeated measures ANOVA comparing the sleep restriction and control group on Total Mood Disturbance scores at baseline and

[1] We previously found that coherence values based on Spearman rank correlations were consistently similar to those based on Pearson correlations (Dinges et al., 1998).

[2] Because distributions of correlations tend to be skewed and therefore biased, statisticians have suggested transformations to account for such bias. Following the recommendations of Silver and Dunlap (1987) we converted each correlation using Fisher's (1921) z transformation, averaged those values, and converted the average z back to an r value. The resulting values were very close to the original r values (differences ranged from -0.03 to 0.04, average 0.02). Because this difference did not affect the interpretation of our results, the original values were used in the analyses reported here.

on the fifth day of sleep restriction revealed a significant mood by condition interaction ($F[1,145]=10.38$, $p=0.002$), suggesting a significant effect of sleep restriction on overall mood. Similar analyses performed using the Profile of Mood States subscales revealed a significant effect of sleep loss on Fatigue ($F[1,145]=7.71$, $p=0.006$), Confusion ($F[1,145]=3.94$, $p=0.049$), and Vigor ($F[1,145]=16.25$, $p<0.001$). There was not a significant group by mood interaction on the subscales of Depression ($F[1,145]=0.92$, $p=0.34$), Anxiety ($F[1,145]=1.56$, $p=0.21$) or Anger ($F[1,145]=0.50$, $p=0.48$) suggesting that these aspects of mood were not sensitive to five nights of sleep restriction.

Effect size estimates (calculated within subjects) revealed that chronic sleep restriction had the largest effect on Fatigue ($d=1.37$) followed by Vigor ($d=0.86$) and Confusion ($d=0.84$). The effect size estimates for the other subscales were in the small to moderate range ($d=0.20$ to 0.34). **Table 1** summarizes these findings. For comparison purposes, subjects' responses to the Stanford Sleepiness Scale (SSS) were also analyzed. The sleep restricted group reported a baseline SSS average of 2.27 (+/-0.79) compared to 3.94 (+/-1.34) after sleep restriction ($d=1.51$).

[Table 1 here]

Changes in reaction time

Repeated measures ANOVA of PVT lapses, defined as reaction times greater than 500 ms, were significantly elevated by sleep restriction ($F[1,145]=10.10$, $p=0.002$). Post-hoc analyses revealed that the sleep restricted and control groups diverged by the second day of sleep restriction ($F[1,145]=5.49$, $p=0.02$). Lapses continued to increase linearly in the sleep restriction group, but not in the control group (see **Figure 1, Panel B**).

[Figure 1 here]

Relationships between mood and reaction time

Pearson correlations were calculated within each subject to determine the strength of relationships between mood scales and reaction time (see **Figure 2** for an example of an individual with high coherence). Individual scores were then averaged to provide a group-level estimate of coherence. Average coherence between the composite mood measure, Total Mood Disturbance, and mean reaction time on the PVT was relatively high (mean r=.48) and significantly different from 0 (t=25.24, $p<.001$). Subsequent analyses revealed that average coherence was significantly greater than 0 for all mood subscales (t range 7.01 to 21.85, all *p* values less than .001). Coherence values were significantly greater for Fatigue (mean r=.44) Vigor (mean r= -.40) and Confusion (mean r=.34) than for Depression (mean r=.15), Anxiety (mean r=.16), and Anger (mean r=.18; all t values greater than 6.52, all *p* values less than 0.001, see **Table 1**).

Paired samples t tests revealed no differences between coherence values of the Stanford Sleepiness Scale (mean r=.50) and those of Total Mood Disturbance scores (t=0.75, $p=.46$). Coherence values associated with sleepiness scores were significantly greater than those associated with Fatigue (t=3.02, $p=0.003$), Confusion (t=7.91, $p<0.001$) and Vigor (t=5.68, $p<0.001$). Overall performance on the PVT on the fifth night of sleep restriction was not associated with coherence values (all r values less than .08, all

p values greater than .30), suggesting that coherence was no better or worse for those who were resilient to the effects of sleep deprivation than for those who were not.

To compare coherence values to traditional correlations, standard Pearson correlations were calculated between PVT performance and daily averages on mood and sleepiness scales on the fifth day of sleep restriction. There was a weak but significant association for Stanford Sleepiness Scale scores (r=.19, *p*=.026). Relationships between PVT and mood scales were not significant (range r=.02 to .15, all *p* values greater than .07).

[Figure 2 here]

Discussion

The overarching goal of these analyses was to improve our understanding of how inadequate sleep influences mood. The study had several unique features including a chronic sleep restriction method that more closely approximated sleep schedules seen in real-world settings, a novel statistical approach that overcomes many of the most serious problems with self report measures, and the largest sample of its kind ever collected. These features allow conclusions to made with more accuracy and better generalizability than has previously been available.

We found that overall mood problems were elevated by chronic sleep restriction, but not all facets of mood were equally affected. Self reported fatigue and confusion increased significantly whereas positive mood and energy decreased significantly,

suggesting a conscious awareness of the decreased energy and cognitive instability that characterizes sleep loss. Equally important were our findings that sleep restriction, under these conditions, did not elevate depression, anxiety, or hostility. These findings are consistent with those of Haack and Mullington (2005) who studied a smaller sample (N=40) but over a longer period (12 days of restriction). This robust finding should be considered when evaluating the mental health of patients who achieve inadequate sleep due to medical conditions or lifestyle demands. Psychiatric symptoms of depression, anxiety and hostility should not be attributed to inadequate sleep alone.

Analyses using the coherence statistics developed by Maislin and colleagues (Dinges et al., 1998) revealed strong relationships between subjective mood and objective performance on a reaction time task within each individual whereas traditional group-level correlations found very weak (and statistically insignificant) associations between these variables. Interpretation using the latter method might lead to the erroneous conclusion that subjective changes during sleep loss are independent of objective performance impairments. Coherence analyses are more appropriate for analyzing relationships between repeated measures of subjective variables, because it is less influenced by noise from different self-report styles. It should be noted however that this method divorces self-report values from any absolute meaning, and may therefore not be appropriate in situations where absolute agreement between subjective and objective measures is relevant.

The finding that subjective responses were closely related to objective performance suggests that the neurobiological changes that produce unstable

performance and those that produce feelings of fatigue and confusion tend to co-occur. Recent efforts to identify the neural substrates of degraded reaction time performance after sleep loss have identified areas in cortical sustained attention network and cortical and subcortical motor systems (Drummond et al., 2005), but these areas are not believed to be associated with conscious affective experience (see Adolphs, 2002; Craig, 2002, for reviews of neural regions that are associated with the conscious experience of feelings). Additional studies are need that focus on the neural basis- of both objective performance deficits and the affective changes that are associated with them.

Although as a group subjects showed a clear relationship between objective performance deficits and related elevation in fatigue and sleepiness, individuals showed considerable variation in the strength of this relationship. Furthermore, we could not predict poor coherence based on attentional lapses, suggesting that there are people who are unable to determine their own cognitive impairment across the spectrum of sensitivity to sleep loss. Those who are extremely sensitive to the neurobehavioral effects of sleep restriction but unaware of their level of impairment represent a subgroup at high risk for motor-vehicle accidents and other potentially dangerous performance impairments. We are currently analyzing our dataset to identify predictors of this performance profile, but additional data from real-world as well as laboratory settings are needed to investigate this phenomenon.

Limitations

Despite the strengths of this study, a few limitation should be emphasized. Most importantly, mood was not intentionally manipulated during this study. In fact, efforts were made to maintain stable affect to prevent drop-out. Therefore, it cannot be concluded that sleep restriction does not influence affective states beyond those we identified, merely that sleep restriction is not sufficient to do so. Only two published studies that we are aware of have experimentally manipulated affective states after sleep deprivation (Franzen, Siegle & Buysse, 2008; Yoo et al., 2007) and much more work is needed in this area before strong statements can be made about how sleep loss influences affective functioning. Similarly, it is important to remember that this was a laboratory-based study where conditions were stable and predictable, thus minimizing stress. There is strong evidence that stress has deleterious effects on sleep (see Akerstedt, 2006 for review) and some evidence to suggest that sleep loss, in turn, potentiates negative affect in response to stressors (Hamilton, Catley & Karlson, 2007). More research is needed to determine if inadequate sleep in combination with stress produces different affective responses than sleep loss alone.

Table 1. Daily averages (standard deviations) of mood scores at baseline and after five nights of sleep restriction.

Mood Scale	Baseline Mean (SD)	Restriction Mean (SD)	Effect Size (within subjects)	Coherence Mean (SD)
Anger	0.75 (2.16)	1.41 (2.17)	0.31	.18 (.25)
Anxiety	3.25 (2.05)	4.02 (2.44)	0.34	.16 (.26)
Confusion*	2.66 (1.62)	4.33 (2.31)	0.84	.34 (.26)
Depression	0.79 (2.03)	1.22 (2.20)	0.20	.15 (.24)
Fatigue**	1.23 (1.71)	6.83 (5.53)	1.37	.44 (.26)
Vigor**	12.02 (7.31)	7.31 (6.32)	0.86	-.40 (.22)
Total Mood Disturbance	**-3.34 (11.89)**	**11.67 (14.48)**	**1.13**	**.48 (.22)**

The coherence value represents the average strength of the relationship between the mood scale and mean reaction time on the PVT.

* Significant between groups effect at 0.05
** Significant between groups effect at 0.01

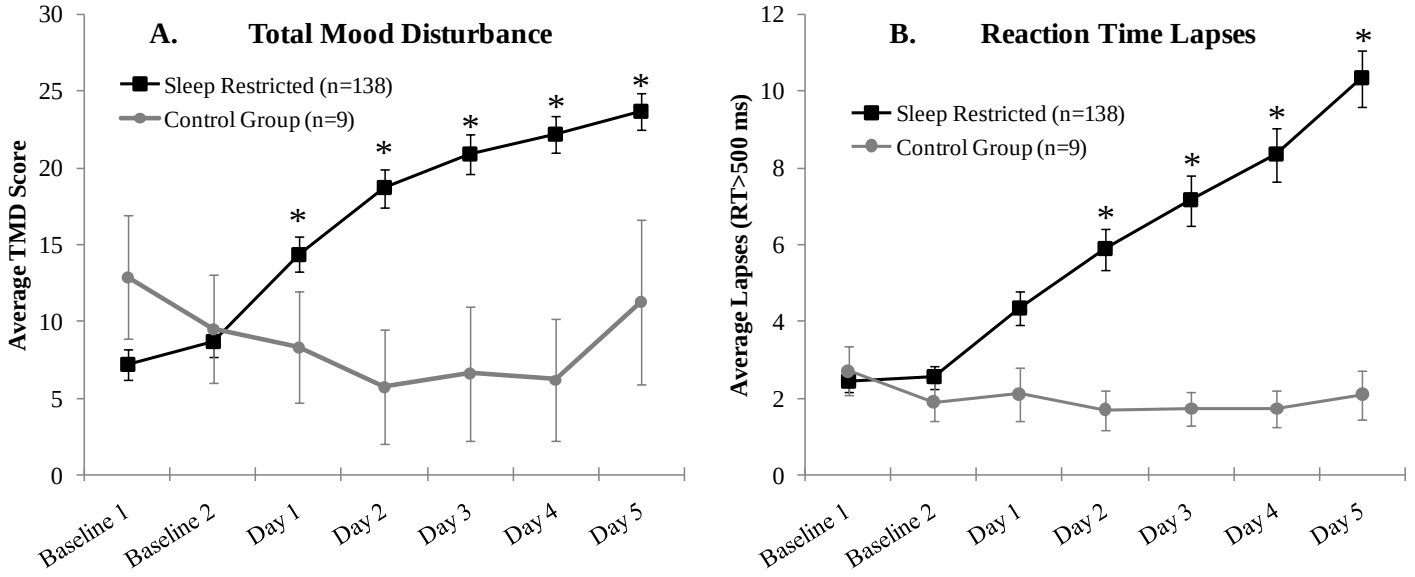

Figure 1. Daily averages for the composite mood scale (Total Mood Disturbance, Panel A) and attention lapses (defined as reaction times greater than 500 ms, Panel B) for the first 7 days of the study. Data from the sleep restriction group (n=138) are shown in the black line. Data from the control group (n=9) are shown in the gray line. Sleep restricted subjects had significantly larger mood disturbance scores than control subjects by the first day of sleep restriction ($F[1,145]=6.49$, $p=0.01$) and significantly more lapses than the control group by the second day of restriction ($F[1,145]=5.49$, $p=0.02$). TMD scores were increased by a constant to improve the clarity of the graph. Bars represent standard errors.

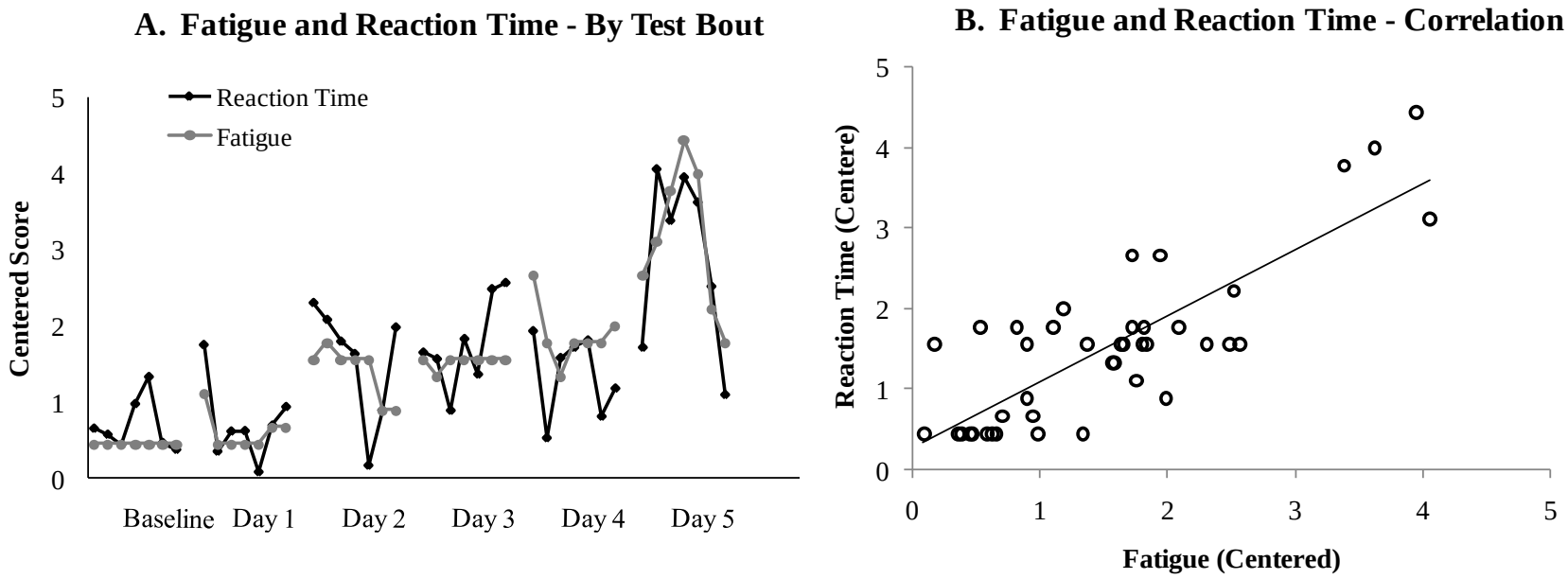

Figure 2. Graphs show data from an individual with high coherence (r=.82) between self-reported Fatigue and mean reaction time on the PVT. Panel A shows reaction time (black line) and Fatigue (gray line) for each test bout. Panel B shows the same data on a scatter plot where each point represents the pair of scores on Fatigue and reaction time for a given test bout. These correlations were calculated for each of the 139 subjects in the sleep restriction condition. Values presented here were centered by adding a constant to z scores to improve the clarity of the graphs.

Appendix A: Profile of Mood States

Composite Scale	**Total Mood Disturbance**					
Subscales	**Depression**	**Confusion**	**Fatigue**	**Vigor**	**Anger**	**Anxiety**
Items	Unhappy Sorry for things done Sad Blue Hopeless Unworthy Discouraged Lonely Miserable Gloomy Desperate Helpless Worthless Terrified Guilty	Confused Muddled Bewildered Efficient Forgetful Uncertain about things Unable to concentrate	Worn-out Listless Fatigued Exhausted Sluggish Weary Bushed	Lively Active Energetic Cheerful Alert Full of pep Carefree Vigorous	Angry Peeved Grouchy Spiteful Annoyed Resentful Bitter Ready to fight Rebellious Deceived Furious Bad-tempered	Tense Shaky On edge Panicky Relaxed Uneasy Restless Nervous Anxious

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Running Head: **SLEEP DEPRIVATION AND EMOTION**

Word count = 2,451

A Night of Sleep Deprivation Reduces the Intensity of Emotional Expressions in Healthy Adults

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Abstract

Past research has established that sleep deprivation has negative effects on cognition, but very little is known about its effects on emotion. We examined the influence of sleep deprivation on emotion by experimentally manipulating sleep duration and measuring responses to emotional stimuli in a laboratory setting. Healthy adult subjects watched positive and negative film clips before and after they were randomly assigned to a night of sleep deprivation or a normal sleep control condition. The intensity of their facial expressiveness while viewing the films was coded by human judges and compared to their subjective emotional responses. Relative to subjects in the control condition, sleep deprived subjects demonstrated less expressiveness, especially in response to positive stimuli. Subjective responses were not significantly different between sleep deprived subjects and rested controls. These results suggest that sleep deprivation is associated with attenuated emotional expressiveness in healthy adults.

A night of sleep deprivation reduces the intensity of emotional expressions in healthy adults

Inadequate sleep is a pervasive problem in modern society. Not only is sleep often impaired by medical and psychiatric problems (Benca et al., 1992; Roehrs & Roth, 2005), but artificial lighting and around-the-clock services have facilitated lifestyles that do not allow for adequate levels of sleep. The resulting "sleep debt" is associated with significant daytime performance deficits that carry considerable social, financial, and personal costs.

Experiments dating back to the 1900's have demonstrated that sleep deprivation has deleterious effects on behavior and cognition, including impairments in vigilant and executive attention, working memory, and divergent higher cognitive functions indicative of instability in wakefulness (see Durmer & Dinges, 2005 and Banks & Dinges, 2007 for recent reviews). Surprisingly little research however has been conducted to determine the effects of sleep loss on emotions. Hypotheses about relationships between sleep and affect have therefore required speculation based on neuroimaging studies of cognitive tasks after sleep deprivation and from clinical populations where sleep restriction cannot be isolated from other variables.

Perhaps the most influential theory of sleep and emotion has been proposed by Dahl & Lewin (2002) who suggested that sleep loss leads to deficits in emotion regulation via its effects on the prefrontal cortex, a region that has been implicated in

inhibitory control of negative emotion in particular (see Ochsner & Gross, 2005 for review). Although compelling, this explanation has had very little empirical evaluation.

Only a handful of studies have been conducted with enough scientific rigor to suggest causal links between restricted sleep and emotional functioning. In a well-designed field study, Zohar et al (2005) used experiential sampling to gather data on sleep and emotion in medical professionals whose sleep fluctuated with the shift they worked. They reported that reduced sleep was associated with a decrease in positive emotion following desirable events and an increase in negative emotion following undesirable events. These findings support the widely held belief that sleep deprivation has deleterious effects on emotional processes in healthy adults.

Yoo et al. (2007) found increased activation of the amygdala and decreased activation in the medial prefrontal cortex in subjects who viewed emotionally negative photographs after sleep deprivation relative to a control group who viewed the same photographs after normal sleep. These findings support Dahl & Lewin's (2002) theory of sleep and emotion because amygdala activation has been found to increase in response to negative emotion probes and the medial prefrontal cortex is implicated in inhibitory control over such states. Nevertheless, no data on behavioral or subjective emotional responses were reported, so it is unknown how these neural changes were expressed.

Franzen et al (2008) completed a similar study where subjects viewed emotionally provocative photographs with and without a night of sleep deprivation, but the primary affective outcome was the change in pupil diameter, a physiological correlate of emotion that has been validated in rested subjects (see Bradley et al, 2008). They reported

increased pupil dilation in response to negative photographs for the sleep deprived group relative to the control group, suggesting that reduced sleep is associated with greater emotional activation in response to unpleasant stimuli.

These studies offer some of the first empirical evidence that restricted sleep influences neural, physiological, and subjective aspects of emotion. The following study was conducted to extend the study of sleep and emotion to facial expressiveness, a component of emotion that has been highly studied since Darwin's Expressions of Emotion in Man and Animals (1871) but not yet investigated by sleep researchers. Facial expressions are of interest because of their crucial role in communicating private emotional states, regulating social interactions, and even influencing subjective and physiological components of emotion (Levenson, Ekman & Friesen, 1990). In the following experiment, we investigated the effects of one night of total sleep deprivation on the intensity of facial expressiveness in response to sad and amusing film clips.

Method

Subjects

Subjects were healthy volunteers recruited from the general community. Fourteen men and 9 women (mean age = 30.8 +/- 6.8 years) completed a 48 hour laboratory-based protocol, approved by the Institutional Review Board of the University of Pennsylvania. All subjects provided informed consent and were compensated for their participation. The sample included 12 Caucasian, 8 African-American, and 3 subjects of other ethnicities.

To participate in the study, volunteers had to be between the age of 22 and 45, have normal sleep wake schedules for the past 60 days, be free from psychiatric disorders, including drug and alcohol abuse, avoid smoking, and be free of debilitating medical conditions. After entry into the study, subjects were removed who were physically ill, had poor sleep the previous night, and/or reported Beck Depression Inventory (BDI-II) scores at or above 14. Five subjects were removed after enrollment.

Procedures

Sleep Deprivation. Subjects were randomly assigned to the sleep deprivation or control condition with approximately 2:1 likelihood of assignment to the deprivation condition. Fifteen subjects (9 males, 6 females) completed the sleep deprivation protocol and 8 subjects (5 males, 3 females) completed the control protocol. Subjects entered the laboratory at 9:00 a.m. and completed consenting procedures. After one day of testing, subjects either received no sleep opportunity (sleep deprivation group) or they were given 9 hours of sleep opportunity (control group) from 11:00 p.m. to 8:00 a.m. A second day of testing was then completed followed by 10 hours of sleep opportunity from 10:00 p.m. to 8:00 a.m. for all subjects. They were informed of their condition at 8:00 p.m., after the first day of testing had been completed.

Subjects completed the experiment with minimal contact with other subjects. Each had a separate room and all testing was done individually. Subjects were monitored continuously by trained staff members using closed-circuit, infrared cameras. Adherence

to sleep condition was further validated by actigraphy, an objective method for estimating sleep based on movement (Ancoli-Israel et al., 2003).

Emotion Induction. Positive and negative emotions were induced between 4:00 p.m. and 6:00 p.m. on two consecutive days of testing. One sad and one amusing clip were presented on the first day of testing (prior to sleep deprivation). Two different clips, one sad and one amusing, were presented on the second day of testing (after sleep deprivation). Three clips were chosen from a library of previously investigated film clips found to elicit target emotions (Gross & Levenson, 1995) and one clip was chosen based on the recommendation of an expert in the field (M. Shiota, personal communication, December 12, 2005).

Measures

Facial Expressiveness. Subjects were videotaped while they watched the emotionally provocative film clips. These videos were later scored without sound in a randomized order. Two raters, one of whom was blind to all conditions, scored all of these videotapes. The videos were scored for overall intensity based on the FACES scoring system (Kring & Sloan, 2007). This system includes a single rating of overall expressiveness rated on a scale from 0-4. To improve reliability, the following anchors were added to the existing 5 point scale: 0 – no emotion, 1 – one or two small displays, 2 – either one big display or several smaller displays, 3 – many small displays or one or more large displays, 4 – several large displays or near constant small displays. The averages of raters' scores were used for statistical analyses.

Reliability was calculated using the intraclass correlation, a ratio of the variance of interest over the sum of the variance of interest plus error (Bartko, 1966). Intraclass correlation coefficients (ICC's) were calculated according to the recommendations of Shrout & Fleiss (1979). Subjects were treated as a random factor and the raters were treated as fixed factors. Measures of absolute agreement rather than consistency were calculated because systematic differences among levels of ratings were determined to be relevant. This is the more conservative statistical choice. ICC's of .70 or greater were considered adequate. When measurements failed to reach this criterion, additional raters were added until the ICC increased to an acceptable value. All ratings were used in analyses by using the average of judges' ratings.

Ratings of subjects' responses to three film clips were determined to be above the reliability threshold (ICC's > .82), but responses to one film clip did not meet our reliability threshold (ICC=.60). An additional rater, blind to sleep condition, rated subjects' responses to this film clip. When these ratings were added, reliability for this clip increased above threshold (ICC=.75). The average ratings from all 3 raters were used in all subsequent analyses.

Subjective Emotional Responses. Immediately after viewing each film clip, subjects completed a post-film questionnaire (Rottenberg, Ray, & Gross, 2007). The instructions were to indicate, on a 9 point scale, the greatest amount of each of 18 specific emotions that they experienced while watching the film clip. The subjects' responses to the item "amusement" were used in all analyses related to the amusing film clips.

Subjects' responses to the item "sadness" were used in all analyses related to the sad film clips.

Statistical Procedures

The effects of sleep loss on subjective emotional responses and facial expressiveness were analyzed using repeated measures analysis of variance to test for a main effect of sleep deprivation as well as an interactions of sleep condition with the type of film clip they viewed (amusing and sad). Where possible, Cohen's *d* effect sizes (Cohen, 1988) were calculated using the mean difference between sleep deprived and control subjects divided by the pooled variance of both groups.

Results

Each subject was videotaped while viewing 4 film clips, producing 92 video segments for scoring. Five of these could not be scored due to equipment malfunction or experimenter error. After each clip, subjects completed a post-film questionnaire, producing 92 questionnaires. Nine of these could not be used in analysis due to subject error in completing the forms.

Sleep manipulation. Actigraphy reports and behavioral monitoring confirmed that all subjects in the control group were in bed with lights out from 11:00 p.m. to 8:00 a.m. and that all subjects in the sleep deprivation condition were awake from the time of their arrival at the laboratory until the second night when recovery sleep was allowed.

Subjective responses to film clips

A manipulation check revealed that the film clips elicited high levels of the intended emotions (based on self-reports, scale range 0-8). The average reported intensity of amusement in response to the amusing clips was 6.1 (+/-1.4) and 6.0 (+/-1.8) on days 1 and 2 respectively. The average reported sadness in response to the sad clips was 6.2 (+/-1.8) and 6.0 (+/-2.0) on days 1 and 2 respectively. Repeated measures analysis of variance revealed no differences in subjective responses between the 2 amusing clips ($F=0.18$, $p=.68$) nor between the 2 sad clips ($F=0.02$, $p=.89$), indicating that although the clips were different, they elicited comparable intensities of the target emotions.

Repeated measures analysis of variance found that the effect of sleep deprivation on subjective responses to films failed to meet criteria for statistical significance ($F=2.30$, $p=.15$). Sleep deprived subjects reported relatively less amusement than controls in response to the amusing film clip ($d=0.80$) and relatively less sadness than controls in response to the sadness inducing clip ($d=0.26$). These results are shown in Figure 1.

Facial expressiveness in response to film clips

There were no significant differences between groups in facial expressiveness prior to sleep deprivation ($F=0.59$, $p=.45$). Repeated measures analysis of variance revealed that sleep deprived subjects were significantly less expressive than control subjects overall ($F=4.57$, $p=.045$). The emotion by group interaction failed to meet criteria for statistical significance ($F=1.81$, $p=.19$), indicating that the effect was not due exclusively to differences in response the positive or negative film clip. There was a

larger effect of sleep deprivation on expressiveness in response to the amusing film clip (d=1.12) than on expressiveness in response to the sad clip (d=0.40). These results are summarized in Figure 2.

Discussion

It is widely believed that inadequate sleep has deleterious effects on emotional functioning, but only a handful of studies have directly investigated this hypothesis in an experimental context. This study is one of the first to examine how sleep deprivation influences basic emotional processes in healthy adults. We found that facial expressiveness, one of the primary ways in which emotion is communicated, was less intense in sleep deprived subjects than in rested control subjects who were exposed to emotionally provocative film clips. Facial expressions in response to the positive film clip showed a particularly large effect, suggesting that positive emotions may be more sensitive to sleep deprivation than negative. This interpretation is consistent with our experience with sleep deprived subjects from many previous protocols who have generally showed a flattening of affect over the course of deprivation.

The reduction in expressiveness did not translate to equivalent reductions in subjective emotional experiences elicited by film clips. The lower self-reported emotional responses in the sleep deprived group relative to the control group failed to meet criteria for statistical significance, but the relatively small sample size prevents strong conclusions from null findings. Nevertheless, effect size estimates suggested that sleep deprivation had a moderate to large effect on subjective responses that was in the same

direction as the effects on facial expressiveness. Additional studies with larger samples are needed to get a more accurate estimate of these effects, but based on our findings we would predict that sleep deprivation decreases the intensity of subjective experiences of emotion as well as its expression.

The larger response of objective indicators of emotion relative to subjective responses may provoke a question of what the "real" influence of sleep deprivation was on emotion. This question is perhaps best addressed by remembering that emotions are multifaceted constructs involving dissociable components of subjective feeling states and emotional expression (Ekman & Oster, 1979). Both are real aspects of emotion, but the former is the private experience of the emotion and the latter is a public display of it. Previous studies, especially in clinical populations, have clearly demonstrated the dissociability of these two features of emotion (see Kring, Kerr, Smith, & Neale, 1993 for example in schizophrenia). Our findings suggest that sleep deprivation may degrade the normal relationship between public and private emotional responses, causing people to appear less emotional than they feel.

People who are chronically unable to attain sufficient sleep, whether due to busy lifestyles or medical conditions, may experience significant consequences from dampened emotional expressiveness. Several decades of research have established many important functions for facial expressions of emotion including eliciting help, primarily through negative emotional displays, and maintaining relationships and reinforcing desired behaviors in others, primarily through positive emotional displays (see Keltner et al., 2003 for a detailed review). A reduction in emotional expressiveness could therefore

have serious consequences for long term social functioning and well being. Interventions to improve sleep are therefore quite important, both in medical settings and in the general population.

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Figure 1. Mean subjective emotional responses to an amusing and a sad film clip reported. The effect of sleep deprivation failed to meet criteria for statistical significance (p=.15). The sleep deprived group (dark gray columns) reported less intense reactions to both the amusing clip (d=0.80) and the sad clip (d=0.26) than the control group (light gray columns). Error bars represent standard errors.

Figure 2. Mean facial expressiveness in response to an amusing and a sad film clip for sleep deprived subjects (dark gray columns) and rested control subjects (light gray lines). There was a significant main effect of sleep deprivation on expressiveness (p=.045). The interaction of sleep condition by type of clip failed to reach statistical significance (p=.19). Sleep deprivation was associated with a larger effect (d=1.12) for the amusing clip than for the sad clip (d=0.40). Error bars represent standard errors.

Running Head: **SLEEP DEPRIVATION AND STRESS**

Word count = 3,009

The Effects of Sleep Deprivation on Stress Induced by Performance Demands

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Abstract

Previous research has established that psychosocial stress can interfere with sleep, but it is not yet known how inadequate sleep influences subsequent responses to stress. This study aimed to investigate the effects of one night of total sleep deprivation on subjective and physiological responses to performance-induced stress. Self reported affective responses and salivary cortisol were studied after low and high stress induction procedures. Fifty-three subjects completed a laboratory-based sleep deprivation experiment where low and high stress was induced on two consecutive days. Subjects in the sleep deprivation group reported significantly greater subjective stress and negative mood after the low-stress induction procedure than subjects in the control group. Subjective reports of stress and mood were similar in both groups after the high stress induction procedure. There were no significant differences between groups in salivary cortisol secretion in response to low or high stress induction procedures. These results suggest that inadequate sleep increases perceived stress and negative affect in response to relatively easy performance tasks, but not to more severe stressors.

The Effects of Sleep Deprivation on Stress Induced by Performance Demands

Introduction

Stress has emerged as an important concept in the theory and practice of psychology, medicine and public health. The physiological changes associated with stress facilitate the detection of and escape from threat, but chronically elevated and excessive stress may damage bodily systems and reduce wellbeing and happiness unnecessarily (Korte et al., 2005). Furthermore, threats to psychological integrity can activate the same physiological responses as physical threats (Gunnar & Quevedo, 2007). In modern societies, this response is often maladaptive, interfering with concentration (e.g, test anxiety) and performance (e.g., public speaking). It is therefore important to improve our understanding of the human response to psychological as well as physical stressors.

There is a well established literature demonstrating the sleep is sensitive to stress (see Akerstedt, 2006 for review). Severe stressors such as life threatening trauma can cause long term, severely disrupted sleep (as seen in posttraumatic stress disorder), but even daily fluctuations in stress levels due to normal life events have been shown to temporarily disrupt sleep. For example, stress due to increased work demands (Akerstedt et al., 2002) and impending exams (Holdstock & Verschoor, 1974) have been shown to reduce sleep quality and duration. A recent field study using in-home recording of sleep physiology found that higher daily stress was associated with lower sleep efficiency, increased wake time, and increase latency to stage 3 sleep (slow wave or deep sleep) on the following night (Akerstedt, Kecklund & Axelsson, 2007).

Less is known about how restricted sleep influences stress responses. Based on findings that sleep deprivation disrupts memory, degrades endocrine function, and alters metabolic processes, McEwen (McEwen, 2006) concluded that sleep deprivation is itself a neurobiologic and physiologic stressor. Animal studies have gone even further in suggesting that sleep deprivation alters both baseline activity of the stress system and physiological responses to subsequent stress (Sgoifo et al., 2006). Similar data in humans however are currently lacking.

At present, no studies have been published that experimentally manipulated stress and sleep, so there is no direct evidence that sleep deprivation alters subjective or physiological stress responses in humans. Studies that have measured biomarkers of stress during sleep deprivation experiments have found inconsistent results (see Leproult et al., 1997; Redwine et al., 2000), possibly because there was no acute stressor administered during the experiments. Nevertheless, indirect evidence from neuroimaging studies supports the hypothesis that sleep deprivation is likely to alter subjective and physiological responses to an acute stressor. Wang and colleagues (Wang et al., 2005) reported that performance-induced stress was associated with activation in several areas of the prefrontal cortex, a brain region that has been found to be sensitive to sleep loss and may function improperly when sleep pressure is elevated (Durmer & Dinges, 2005; Horne, 1993). Because the prefrontal cortex plays a central role in inhibitory control of negative emotions (Davidson, 2004; Ochsner & Gross, 2005), impaired function due to sleep loss would be expected to result in disinhibited (i.e., more intense) stress responses.

The present study was conducted to investigate the influence of sleep deprivation on subjective and physiological responses to a psychosocial stressor in healthy adult volunteers. To the best of our knowledge, it is the first study to experimentally manipulate both stress and sleep duration in humans. A previously validated stress induction procedure (Dinges et al., 2005) was used that altered task difficulty and feedback about performance to create low stress and high stress conditions. Subjects were randomly assigned to sleep deprivation or a control condition and completed identical stress induction procedures in a controlled laboratory setting.

Methods

Data from two studies with a very similar design were combined for the present analyses. In both studies, subjects completed low and high stress induction procedures on two consecutive days. After the first day, subjects were randomly assigned to either one night of total sleep deprivation or to a control condition in which they were given 9 hours of sleep opportunity. Subjective (self report) and physiological (salivary cortisol) responses to the stress induction procedures were assessed. Study 1 (n=30) and Study 2 (n=23) had different screening procedures, slightly different stress induction procedures, and different frequencies of saliva collection (see below for details).

Subjects

Subjects were 53 healthy volunteers recruited from the general community. Twenty-seven men and 24 women (mean age = 30 +/- 6.9 years) completed a 48 hour

laboratory-based protocol, approved by the Institutional Review Board of the University of Pennsylvania. All subjects provided informed consent and were compensated for their participation. The sample included 21 African-American subjects, 26 Caucasian subjects, and 6 subjects of other ethnicities.

To participate in the study, volunteers had to be between the age of 22 and 45, have normal sleep wake schedules for the past 60 days, be in good medical health, avoid smoking, and be free from psychiatric disorders, including drug and alcohol abuse. Volunteers for Study 1 completed a structured clinical interview (SCID I, (First et al., 1997)) to ensure that they did not meet criteria for any Axis I psychiatric disorders. Volunteers for Study 2 did not complete a structured clinical interview because less intensive screening was found to be equally effective. After entry into the study, subjects were removed who were physically ill, had poor sleep the previous night, or reported Beck Depression Inventory (BDI-II) scores at or above 14. Six subjects were removed from the experiment based on these criteria.

Measures

Subjective responses to the stress induction procedures were measured by self reports of stress and mood. Stress was measured after each induction procedure by a computer-administered visual analog scale (0-8) with a range of "not stressed at all" to "extremely stressed." Mood was measured after each induction procedure by a computerized version of the Profile of Mood States (McNair & Heuchert, 2005; McNair, Lorr & Droppleman, 1971), a 65 item adjective checklist where each item is rated on a 5-

point scale that ranges from “not at all” to “extremely.” Based on factor analytic studies (see (McNair & Heuchert, 2005) the items are organized into the following subscales: Depression, Anxiety, Anger, Fatigue, Confusion, and Vigor. These subscales are combined to give a single composite score, Total Mood Disturbance.

Physiological responses to the stress induction procedures were measured by salivary cortisol. Saliva was collected using salivettes with cotton inserts placed between the tongue and roof of the mouth and subjects’ food and water intake was carefully controlled prior to collection. Samples were spun down by centrifuge and stored on site in a -80° C freezer. They were later thawed and assayed for cortisol at the Biochemistry Core Laboratory, located in the Hospital of the University of Pennsylvania using standard salivary immunoassay kits from Salimetrics LLC. Subjects in both studies gave baseline saliva samples in the morning of each day of testing, prior to stress induction procedures, and again after each low stress and high stress induction procedure. Additional saliva samples were collected from subjects in Study 2 immediately before low and high stress induction procedures as well.

Procedures

Sleep Deprivation. Subjects were randomly assigned to the sleep deprivation or control condition. In Study 1, subjects had an equal likelihood of assignment to either group. In Study 2, subjects were randomly assigned with approximately 2:1 likelihood of receiving the deprivation condition. Twenty-nine subjects (17 males, 12 females) completed the sleep deprivation protocol and 24 subjects (12 males, 12 females)

completed the control protocol. Subjects entered the laboratory at 9:00 a.m. and completed consenting procedures. After the first day of testing, subjects either received no sleep opportunity (sleep deprivation group) or they were given 9 hours of sleep opportunity (control group) from 11:00 p.m. to 8:00 a.m. At night, subjects in the sleep deprived condition completed 10 minute reaction time tasks every 2 hours. They were allowed to read magazines, complete puzzles, and interact with staff to maintain wakefulness, but no television or electronics were available and contact between subjects was strictly prohibited. A second day of testing was then completed followed by 10 hours of recovery sleep opportunity from 10:00 p.m. to 8:00 a.m. for all subjects. Subjects were informed of their condition at 8:00 p.m., after the first day of testing had been completed.

Subjects completed the experiment with minimal contact with other subjects. Each had a separate room and all testing was done individually. Subjects were monitored continuously by trained staff members using closed-circuit, infrared cameras. Adherence to sleep condition was further validated by actigraphy, an objective method for estimating sleep based on movement (Ancoli-Israel et al., 2003).

Stress Induction. Subjects completed test batteries under conditions designed to induce low stress and high stress that were previously validated in our laboratory (Dinges et al., 2005).

The high stress inductions involved more difficult performance tasks, negative social feedback, and greater time pressure relative to the low stress inductions. In Study 1, negative feedback was given both verbally during testing and by computer after testing. In Study 2, negative feedback was given only by computer.

We adapted mental arithmetic tasks for the primary stressor. In the high stress condition, subjects responded verbally to a serial subtraction task (i.e., subtraction of 13 from a four-digit number, Kirschbaum, Pirke & Hellhammer, 1993; Wang et al., 2005) and a descending subtraction task (Dinges et al., 1981). In Study 1, subjects also completed the Stroop color-naming task (Stroop, 1935) and a divided attention task (Synwork; Elsmore, 1994). In Study 2, subjects completed mental arithmetic tasks only. In order to assess the possibility of aptitude influencing perceived stress in response to these tasks, IQ was measured with a previously validated seven subtest short form of the Wechsler Adult Intelligence Scale Third Edition (WAIS-III; (Wechsler, 1997)). This short form has been found to correlate near perfectly (r=.97) with the full scale IQ measurements using the full version of the WAIS III (Ryan & Ward, 1999).

Subjects completed stress testing on both days of the experiment. To control for circadian effects, testing occurred at the same time on both days (between 4:00 p.m. and 6:00 p.m.). Tasks were completed in an unfamiliar, brightly lit room that contained minimal furniture, giving it an austere appearance. Subjects completed all testing alone. A trained staff member, unfamiliar to the subjects, delivered instructions for the tasks by intercom. Cameras were clearly visible in front of and above the subject.

Subjects first completed testing under low stress conditions, then returned to their rooms to complete questionnaires. Approximately 1 hour later, they completed testing under high stress conditions. All subjects were informed of the true nature of the experiment immediately following the final stress induction procedure. Debrief

interviews confirmed that subjects were unaware that the procedures were primarily intended to elicit stress.

Data analysis

Differences between sleep deprived and rested control subjects in subjective responses to the low and high stress induction procedures were analyzed with independent samples t tests. Between groups differences were also analyzed using change scores to control for baseline responses. Change scores were calculated by subtracting baseline values from responses after the sleep manipulation. Cohen's *d* effect sizes (Cohen, 1988) were calculated using the mean difference between sleep deprived and control subjects divided by the pooled variance of both groups.

Cortisol levels were checked for normality prior to analysis using Shapiro-Wilks test and log transformed as needed to improve fit with a normal distribution. The log transformed scores were then compared within and between groups using paired and independent samples t tests. Non-parametric analyses of mean differences were also completed using the original (non-transformed) values. Within groups differences were compared with Wilcoxon signed-rank tests and between groups differences with Mann-Whitney U tests.

Results

Subjective Responses

Self Reported Stress. A manipulation check confirmed that procedures induced the intended subjective effects. On the first day of the study (prior to any sleep manipulations) subjects reported greater subjective stress after the high stress relative to the low stress induction (mean low = 1.83, mean high = 3.25, t=6.36, $p<0.001$). There were no differences in self-reported stress between sleep deprived and control subjects prior to the sleep manipulation (*p* values greater than 0.82), indicating that the randomization procedure was successful. Estimated IQ was not significantly correlated with self-reported stress after the low stress (r=.06, $p=.67$) or high stress (r=.11, $p=.45$) induction procedures. Paired samples t-tests revealed that the control group's self-reports of stress did not differ significantly between Day 1 and Day 2 for low stress (t=1.37, $p=0.19$) or high stress (t=0.48, $p=0.63$) induction procedures, indicating that repeated exposure to the stress induction procedures did not significantly alter the subjective stress response.

Analysis of responses after the experimental manipulation revealed that the sleep deprived group reported significantly greater subjective stress in response to the low stress condition than subjects in the control condition (t=2.12, $p=.04$, $d=0.57$), but there was not a significant difference between these groups in subjective responses to the high stress procedure (t=0.60, $p=.55$, $d=0.17$; **See Figure 1**). Analyses using change scores (subjective stress on Day 2 minus Day 1) to control for individual differences in reporting styles confirmed these results. Sleep deprived subjects reported significantly larger change scores (indicating significantly greater stress responses on Day 2 relative to Day

1) than control subjects in response to the low-stress inductions (t=2.49, p=.02, d=0.77) but not for the high stress inductions (t=0.83, p=.41, d=0.24).

[Figure 1 here]

Self Reported Mood. A manipulation check of responses prior to the sleep manipulation (Day 1 only) revealed that Total Mood Disturbance, the composite score for the Profile of Mood States (POMS), was greater following the high stress induction than following low stress induction (t=6.36, p<0.001). Post hoc analyses revealed that all six of the POMS subscales indicated elevated mood disturbance after the high stress induction procedure relative to the low stress induction procedure (all p values less than 0.015).

Analyses of the combined effects of stress and sleep deprivation revealed that Total Mood Disturbance scores were significantly elevated for the sleep deprived group relative to the control group after both low stress (t=5.25, p<.001, d=1.51) and high stress (t=2.60, p=.01, d=0.72) induction procedures (see **Table 1**). Post-hoc analyses were conducted to determine the relative contribution of each subscale score to the overall elevation in mood disturbance. After the low stress induction procedure, sleep deprived subjected reported significantly more Fatigue (p<0.001, d=2.33), Confusion (p<0.001, d=1.19), Anger (p=0.003, d=0.91), and Anxiety (p=0.005, d=0.81), and significantly less Vigor (p=0.006, d=0.74) than control subjects. Only Depression subscale scores did not differ significantly between sleep deprived and control subjects after low stress induction procedures (p=0.06, d=0.56). After the high stress induction procedure, sleep deprived

subjects reported significantly greater Fatigue ($p<0.001$, $d=1.67$) and lower Vigor ($p=0.006$, $d=0.80$). There were no significant differences between sleep deprived and control subjects after the high stress induction procedure on Anger, Anxiety, Confusion, or Depression (all p values > 0.10).

[Table 1 here]

Physiological Results

Two samples could not be assayed for cortisol due to low saliva volume. Analyses using Shapiro-Wilks tests revealed that the cortisol values were not normally distributed (p values < 0.01). After log transformation, the data were found to have acceptable fit with a normal distribution (all p values greater than 0.13). A manipulation check using only subjects from Study 2 revealed that the high stress induction procedure was unsuccessful in eliciting cortisol elevations. Neither the low nor high stress induction procedure was associated with a significantly elevated cortisol level (p values greater than 0.10). Analyses using nonparametric Wilcoxon signed-rank tests on the raw cortisol values confirmed this result.

Analyses of physiological responses between groups after the sleep manipulation found no effect of sleep deprivation on salivary cortisol concentration. An independent samples t-test revealed no differences between sleep deprived and control subjects in salivary cortisol concentration after the low stress (t=0.49, $p=0.62$) or high stress (t=0.14, $p=0.89$) induction procedures. A Man Whitney U test on the original cortisol values also found no differences between sleep deprived and control subjects following the low stress or high stress induction procedures (p values greater that 0.77).

Discussion

The purpose of this experiment was to investigate the effects of sleep deprivation on psychosocial stress responses in healthy adult volunteers. Although we found no differences between sleep deprived and control subjects in the physiological response to stress, we found that sleep deprived subjects reported significantly greater subjective stress in response to the low stress (but not to the high stress) induction procedure than rested control subjects. Subjective reports of mood also suggested that sleep deprivation had broader effects in the low stress condition than in the high stress condition with the sleep deprived group reporting significantly higher levels of Anxiety, Anger, and Confusion in addition to the increased Fatigue and decreased Vigor we would expect from sleep deprivation alone. The influence of sleep deprivation on affective responses to the high stress induction were much more mild by comparison, showing significant differences in Fatigue and Vigor only. These results suggest that sleep deprived subjects may subjectively over-respond to mildly stressful situations while responding normally to more severe stressors.

Previous research established that subjective stress during the day interferes with sleep at night (Akerstedt, 2006). Our findings complement this research by showing that inadequate sleep at night may then increase negative affect in response to relatively minor stressors encountered the following day. This finding highlights the importance of stress management in people who obtain inadequate sleep due to medical conditions or occupational demands. In people with psychiatric conditions such as depression and

chronic insomnia however, avoidance of stressors often serves to maintain problematic affective states and maladaptive behaviors (Ferster, 1973; Harvey, 2002) so care must be taken in extending these findings to clinical populations.

The primarily limitation of this study was the failure of the stress induction procedure to elevate cortisol levels. Although we used a standard, previously validated psychosocial stressor, it failed to elicit the intended responses in this study. We were therefore unable to investigate how physiological stress reactions are altered by sleep deprivation and can only report that resting levels of cortisol were not sensitive to sleep loss. It is therefore still an open question whether or not sleep deprivation influences HPA axis reactivity to psychosocial stress.

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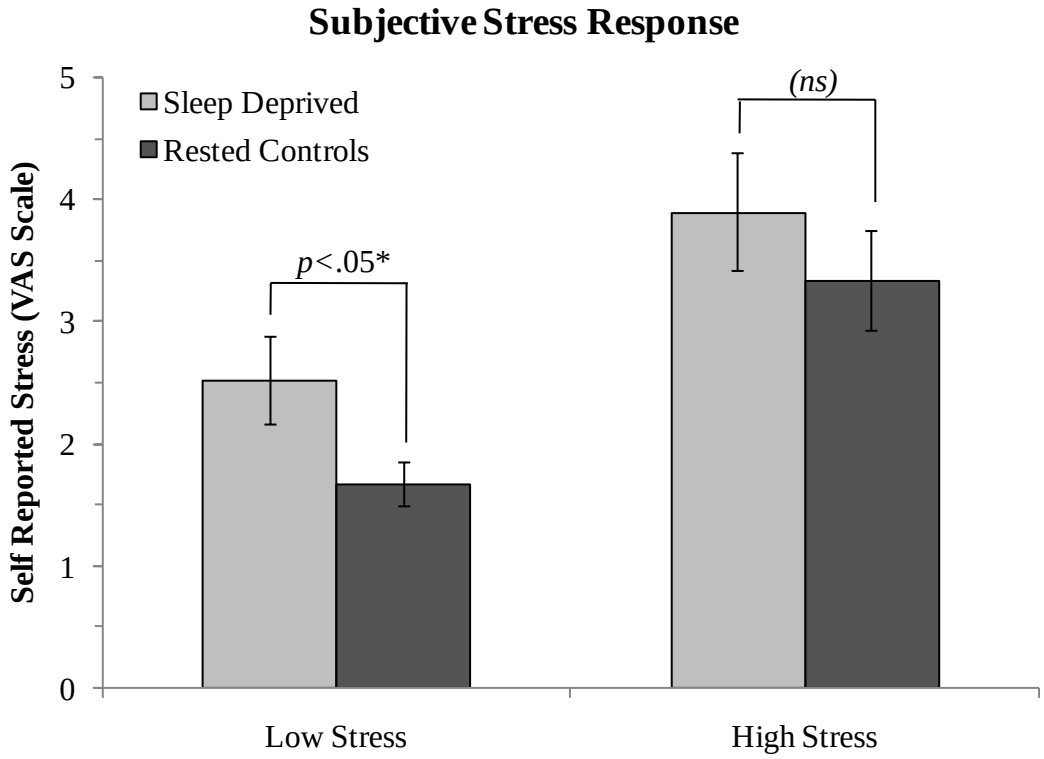

Figure 1. Subjective stress responses to low and high stress inductions for sleep deprived (light gray bars) and control subjects (dark gray bars). Sleep deprived subjects reported significantly greater stress in response to the low-stress condition than control subjects (t=2.12, *p*=.04, *d*=0.57). Group differences in response to the high stress induction were not significant (t=0.60, *p*=.55, *d*=0.17). Error bars represent standard errors.

Table 1

Profile of Mood States Scores After Low and High Stress Induction for Sleep Deprived and Control Subjects

Condition	Variable	Control Group	Sleep Deprived Group	Effect Size Cohen *d*	*p* value
Low Stress	Anger*	0.50 (1.06)	2.14 (2.50)	.91	.003
	Anxiety*	3.88 (2.42)	6.24 (3.40)	.81	.006
	Confusion*	3.29 (1.99)	6.48 (3.36)	1.19	<.001
	Depression	0.75 (1.36)	1.97 (2.97)	0.56	.056
	Fatigue*	1.67 (2.22)	11.45 (6.19)	2.33	<.001
	Vigor*	12.13 (8.70)	6.10 (7.64)	0.74	.01
	*Total Mood Disturbance**	*-2.04 (12.46)*	*22.17 (19.53)*	*1.51*	*<.001*
High Stress	Anger	3.21 (5.41)	2.79 (4.32)	0.09	.76
	Anxiety	6.50 (4.05)	7.75 (5.53)	0.26	.36
	Confusion	5.08 (3.76)	6.82 (3.82)	0.46	.11
	Depression	2.63 (6.47)	2.14 (3.67)	-0.10	.74
	Fatigue*	2.96 (3.605)	11.11 (6.14)	1.67	<.001
	Vigor*	10.67 (8.580)	4.82 (6.12)	0.80	.006
	*Total Mood Disturbance**	*9.71 (22.072)*	*25.79 (22.35)*	*0.72*	*.012*

* Between groups difference significant at the 0.05 level (two tailed).

A negative effect size indicates an unexpected benefit of sleep deprivation on mood.

DISCUSSION

The overarching goal of the studies presented here was to improve our understanding of the influence of sleep loss on affective functioning in healthy adults. Study 1 (Sleep and Mood) found three facets of mood (Fatigue, Vigor and Confusion) to be sensitive to sleep restriction, increasing in a dose-response manner as wakefulness was extended and covarying with a well validated behavioral assay of alertness (the PVT reaction time task). Three other facets of mood (Depression, Anxiety, and Anger) were not sensitive to sleep restriction and did not covary with performance on the PVT. Study 2 (Sleep and Emotion) found that sleep deprivation decreased expressiveness in response to positive and negative emotion probes. Although the effects on self-reports were not statistically significant, there was a trend toward decreased intensity of subjective emotional reactions for both positive and negative emotions for sleep deprived subjects as well. Study 3 (Sleep and Stress) found that sleep deprivation was associated with a heightened subjective response to a mild stressor, but not to a more intense stressor. When taken together, these studies offer new insights into the relationship between sleep and affect. In this final section of the dissertation, I would like to review emerging themes across these studies and to propose suggestions for future studies, some of which we have already been implemented in our own laboratory.

Sleep loss, de-arousal, and affect

Previous studies of sleep deprivation have established robust effects of sleep loss on behavior and cognition that should not be ignored in studies of sleep deprivation and

affect. Among the most robust findings are that cognitive processing slows and performance becomes more variable (Durmer & Dinges, 2005). Dinges (Doran, Van Dongen & Dinges, 2001; Durmer & Dinges, 2005; Minkel, Banks & Dinges, 2009) has proposed that these changes reflect neural instability caused by a conflict between wake-promoting and sleep-initiating mechanisms. Studies 1 and 2 (Mood and Emotion) highlight the effect of such instability on affect. Positive mood and energy declines while fatigue and confusion increase, dampening the overall emotional response to affective probes. This de-arousal represents an important influence of sleep loss on affective functioning that has so far been overlooked in explanations of sleep and emotion.

Findings in Study 3 (Sleep and Stress) however are not well explained by de-arousal. Sleep deprived subjects reported a more intense affective response than the control group, but primarily in response to the low stress induction. This difference probably reflects different cognitive appraisals of coping potential between sleep deprived and rested control subjects. Perceived stress is understood to be determined by an individual's appraisals of both the stressor and his ability to cope with that stressor. In the context of performing arithmetic and other cognitive tasks, the sleep deprived group may have had significantly different appraisals of their coping abilities for the relatively easy tasks. The high stress condition may have simply involved tasks that were so difficult that both groups of subjects reported relatively high stress. Furthermore, subjects knew that the high stress task was the final performance task to be completed in the experiment. The reduction in anticipatory anxiety for future tasks may also have produced this difference.

Explanations of sleep deprivation and emotion

There are currently two published explanations for changes in affective functioning associated with sleep loss. The more popular hypothesis posits that sleep loss causes emotional dysregulation through its deleterious influence on the prefrontal cortex (Dahl & Lewin, 2002). This explanation assumes that sleep loss potentiates emotional responses, especially those related to negative emotions and strong appetitive drives. Although this hypothesis was proposed to explain adolescent risk taking behavior, the same arguments should hold for healthy adults who consistently show altered prefrontal cortex activity during cognitive tasks, including those specifically related to inhibitory control (Chuah et al., 2006). Findings here do not support that hypothesis. Study 2 (Sleep and Emotion) found reductions in behavioral and subjective aspects of emotion when the Dahl & Lewin (2002) hypothesis would predict increases. Study 3 found a significant effect of sleep loss on subjective responses to low stress when the Dahl & Lewin (2002) hypothesis predicts greater responses to the high stress. It appears that although it is true that the prefrontal cortex is sensitive to sleep loss (as reported by (Yoo et al., 2007), other neural mechanisms may buffer or mask the effects on the feeling and expression of emotion. If de-arousal is more potent that the corresponding increase from disinhibition, then the net change would still be a decrease in emotional intensity. Additional neuroimaging studies needed that measure subjective as well as neural responses to emotion probes after sleep deprivation.

A second explanation for emotional changes associated with sleep loss has been proposed by Zohar and colleagues (Zohar, Tzischinski & Epstein, 2003; Zohar et al., 2005) based on field studies rather than laboratory-based experiments. They suggest that "cognitive energy" associated with sleep loss is required both for coping with negative events and for capitalizing on new opportunities offered by positive events. When cognitive energy is depleated by sleep deprivation, positive events are associated with dampened positive emotion and negative events are associated with potentiated negative emotion. This theory accurately predicts some of the findings from the studies presented here. Positive affect was dampened by sleep deprivation in all three studies, but negative affect was only potentiated in response to stress induced by performance demands, not in response to sadness induced by a film clip. This may reflect the difference in methodology (experiential sampling in a field study vs. laboratory-based experimentation) used to develop this theory. Zohar and colleagues (ref) reported increased negative affect in medical residents exposed to goal-discordant events after sleep loss. These events were likely much more stressful than passively viewing a sad film clip. The cognitive energy explanation may therefore be most relevant for explaining stress responses while the de-arousal explanation offered above explains reactions to non-threatening events. Both explanations are admittedly vague and will require additional studies to ground them biological principles. Nevertheless, together they offer the best explanation of the available data.

Future directions

Sleep deprivation and mood

The study of sleep deprivation and mood is fairly advanced compared to investigations of other affective constructs, such as stress and emotion. Study 1 (Sleep and Mood) presented here was conducted with an extremely large sample and largely replicated previous findings from our lab and others (Dinges et al., 1997; Haack & Mullington, 2005). The more interesting area to pursue now is individual differences in coherence between reaction time and mood. The study of individual difference in mood has been restricted by the limitations of self report. One cannot be sure if subjects who report less fatigue actually experience less or simply report it differently. For example, in Study 1, African-American subjects reported only half the level of mood disturbance as Caucasian subjects (data not reported in manuscript), but we cannot assume that they only felt half the effects because cultural differences in response style cannot be ruled out. The coherence approach is robust to such differences in reporting style, allowing the researcher to focus on whether or not changes in mood correspond to changes in objective performance. Future studies of mood would do well to focus on objective-subjective discrepancies rather than on absolute values of mood change.

Sleep deprivation and emotion

The study of sleep deprivation and emotion is extremely new with only two published reports of experiments that manipulated sleep duration and emotional states (i.e., Franzen, Siegle & Buysse, 2008; Yoo et al., 2007). In addition to using larger samples, future studies would be more compelling if they used a greater variety of

emotion induction procedures. Both published studies of sleep deprivation and emotion used photographs to elicit emotions, an induction method that we found problematic and quickly abandoned. A substantial portion of sleep deprived subjects in our studies experienced attentional lapses and slow eyelid closures, even while viewing highly provocative photographs (e.g., erotica and bodily injury). It is therefore difficult to interpret findings based on such methods. For example, it is possible that the subjects in the Yoo et al. (2007) showed greater activation in neural networks associated with fear because they were startled out of microsleeps by the noise of the fMRI magnet. Future studies must take care to use methods that are not likely to be contaminated by known correlates of sleep deprivation.

Our own studies of sleep deprivation and emotion have focused on film clips for emotion elicitation because they offer the same level of experimental standardization as photographs and are easier for subjects to tolerate when sleep deprived. We have expanded the emotions we elicit with film clips to include disgust and anger as well as amusement and sadness. It would also be of interest to include films that elicit mixed emotions (e.g., bitter-sweet reactions) to investigate asymmetries in the sensitivity of positive and negative emotions to sleep loss. We are also piloting new methods for emotion induction that involve face to face interviews about emotionally provocative memories and role-plays of emotional situations. These new methods appear to elicit more intense emotions with more dramatic (and more varied) facial expressions. These methods are more difficult to standardize, but offer greater ecological validity and may

prove to be a useful addition to a more comprehensive emotion-elicitation battery in future experiments.

Sleep deprivation and stress

Study 3 (Sleep and Stress) is the first experiment to elicit stress in humans after sleep deprivation. Our laboratory has expanded this study with several important improvements. Because cortisol was not elevated by our previous induction procedure, we added the best-validated psychosocial stressor (a combined public speaking and mental arithmetic task; (Kirschbaum, Pirke & Hellhammer, 1993) and adjusted the timing of saliva collection to reflect the best practices in the field (Gordis et al., 2006). Preliminary data on 10 subjects suggests that this method successfully elicits cortisol elevations and allows us to investigate the temporal profile of the physiological stress response rather than just the peak (see **Figure 1**). In addition, preliminary analyses of video tape during stress induction suggest that subjects make displays that are not captured by Ekman's basic emotions (Ekman & Oster, 1979) including confusion and concentration displays described by Rozin & Cohen (Rozin & Cohen, 2003). We are currently working with colleagues in computer science to develop an automated, computerized method for scoring stress displays that will make detailed scoring of large samples feasible (at present, such scoring is too labor intensive).

Finally, all experiments of sleep deprivation and affect could be expanded to include subjects across a wider spectrum of psychopathology. The relationship among inadequate sleep and depression appears to be particularly strong and ripe for

investigation. Progress in the basic science of sleep, emotion and psychopathology is likely to result in novel and more effective treatments for pervasive mental health problems as well as a slightly better understanding of the human condition more generally.

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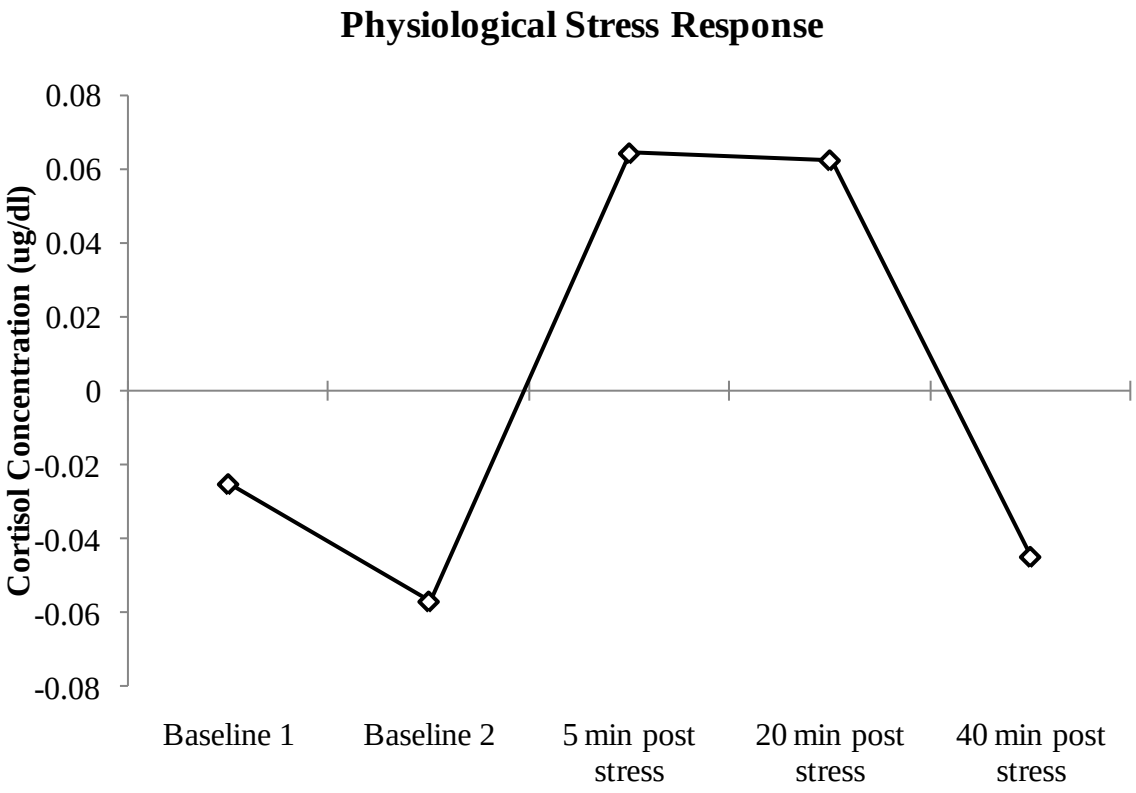

Figure 1. Figure shows average salivary cortisol secretion from N=10 subjects in response to the Trier Social Stress Test. Values were normalized by subtracting each subject's mean from every score. Baseline samples were taken 20 minutes and 5 minutes before the stressor. Cortisol decreased during baseline, rose sharply in response to the stressor and returned to baseline within 40 minutes. This method will allow for a more powerful comparison between sleep deprived and control subjects than the previous method.