The Effects of Sleep Manipulation on Emotional Processing and Mood

by

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Abstract

Sleep manipulations have often been used to attempt to reveal the role of sleep. Early research, however, has also implicated certain sleep manipulations including late partial sleep deprivation, and REM-deprivation as temporarily mood enhancing in depressed individuals. These initial findings have prompted the present three-paper dissertation to explore the potential impact that three distinct sleep manipulations, a homeostatic sleep delay challenge, slow-wave sleep disruption, and napping may have on mood and emotional processing. The first study will examine a three-hour sleep delay and the associated effects on mood disturbance, in a sample of healthy and depressed adults. The second study explores the impact of disrupting slow-wave sleep on an aspect of emotional processing, the recognition of positive and negative words, in healthy individuals and those with depression. Finally, the third study will investigate the potential benefits of napping on frustration tolerance and impulsive behavior in a sample of healthy adults. If our results indicate that sleep manipulation does indeed show positive effects on mood and emotional processing, this may help inform treatment strategies for psychiatric disorders such as major depressive disorder, or help develop intervention approaches for vulnerable populations who have been shown to be prone to emotional dysregulation

Chapter 1: General Introduction

Although its role is still unclear, sleep has been shown to be necessary for adequate functioning. Research on the effects of organic and experimental sleep deprivation has been conducted for the last century, and has documented several cognitive and physiological effects, including decreased attention and alertness, memory disturbance (Durmer & Dinges, 2005), decreased immune functioning (Haack & Mullington, 2005), and increased risk for high blood pressure and heart disease (Shahar et al., 2001). Anecdotally, the emotional consequences of sleep loss have been noted frequently, including emotional lability, increased irritability, and decreased tolerance for distress or frustration. Although the current literature is beginning to support these claims, research on the emotional effects of sleep loss is only in its infancy. Dinges and colleagues (1997) showed that across a 7-day period of sleep restriction, emotional disturbance was increased, indicated by Profile of Mood Symptoms scores and Kahn-Greene (2007) showed that self-reported depressed mood, anger and frustration all increased following sleep loss. Additionally, sleep loss may not only affect mood directly but may affect how individuals interpret and manage difficult situations. Zohar and colleagues (2005) demonstrated that medical residents who experienced sleep loss and a disruptive daily event reported more negative emotion than those who did not have limited sleep and Killgore (2008) showed that sleep deprivation limits coping skills and may increase one's perception of stress. Taken together, these recent studies give preliminary empirical support to the subjective accounts that sleep disruption has a largely negative impact on emotional functioning.

In contrast, studies have also indicated that individuals with major depressive disorder (MDD) show a curious deviation from the sleep pattern shown by healthy individuals. In response to sleep deprivation, those with MDD show brief symptom improvement which typically lasts until recovery sleep occurs (Gillin et al., 2001). These results have not only been found in response to total sleep deprivation, but also to REM-deprivation, and late-night sleep deprivation (Giedke & Schwarzler, 2002; Giedke, Klingberg, Schwarzler, & Schweinsberg 2003). However, some researchers have argued that it is not the timing of the sleep disruption that is critical, but the amount of sleep fragmentation or the sleep deficit experienced (Bonnet, 1985). The interest in the clinical use of sleep deprivation as an intervention for MDD, however, has not continued as clinicians and researchers have noted that depressive symptoms return quickly after recovery sleep. However, some researchers have noted that the effects of antidepressant medication on sleep macroarchitecture, specifically in reducing REM sleep (Wilson & Argyropoulos, 2005), is evidence that sleep manipulations may still be an important target for interventions for depression (Vogel, Vogel, McAbee, & Thurmond, 1980).

There has been a renewed interest in the use of a specific kind of sleep disruption, slow-wave sleep disruption, as a method to reduce depressive symptoms. Slow-wave activity (SWA) or delta activity, brain activity that exhibits a frequency between 0.5-3.9 Hz can be experimentally decreased, with the use of auditory tones, without impacting total sleep time. Utilizing this methodology, Landness and colleagues (2011) demonstrated that a 37% decrease SWA resulted in a 10% decrease in depressive symptoms. Moreover, a very recent study from our own group has demonstrated that a reduction in delta activity following experimentally disrupted slow-wave

sleep, visually scored sleep containing brain waves with amplitude of at least 75 µV, reduced

negative affect in those with MDD (Cheng et al., 2015). Taken together, these results suggest

that decreasing slow-wave sleep improves mood in MDD. If reducing slow-wave sleep improves

mood in MDD, it may also follow that increasing slow-wave sleep will disturb mood. Wu and

Bunney (1990) have indeed suggested that recovery sleep following sleep deprivation, known to

be high in slow-wave activity, may be depressogenic for those with MDD. This theory has also

been supported by a preliminary study that demonstrated that increased slow-wave activity

decreased positive mood in those with MDD. Collectively, slow-wave activity is postulated to be

important for healthy emotional functioning, and therefore understanding the associated

emotional changes resulting from experimentally increasing or decreasing slow-wave activity

will be important to further understand its role.

Sleep as an intervention for mood improvement has also been considered in other contexts,

including the use of naps in healthy individuals. Napping has been shown to be one of the most

effective countermeasures to fatigue and sleepiness (Horne & Reyner, 1996). With regard to

subjective mood, although only a limited number of studies have examined the direct effect of

naps on mood, the results have been mostly consistent, demonstrating that naps improve positive

affect. Taub, Tanguay, and Clarkson (1976) demonstrated that napping increased subjective

energy, while Hayashi, Watanabe, and Hori (1999) and Luo and Inoue (2000), found that

napping increased motivation, and joy, respectively. More specifically, Kaida, Takahashi,

Otsuka (2007) found that a brief nap improved dimensions of positive mood status as measured

by the Mood Checklist 3. Additionally, women in the late-luteal phase of their menstrual cycle,

Lamarche, Driver, Forest, & Koninck (2010), showed that napping improved mood and

alertness. With regard to negative affect, a very recent study showed that toddlers who napped showed fewer negative responses to an unsolvable task than did those who did not nap (Berger, Miller, Seifer, Cares, & Lebourgeois, 2012), which may provide preliminary evidence that napping can facilitate control of negative emotions in children, and perhaps adults, as well. Although not conclusive, taken together, these studies provide preliminary support for the role of naps as a potential intervention strategy for improving mood or controlling negative emotional responses.

Manipulating slow-wave sleep or napping may represent novel therapies to improve mood in both depressed and healthy individuals. Both methods are safe and may be relatively cost-efficient, but before implementation can be considered, adequate research is still required. The first paper of this three-paper dissertation aims to investigate the effects of delaying sleep, previously shown to increase the homeostatic drive for sleep and increase slow-wave activity, on subjective mood as measured by the Profile of Mood States Questionnaire (POMS). These data will be used to examine if increased slow-wave activity is associated with increased mood disturbance in depressed and healthy individuals, which may help to further elucidate the contribution of slow-wave activity to healthy emotional functioning.

The aim of the second paper is to determine whether slow-wave sleep disruption will result in emotional memory biases in healthy research participants and those with MDD. Research has shown that healthy individuals show a memory bias for emotional, as compared to neutral, information (Phelps, 2004). Moreover, in addition to the bias for emotional information, individuals diagnosed with MDD show biases for negative, as compared to positive, information

(Gotlib et al., 2005; Gotlib et al., 2004). It is not clear, however, why depression would be associated with these cognitive changes. It is possible that these biases are related to the sleep changes noted in MDD, including sleep fragmentation or an overall decrease in total sleep time, as research has also shown that sleep deprivation in healthy participants results in emotional and mood dysfunction. In order to test the hypothesis that sleep disturbances affect emotional reactivity, participants will also complete computer-based tasks to examine reactivity to emotional stimuli following baseline, and slow-wave disrupted sleep. These data will be used to explore if reducing slow-wave sleep will differentially increase reactivity and result in biases to specific emotional stimuli. These data may lead to further understanding of how slow-wave sleep deprivation, and conversely slow-wave sleep, may affect daytime cognition in healthy participants and those with MDD.

The third and final paper aims to assess the impact of a brief, midday nap on frustration tolerance and impulsivity in a sample of participants. These data will be used to explore the hypothesis that napping will decrease subjective impulsivity, and increase tolerance for frustration. Utilizing this information, we may reveal that napping, a safe and easy to implement practice, may be a relatively straightforward intervention to increase emotional control.

As a whole, this dissertation explores the emotional effects of sleep manipulations, including sleep delay, slow-wave sleep disruption, and napping. Delaying bedtime by three hours, and potentially increasing slow-wave activity by increasing the homeostatic drive for sleep, may result in a differential pattern of mood changes in healthy and depressed participants. Depending on the pattern, this information could aid in the understanding of the pathophysiology of

depression, or the role of slow-wave activity in healthy emotional functioning. Decreasing slow-wave sleep may result in biases to emotional stimuli. As reactivity and reaction time are generally below the threshold of conscious control, this study may suggest that sleep loss biases limited attentional resources. Moreover, the opportunity to nap, and decrease the homeostatic drive for sleep, may result in decreased impulsivity and increased tolerance for frustration. Manipulations of the sleep system, in various forms including may represent an important target for potential clinical interventions.

Specific Aims

1. To investigate the effects of sleep delay, potentially resulting in increased slow-wave activity, on mood disturbance, as measured by the Profile of Mood States Questionnaire, in a sample of healthy and depressed participants. It is expected that sleep delay will result in increased mood disturbance in those with MDD, and no change in mood disturbance in healthy controls.

2. To determine if individuals who experience slow-wave sleep loss will demonstrate differential reactivity to emotional stimuli. Using a slow-wave sleep disruption paradigm, it is expected that healthy control participants will show a positive bias after the disruption paradigm in contrast to following baseline sleep. Additionally, it is expected that participants with major depressive disorder will show a similar, albeit blunted, bias following the disruption paradigm as the healthy control group.

3. To assess the impact of a daytime nap on impulsive behavior and frustration tolerance. It is expected that a brief, midday nap will increase one's ability to control negative emotions responses, by increasing frustration tolerance and decreasing impulsivity. Additionally, it is expected that maintaining wakefulness throughout the study period will result in a decreased ability to control these negative emotions.

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Exploring the Effects of Sleep Delay on Mood Disturbance in Healthy and Depressed Adults

Introduction

Research has demonstrated that getting an insufficient amount of sleep is associated with mood disturbance. For example, following experimental sleep deprivation, Pilcher and Huffcutt (1996) showed that measures of mood were significantly more disturbed compared to other measures of performance. Similarly, Dinges and colleagues (1997) showed that over a 7 day period of chronic sleep restriction to 4 hours, mood continued to show degradation, while alertness showed a brief plateau effect. Moreover, Talbot et al. (2010) also demonstrated that sleep restriction resulted in a loss of positive mood using the Positive and Negative Affect Schedule. Taken together, these studies demonstrate that sleep loss in the form of sleep deprivation or restriction is associated with an increase in subjective mood disturbance in healthy individuals.

In contrast to the mood worsening effects in healthy individuals, total sleep deprivation has been shown to alleviate depressive symptoms in approximately 40-60% of individuals with MDD (Wirz-Justice and Van den Hoofdakker, 1999; Gillin et al., 2001). Because of the clinical relevance of these findings, researchers have attempted to identify the mechanism of the antidepressant effect of total sleep deprivation by experimentally decreasing certain components

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[1] Chapter 2 corresponds to the publication Goldschmied et al., in preparation

of sleep, including REM and slow-wave sleep, to reveal their unique contribution. In a study examining selective REM deprivation, results revealed that REM deprivation was no more effective at producing an antidepressant response than total sleep deprivation. The authors concluded that REM deprivation may only yield an antidepressant response as a result of decreasing total sleep time (Giedke and colleagues, 2002). In contrast, Landness and colleagues (2011) demonstrated that a 37% decrease in slow-wave activity resulted in a 10% decrease in depressive symptoms in those with MDD. Moreover, a recent study by Cheng and colleagues (2015) showed that a slow-wave disruption paradigm, resulting in reduced delta power, predicted an improvement in negative affect. The results of these studies suggest that it may be a reduction of slow-wave activity that leads to the antidepressant effects in MDD.

If decreasing slow-wave activity results in improved mood, it may also follow that increasing slow-wave activity will worsen mood. Researchers have consistently demonstrated that total sleep deprivation increases slow-wave activity during recovery sleep in an exceedingly predictable manner as a result of increasing the homeostatic drive to sleep. Exploring alternatives to sleep deprivation paradigms, Armitage and colleagues (2007, 2012) have demonstrated that a sleep delay paradigm, which extends prior wakefulness by three hours, can likewise increase the homeostatic drive to sleep. While both total sleep deprivation and sleep delay increases this drive to sleep, in contrast to total sleep deprivation, recovery sleep can occur in the same night following sleep delay. This sleep delay paradigm has also been shown to be associated with consequent changes in mood. In a preliminary study, Cheng and colleagues (2010) showed that following sleep delay, healthy controls displayed an increase in positive mood, while individuals with depression exhibited a decrease in positive mood. Neither healthy controls nor individuals

with MDD, however, showed any changes in negative mood. Although the current research on the effects of SWS manipulations on mood are limited, there is evidence that altering the quantity of slow-wave activity (SWA) may have differential effects on mood in major depressive disorder and healthy controls.

As previously mentioned only 40-60% of individuals with MDD have been shown to exhibit decreased depressive symptomatology following total sleep deprivation (Wirz-Justice and Van den Hoofdakker, 1999; Gillin et al., 2001). Cheng and colleagues (2015) found the same pattern following slow-wave disruption, with approximately 50% of their sample showing a significant improvement in negative affect, while the remaining participants showed no change or worse mood. While Wu and Bunney (1990) postulate that 'responders' may have a different level of sensitivity to sleep manipulations than 'non-responders,' it is currently unclear why the antidepressant response following total sleep deprivation and slow-wave disruption occurs in only 50% of individuals with MDD. Although we may not understand why some participants respond to sleep deprivation and slow-wave disruption with improved mood, while others show the opposite effect, these findings demonstrate the necessity to examine individual differences following a sleep manipulation.

The aim of the current study is to determine if the amount of SWA following a 3-hr sleep delay will be predictive of mood disturbance in a sample of depressed and healthy adults, as measured by the Profile of Mood States, or POMS. The total mood disturbance (TMD) measure of the POMS can be viewed as a proxy for general negative affect as it the sum of the five negative

subscales of the POMS including depression, tension, anger, confusion and fatigue with the one positive POMS subscale, vigor, subtracted from this sum.

Given preliminary evidence that decreasing SWA decreases negative affect in those with MDD, we hypothesize that following a 3-hr sleep delay, an increase in the amount of SWA will be associated with an increase in negative affect, or increased mood disturbance on the POMS. Additionally, given the preliminary evidence that a sleep delay paradigm resulted in no change to negative mood in healthy controls, we hypothesize that SWA will not be predictive of POMS mood disturbance.

Lastly, because research has indicated that approximately 40-60% of depressed individuals respond to sleep manipulations, including total sleep deprivation and slow-wave disruption, we hypothesize that an increase in mood disturbance will only occur in approximately 50% of participants, while the remaining participants will show no change or decreased mood disturbance.

Methods

Participants

Participants were recruited from the Sleep and Chronophysiology lab at the University of Texas Southwestern Medical Center at Dallas (UTSW) and the University of Michigan (UM), under the same conditions. Participants were self-referred, and responded to advertisements in the community, and habitually slept between 6-8 hours per night. Inclusion criteria for the study required two consecutive nights of polysomnographic recording without any difficulties or deviations from the protocol.

Participants did not have any significant previous or concurrent general medical illness, significant head injury, seizure or unconsciousness for more than 5 minutes. As determined by medical history or polysomnogram, participants were free of sleep disorders including narcolepsy, sleep apnea, bruxism, or periodic limb movements, and were not engaged in shiftwork. All participants were unmedicated, other than non-steroidal anti-inflammatory drugs, prior to sleep study for 4 weeks or more. Females were not pregnant or lactating. All subjects provided written informed consent, and the protocol was approved by the Institutional Review Boards at UTSW and UM.

Individuals with MDD

The sample includes 37 adults, between the ages of 20 and 40, diagnosed with MDD. All diagnoses were based on the Structured Clinical Interview for DSM-III-R and IV (SCID; First et al., 2002). Participants met criteria for non-psychotic MDD, but no other current Axis I disorders, or substance abuse within 12 months prior to baseline study. Participants were not

currently undergoing antidepressant therapy or counseling, and had no significant suicidal

ideation (as judged clinically), or previous suicide attempt. The 17-item Hamilton Rating Scale

for Depression (HRS-D; Hamilton, 1960) was used to assess symptom severity.

Healthy Controls

The Healthy Control (HC) group consisted of 59 healthy adults, 20–40 years of age. The HCs

also underwent SCID to confirm the absence of current or past personal or family history of

psychopathology. All healthy controls subjects had Hamilton Rating Scale for Depression scores

≤2.

Procedures

For 5 days prior to study, participants kept an 11pm-6am sleep schedule, as verified by sleep

diary and actigraphy[2]. Participants spent three consecutive nights in the sleep lab. The first night

served as an adaptation to the laboratory environment and screening for independent sleep

disorders, while the second served as the baseline. Bedtime and rise time were delayed by 3

hours on the third night, the SWA regulation challenge. Total available sleep time was held

constant at 7 hours for adults on all nights. Self-report scales including the Profile of Mood

States (POMS-SF) were administered in the morning after the baseline sleep night and in the

morning after the sleep challenge night. Subjects refrained from napping, using alcohol and

drugs, and limited caffeine use to one caffeinated beverage before noon for the 5 days before the

study, confirmed by sleep diary and urine screening.

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[2] As this was a sleep challenge study, it was necessary to fix total sleep time across participants. Since there is individual variation in sleep time, we specifically recruited those who slept 6-8 hours, habitually. Selecting a 7 hour bedtime guarantees that none of our participants will have a sleep opportunity that differs for more than 1 hour from their habitual sleep schedule.

Profile of Mood States – Short Form

The POMS-SF (Shacham, 1983) is a measure consisting of 30 adjectives describing feelings, designed to assess transient, fluctuating subjective mood states. Utilizing a 5-point scale, participants select the degree to which each adjective describes their present mood. The POMS-SF produces a Total Mood Disturbance score (TMD), in addition to six subscale scores, Depression-Dejection, Tension-Anxiety, Anger-Hostility, Confusion-Bewilderment, Fatigue-Inertia, and Vigor-Activity. TMD is defined as the sum of five of these POMS subscale scores (depression, tension, anger, confusion and fatigue) minus the sixth subscale score, vigor. TMD and each individual subscale score have been shown to be reliable and valid indicators of affective state (McNair et al., 1992).

Sleep EEG

Standard laboratory procedures were followed (Armitage et al., 2012). On the first overnight in the laboratory, leg leads, chest and abdomen respiration bands, and nasal–oral thermistors were used, in addition to a full EEG montage. On each successive night, the montage included C3, C4, F3, F4, P3, P4, O1, and O2 EEG, left and right EOG, and a bipolar EMG. The reference electrode was comprised of linked earlobes passed through a 10 KΩ resistor to minimize possible artifacts. All impedances remained below 2 kΩ, and EEG was monitored throughout the sleep delay period to verify that subjects did not fall asleep. Research personnel visually scored sleep records following standard criteria (Rechtschaffen and Kales, 1968), after training to a ≥90% agreement on an epoch-by-epoch basis. Thereafter, any epochs that contained movement, breathing muscle artifact, or recording difficulties were omitted from further analysis.

Data from UTSW were collected on a GRASS™ P511 amplifier-based paperless polygraph described in detail elsewhere (Armitage et al., 2002). Data from the UM lab were collected on a Vitaport™ III digital data acquisition system, described in detail in Armitage et al., 2012. Both data systems were cross-validated, simultaneously recording and analyzing data from 10 subjects.

The main dependent sleep variables used presently, SWA across the night at baseline, $F(1,94) = 1.808$, $p>0.05$, and following SDC, $F(1,94) = 2.328$, $p>0.05$, in addition to SWA during NREM1, $F(1,94) = 1.787$, $p>0.05$, NREM2, $F(1,94) = 0.378$, $p>0.05$, NREM3, $F(1,94) = 0.003$, $p>0.05$, and NREM4, $F(1,94) = 0.281$, $p>0.05$, were compared and did not differ between data systems.

Power spectral analysis (PSA), was performed on the EEG data in 2-sec blocks using an algorithm based on a fast Fourier transform (512 samples for each 2 s). The sampling rate was set to 256 Hz, with a Hanning window taper to reduce overlap between adjacent frequencies. The PSA generates power in all five frequencies, but the analysis for the present paper was restricted to the delta activity expressed as μV^2.

Delta power was averaged in 30-s epochs to provide identical epoch lengths to the stage-score data and sorted by NREM period for each subject on each night in the lab. NREM period was defined as the succession of stages 2, 3, or 4 of $\geq$ 15-min duration and terminated by stage REM or a period of wakefulness of $\geq$ 5 minutes. Stage 1 sleep epochs were excluded. No minimum REM duration was required for the first or last REM period. Delta power was summed and then averaged relative to the number of epochs in each NREM period, for each subject, henceforth

referred to as slow wave activity (SWA). For statistical purposes, only the first four NREM periods were included for analysis, since not all subjects had more than four NREM periods across the night.

In addition to the raw SWA power, percentage of SWA was included (BL-Normalized SWA), expressing SWA in each NREM period on the delay night relative to SWA on the baseline night, in order to normalize power and control for any potential individual differences across subjects. EEG analyses were focused exclusively on the central leads as slow-wave activity is known to be fronto-centrally distributed.

Data analysis

Initially, in order to explore if the SDC had a significant effect on the amount of SWA, microarchitectural sleep variables, including SWA across the night and during each NREM period, were examined at baseline and following SDC.

Next, in order to explore if the amount of SWA resulting from the SDC had a direct effect on TMD, regression analyses were conducted with BL-Normalized SWA in each of the four NREM periods (NREM 1-4), individually, as the predictor variable, and TMD at post as the outcome variable. Amount of Stage 1 sleep, Stage 2 Sleep, REM, and Awake & Movement were entered as covariates to control for the non-slow wave components of sleep.

Finally, in order to examine individual differences in response to SDC in depression, a difference score was calculated by subtracting TMD following baseline from TMD following SDC.

Utilizing this difference score, participants were then divided into two groups, those whose difference score indicated increased mood disturbance and those whose did not. Repeated Measures ANOVA was then utilized to explore if POMS scores significantly increased following delay night in this subset of individuals. Additional, post-hoc analyses included univariate analyses to determine factors that could differentiate those who exhibited increased mood disturbance from those who did not. All analyses were performed using the software program IBM SPSS v20.0, with $P < 0.05$ considered significant.

Results

Baseline Variables- Participant Characteristics

Demographic and mood variables (Table 2.1) were compared between the HC group and

participants with MDD. As expected, the MDD group had higher levels of depression as

measured by the BDI, but did not differ from HC in age or number of females.

Macroarchitectural Variables

Polysomnographic variables were likewise examined at baseline and following SDC (Table 2.2).

As compared to HC, those with MDD had less stage 2 sleep. No other baseline group differences

emerged. Following the sleep delay, the HC exhibited shorter sleep onset latency, less stage 2

sleep, more REM sleep, shorter REM latency than at baseline, while the MDD group exhibited

shorter sleep onset latency, and shorter REM latency.

Sleep Delay Challenge Manipulation Check – Microarchitectural Variables

SWA variables were then analyzed to examine the effectiveness of the SDC in evoking a slow-

wave response (Table 2.3). As expected, the HC group exhibited significantly more average delta

power across the night following the sleep delay, and during the first and fourth NREM periods,

specifically. In contrast, the SDC did not result in increased delta power across the night in the

MDD group, as indicated by a significant Condition x Group interaction, $F(1,92) = 4.364$,

$p=0.039$.

The HC group exhibited more SWA during both baseline and following SDC than those in the MDD group, Group, $F(1,92) = 9.371$, $p<0.01$. Additionally, collapsed across groups, SWA was higher following SDC than baseline, Condition, $F(1,92) = 4.558$, $p=0.035$.

Regression Analyses

Regression analysis was used to test if the amount of SWA following SDC, during each NREM period, significantly predicted mood disturbance. BL-Normalized SWA only in NREM 2 significantly predicted TMD following SDC, even after controlling for covariates, $b=.221$, $t(30)=2.301$, $p<0.05$. As expected, a significant effect of TMD at baseline was also detected in the model, in addition to percent of awake and movement (Table 4). The results of the regression for the MDD group indicated that the model accounted for 76.8% of the variance, $F (6,30)$ $=16.58$, $p<0.01$ (Figure 2.1). BL-Normalized SWA during NREM 1, NREM 3 and NREM 4 were not predictive of mood disturbance for HC or the MDD group.

When looking at the subscales of the POMS, increased BL-Normalized SWA in NREM 2 was specifically associated with increased POMS depression ($r=0.540$, $p<0.01$) and increased POMS tension ($r=0.502$, $p<0.01$) following SDC, but not Anger-Hostility, Confusion-Bewilderment, Fatigue-Inertia, and Vigor-Activity.

The results of the regression for the HC group indicated that the model accounted for 80.0% of the variance, $F (6,52) =34.71$, $p<0.01$. The model, however, demonstrated that only TMD at

baseline significantly predicted TMD following SDC, b=.861, $t(52)=12.968$, $p<0.01$. BL-Normalized NREM2 did not predict TMD following SDC (Table 2.5).

Individual Differences in MDD

As previously mentioned, difference scores were calculated by subtracting TMD following baseline from TMD following SDC. Utilizing this difference score, participants were then divided into two groups, those whose difference score was above 0, indicating increased mood disturbance and those whose did not.

Half of the sample of those with MDD (n=18), exhibited significantly increased mood disturbance following SDC, as indicated by a significant Condition x Mood Disturbance Status interaction, $F(1,35) = 55.923$, $p<0.01$.

Additionally, those who demonstrated increased total mood disturbance following SDC, also exhibited significantly increased depression, $t(17) = -3.453$, $p<0.01$, and significantly decreased vigor, $t(17) = 3.462$, $p<0.01$, following SDC, while those who reported no change or decreased mood disturbance did not (Table 2.6).

Post-hoc univariate analyses also revealed that those who reported increased mood disturbance had higher BDI scores, $F(1,33) = 5.05$, $p=0.031$, and shorter REM latency following SDC, $F(1,35) = 4.83$, $p=0.035$ than those who did not.

Discussion

The present study demonstrated that an increase in the amount of BL-Normalized SWA from the 2nd NREM period following a sleep delay paradigm predicted an increase in total mood disturbance in individuals with MDD. This effect was driven by a subset of the MDD group who showed a significant increase in TMD, and depression and significantly decreased vigor following the SDC. These results add to the increasing body of literature indicating that the amount of SWA following a sleep manipulation may impact mood, and that increased SWA may contribute to worsening mood in a subset of those with MDD.

These results are consistent with recent research examining the impact of a slow-wave disruption paradigm on mood in those with MDD (Cheng et al., 2015). Results from that study demonstrated that a reduction in average SWA across the night predicted improvement in negative affect. If a reduction of SWA improves negative affect, it should then follow that increased SWA should predict an increase in negative affect, or increased mood disturbance, as was demonstrated presently.

These results are also consistent with the research demonstrating the antidepressant effect of total sleep deprivation. Given the previously mentioned research on SWA disruption, it is wholly possible that it is indeed the lack of SWA during total sleep deprivation that drives the decrease in depressive symptoms. Giedke and colleagues (2003) explored this possibility by examining the resultant mood effects of total sleep deprivation contrasted with late partial sleep deprivation. Late partial sleep deprivation involves depriving the individual from sleep which occurs in the latter half of the night, known to be dominated by REM sleep in contrast to slow-wave sleep.

Although late partial sleep deprivation was better tolerated by participants, they found that total sleep deprivation was more effective in reducing depressive symptoms. These results lend further support to the claim that it may be the reduction in SWA, inherent to total sleep deprivation that results in the transient antidepressant effects.

Somewhat surprisingly, it was increased BL-Normalized SWA during the 2nd NREM period, specifically, that was predictive of increased mood disturbance in those with MDD. Following homeostatic sleep challenges including total sleep deprivation and sleep delay, studies have shown that SWA increases during the first NREM period as an indicator of the increased homeostatic drive for sleep followed by a prompt decrease, indicative of the healthy dissipation and regulation of SWA. The results found presently may suggest that the pattern in which SWA dissipates in MDD from the first to the second NREM period following a homeostatic sleep challenge contributes to mood disturbance, with more residual SWA at NREM 2 indicative of less SWA dissipation, resulting in more disturbed mood.

These results, however, should be interpreted in light of some limitations. First, as this was a study of the homeostatic response to sleep delay, total sleep time was required to be kept constant and consistent among all participants. Therefore, every participant kept an 11pm-6am sleep schedule, allowing a 7-hour sleep opportunity. This amount reflects the current recommendation for the amount of sleep for adults according to the Consensus Panel of the Sleep Research Society and American Academy of Sleep Medicine (Watson et al., 2015). Additionally, inclusion criteria required all participants to have a habitual sleep time between 6 and 8 hours, which would limit the maximum adjustment to study bedtime to only 1 hour.

Despite this data, there is still a possibility that some study participants required more than 7 hours of sleep per night, which could result in a subset of the participants being sleep deprived during the study protocol. Chronic sleep restriction has been shown to affect measures of mood (Talbot et al., 2010), and one could expect that this may impact mood measures in the present study. In order to prevent this from occurring, future studies may consider only including participants who have a habitual sleep schedule that exactly mirrors study parameters.

Second, mood effects were limited to those measured by the POMS SF, and more specifically to the TMD measure of the POMS SF. Although the POMS SF has been shown to be a good alternative to the full length POMS (Curran, Andrykowski & Studts, 1995), and has been used extensively to measure state mood changes during sleep manipulations (Dinges et al., 1997; Penetar et al., 1993; Scott, McNaughton & Polman, 2006) in order to more accurately examine the mood changes associated with SWA changes, it would be useful to incorporate additional state measures of mood including visual analogue scales, which have been shown to have high degrees of sensitivity (McCormack, de L Horne & Sheather, 1988).

Lastly, whereas SWA significantly increased in HC, as expected, SWA in the MDD group, as a whole, did not change following SDC. Previous studies have demonstrated that individuals with MDD do not respond to sleep challenges as robustly as HC, and that this may be an indicator of a dysfunctional homeostatic sleep drive. It is also possible that individuals with MDD require a fairly long period of time spent awake to elicit an associated increase in SWA. However, those in the MDD group did exhibit shorter sleep and REM latency following the SDC suggesting that the challenge did indeed have an effect on sleep, but not SWA, specifically. Future studies could

address this by utilizing a total sleep deprivation paradigm to examine whether SWA can be increased the following night predictably in those with MDD, and if this increase would be associated with subjective changes in mood.

In summary, this study examined if the amount of SWA following a 3-hr sleep delay would be predictive of mood disturbance in HC and individuals with MDD. Results revealed that, in those with MDD, increased SWA in the 2nd NREM period following sleep delay relative to baseline was predictive of increased total mood disturbance. This pattern, however, was not found in the HC group. These findings support previous research that has demonstrated that decreased SWA predicts improved mood by similarly demonstrating that events resulting in increased SWA may predict further mood disturbance in those with MDD.

Table 2.1

Demographic Variables, by group and condition

	Healthy Control	Major Depressive Disorder
N (No. female)	59 (32)	37 (21)
Age (SD)	29.03 (5.77)	27.65 (6.30)
Beck Depression Inventory Score	0.72 (1.44) †	25.23 (8.74) †
Means, standard deviations (within parenthesis) and ANOVA results.		

† indicates group difference

Table 2.2

Means and standard deviations of polysomnographic variables, by group and condition.

	HC		MDD	
	Baseline	**Delay**	**Baseline**	**Delay**
Time in Bed (min)	416.04 (7.90)	413.22 (20.95)	418.20 (5.82)	410.50 (27.51)
Sleep Efficiency (%)	95.15 (2.51)	94.90 (4.26)	93.82 (4.97)	95.25 (3.25)
Sleep Latency (min)	7.56 (6.21)	4.15 (3.02)*	12.51(18.50)	4.57 (4.19)*
% Stage 1	6.35 (5.31)	6.46 (5.44)	5.35 (5.28)	6.05 (5.66)
% Stage 2	56.19 (7.66) †	53.10 (7.55)*	52.69 (8.16) †	50.58 (7.61)
% SWS	11.32 (9.01)	11.90 (9.13)	13.76 (8.31)	13.82 (9.19)
Awake & movement (%)	2.83 (1.96)	3.17 (2.57)	3.16 (3.05)	3.29 (2.72)
REM (%)	23.32 (5.82)	25.37 (7.10)*	25.04 (6.38)	26.26 (5.59)
REM Latency	75.95 (24.50)	68.38 (29.54)*	79.93 (40.76)	57.73 (23.71)*

†denotes significant group difference;* denotes significant, within group condition difference

Table 2.3

Means and standard deviations of Slow Wave Activity, by group and condition.

	HC		MDD	
	Baseline	**Delay**	**Baseline**	**Delay**
Average Delta across the night	427.34 (81.01)	450.48 (91.98) *	392.39 (62.35)	393.19 (77.51)
Delta in 1st NREM	569.52 (119.86)	593.70 (136.21)*	510.42 (113.76)	507.31 (113.54)
Delta in 2nd NREM	449.37 (112.12)	472.25 (126.10)	422.65 (102.00)	421.19 (105.88)
Delta in 3rd NREM	368.97 (69.93)	377.23 (78.08)	336.35 (60.48)	336.54 (78.41)
Delta in 4th NREM	321.49 (78.59)	358.74 (83.54)*	300.14 (56.05)	307.74 (75.38)

*indicates significant within group condition difference

Table 2.4

Summary of Linear Regression Analysis for TMD following SDC in MDD

	B	Std. Error	Beta	t	Sig.
(Constant)	-41.405	21.890		-1.892	.068
BL-Normalized SWA NREM2	.204	.089	.221	2.301	**.029**
% Stage 1	-.051	.324	-.015	-.159	.875
% stage 2	.341	.238	.136	1.432	.163
% REM	-.012	.334	-.004	-.036	.972
% Awake and Movement	1.531	.675	.219	2.268	**.031**
TMD at Baseline	.929	.115	.755	8.104	**.000**

Note. Adjusted R^2=.722, bold indicates p<0.05

Table 2.5

Summary of Linear Regression Analysis for TMD following SDC in HC

	B	Std. Error	Beta	t	Sig.
(Constant)	-8.464	8.187		-1.034	.306
BL-Normalized SWA NREM2	.002	.038	.004	.061	.952
% Stage 1	-.040	.157	-.020	-.255	.800
% stage 2	.034	.096	.024	.354	.724
% REM	.172	.116	.114	1.475	.146
% Awake and Movement	.553	.333	.132	1.662	.103
TMD at Baseline	.915	.071	.861	12.968	**.000**

Note. Adjusted R^2=.777, bold indicates $p<0.05$

Figure 2.1

Scatter plot of amount of BL-Normalized SWA in NREM 2 and TMD following SDC in MDD
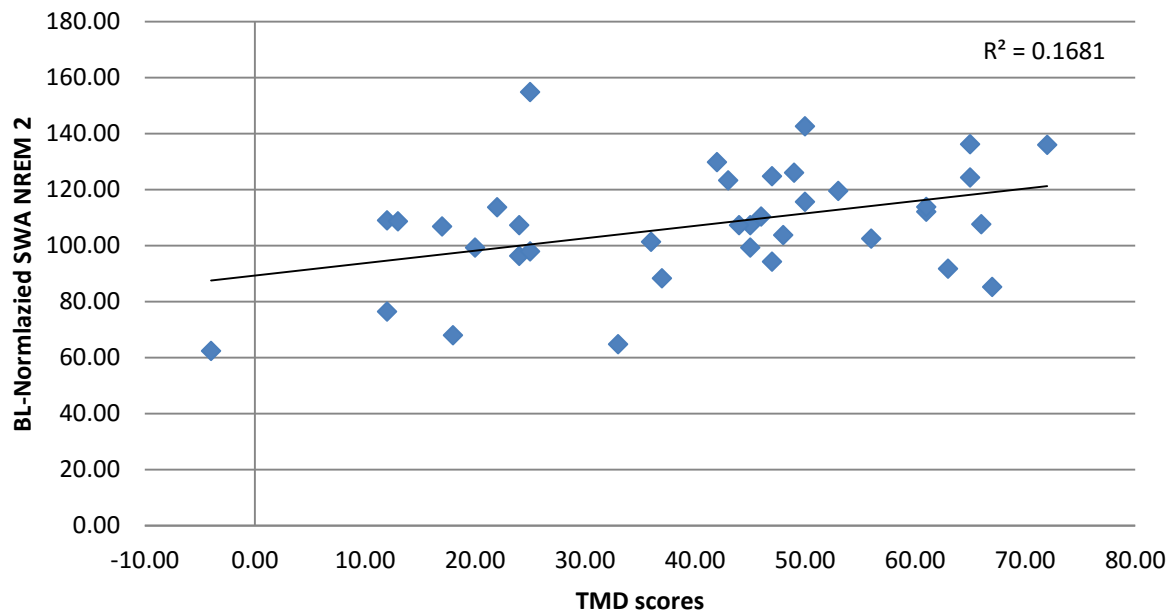
Table 2.6

Means and standard deviations of POMS scores, by Mood Disturbance Status and Condition

	MDD – Increased Scores (N=18)		MDD – Non-Increased (N=19)	
	Baseline	**Delay**	**Baseline**	**Delay**
TMD	42.78 (14.97)	50.67 (15.39)*	39.79 (16.24)	30.89 (17.37)*
Depression	10.56 (4.96)	12.72 (4.81)*	9.63 (5.50)	7.84 (4.90)*
Tension	7.83 (3.40)	9.33 (3.38)	7.74 (4.09)	6.26 (4.15)*
Anger	8.33 (4.60)	9.06 (4.58)	8.16 (4.52)	5.84 (4.41)*
Confusion	9.00 (3.82)	9.72 (4.11)	6.58 (3.08)	6.00 (3.45)
Fatigue	11.61 (4.85)	12.78 (4.52)	11.79 (4.40)	9.74 (5.17)*
Vigor	4.56 (2.66)	2.94 (2.07)*	4.11 (2.96)	4.79 (3.84)

*indicates significant within group condition difference

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<center>**Chapter 3[3]**</center>

<center>Slow-wave Disruption Enhances the Accessibility of Positive Memory Traces</center>

<center>**Introduction**</center>

Over the last several years, research has begun to show that decrements in sleep may provoke a hedonic response that results in behavior aimed towards reward-related stimuli. This type of response has been demonstrated in both animal and human models, to many forms of rewarding stimuli, including alcohol, drugs, food, money, and pleasurable pictures. For example, following acute sleep deprivation, Puhl and colleagues (2009) showed that rats increased self-administration of cocaine, while Hanlon et al. (2005) indicated that REM-deprivation in rats increased motivation for food reward. Increased food intake has also been recognized in humans following partial sleep deprivation (Brondel et al., 2010). Additionally, neuroimaging work has shown that there is a significant relationship between sleep loss and increased activation during monetary reward tasks in reward-related brain areas, such as the ventral striatum (Mullin et al., 2013; Venkatraman et al., 2007). Similarly, Gujar and colleagues (2011) demonstrated increased activity within the same region, to positive images following sleep deprivation, while behavioral evidence showed that participants showed an increase in the number of visual stimuli rated as positive.

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[3] Chapter 3 corresponds to the publication Goldschmied et al., revise and resubmit

<center>39</center>

This hedonic response following sleep disturbance is also evident in psychiatric disorders. Sleep disturbance has been shown to prompt manic episodes in those with bipolar disorder (Plante & Winkelman, 2008) in addition to being associated with the risk of relapse in alcoholics (Brower & Perron, 2010). Additionally, several influential studies have demonstrated an antidepressant effect of total sleep deprivation and selective-REM deprivation in those with major depressive disorder (MDD), which is quickly reversed with recovery sleep (For review, Wu & Bunney, 1990).

In addition to increasing the hedonic drive for rewarding stimuli, sleep deprivation has also been shown to improve mood (Selvi et al., 2007). If sleep deprivation increases positive mood, it suggests that it may also prompt a positivity bias on other forms of cognition, including memory. Understanding the effects on memory is especially important as memory has been shown to impact other higher-order cognitive functions including learning and decision-making. The literature has indeed indicated that there is an intimate relationship between sleep and memory (Plihal & Born, 1997; Daurat et al., 2007; Stickgold, 2005) such that sleep following encoding has been shown to improve memory in contrast to a period without sleep (Baran et al., 2012). Moreover, sleep is also thought to preferentially consolidate emotional memory (Payne et al., 2008), especially when containing REM sleep (Wagner et al., 2001; Nishida et al., 2009; Groch et al., 2013). The majority of studies that have examined the benefit of sleep on emotional memory have, to some extent, restricted their analyses to negative memory traces, showing that sleep consolidates negative memories better than an intervening period of wake. However, a very recent study by Chambers & Payne (2014) which examined the effect of sleep on humorous

stimuli provided preliminary evidence that sleep does benefit memory for novel positive and

arousing stimuli (Chambers & Payne, 2014), as well. With regard to studies exploring the effects

of sleep deprivation on emotional memory, most research has also been restricted to the

examination of negative memory traces. These studies have generally shown that sleep loss

blocks the ability to create new fear memories (Graves et al., 2003; Kumar & Jha, 2012; Menz et

al., 2013) which may suggest a bias towards positive memory following sleep loss. There have

not been any studies to date, however, that have examined that direct impact of sleep deprivation

on emotional memory with a focus on positive memory traces.

As a result of the research showing that emotional memory specifically benefits from REM

sleep, some have theorized that selective REM deprivation should impact the accuracy of

emotional memory. In contrast to what most would predict, a recent study demonstrated that

selective REM deprivation did not affect accuracy for emotional memory (Morgenthaler et al.,

2014). The authors suggest that their results may implicate other aspects of sleep, not affected by

REM-deprivation, in supporting emotional memory processes. Indeed, slow-wave sleep (SWS)

has also been shown to be essential to memory consolidation. In a seminal study, Plihal & Born

(1997) showed that late sleep, dominated by REM and stage 2 sleep, improved procedural

memory, while early sleep, typically dominated by SWS improved declarative memory such as

recall and recognition. There has been no research, however, on the effects of slow-wave

deprivation on emotional memory accuracy.

Slow-wave deprivation (SWD) may actually be a far better method than selective-REM

deprivation or total sleep deprivation procedures to examine emotional memory since the latter

paradigms result in many cognitive deficits, including general slowing of reaction time and decreases in attention, which could potentially interfere with observing the consequences on emotional memory. To this end, studies by Ferrara (1999) and others (Lentz et al., 1999) have shown that SWS can be reduced without waking the subject, or decreasing total sleep time. This elegant paradigm, using auditory tones to reduce SWS, offers a unique opportunity to explore the consequences of slow-wave loss. Utilizing this paradigm, Landsness and colleagues (2011) recently explored the effects of SWD on individuals with MDD, and showed that a 37% decrease in slow-wave activity resulted in a 10% decrease in depressive symptoms.

Although the current research has shown that selective REM deprivation does not affect accuracy for emotional memories, it is still possible that sleep deprivation may result in a bias towards positive memories. Although most studies of memory examine measures of accuracy, some researchers have noted that reaction time may actually reflect a distinct process from accuracy in recognition memory tasks (Santee & Egeth, 1982). In this way, whereas accuracy represents a measure of memory strength, reaction time can be used as a metric to measure the difficulty or ease of retrieving an item from memory (Sternberg, 1969; Wattenbarger & Pachellat, 1972). It is possible, then, that a hedonic bias that may not be observed in accuracy may actually be present in reaction time. In this way, positive words may not be remembered better than negative words following sleep deprivation, but may be accessed *faster* than negative words. Accessibility of emotional memories is particularly important because it emphasizes which types of information are more readily available for further processing. For example, if the memories of the hedonic factors of alcohol consumption are more available than the adverse consequences, this may impact decisions that relate to sobriety and remission.   In order to more

thoroughly understand how sleep loss impacts memory, it is imperative to examine both accuracy and reaction time.

The aim of the current study was to investigate the effects of SWD on positive and negative word recognition in both healthy control participants and individuals diagnosed with MDD using an emotional memory task. Given that sleep deprivation results in a hedonic response in behavior to positive stimuli in healthy individuals, and that there is mixed evidence with regard to the effects on emotional memory accuracy, we hypothesized that healthy controls would recognize positive words with equal accuracy, but faster than negative words after the SWD paradigm. Additionally, given that total sleep deprivation and SWD have been shown to ameliorate depressive symptoms, we inferred that those with MDD would show a similar pattern to healthy controls, recognizing positive stimuli faster than negative stimuli. However, because there is evidence that those with MDD already exhibit decreased SWS (Armitage, 2007; Pillai et al., 2011), we expected the effect to be attenuated as compared to HC.

Methods

Participants

26 participants were recruited by flyers and internet recruitment sites from the Ann Arbor area.
In order to determine study eligibility, all participants underwent an initial phone screen.
Inclusion criteria included English fluency, habitual sleep time between 6-8 hours, with a
habitual bed time between 10pm-12am, and ability to keep a consistent sleep schedule.
Exclusion criteria included current use of medications that are thought to impact sleep, including
antidepressants, history of serious, unstable medical illnesses including hepatic, renal,
gastrointestinal, respiratory, or hematologic disease, uncorrected hypothyroidism or
hyperthyroidism, neurological disorders, and sleep disorders.
The study was approved by the Institutional Review Board at the University of Michigan, and all
participants provided written, informed consent.

Individuals with MDD. The sample included 14 individuals, 18-48 years of age (9 women; mean
age 25.0±7.7) diagnosed with MDD. All diagnoses were based on the Structured Clinical
Interview for DSM-IV. Participants met criteria for MDD, and no other current Axis I disorders,
including substance dependence or substance abuse within 12 months prior to baseline study,
with the exception of Anxiety Disorders. Participants were medication-free for at least 6 weeks
prior to study. Those with MDD were moderately depressed (BDI-II mean score 27.86 ± 6.0;
Range 18-38).

Healthy Controls. The Healthy Control (HC) group consisted of 12 adults, 18–40 years of age (8 women; mean age 24.5±6.8). The HCs also underwent SCID to confirm the absence of current or lifetime major depression.

Experimental Design

All participants were instructed to refrain from alcohol and limit caffeine intake to two caffeinated beverages before noon for the 24 hours before and during the entire course of the study participation. Participants maintained consistent bedtimes and wake-times, and refrained from napping for one week prior to study participation, as verified by sleep diary and actigraphy.

During the course of the study, participants spent three consecutive nights in the sleep lab, with a nightly 7-hour sleep opportunity. As this was a sleep challenge study, it was necessary to fix total sleep time across participants. Since there is individual variation in sleep time, we specifically recruited those who slept 6-8 hours, habitually. Selecting a 7 hour bedtime guarantees that none of our participants will have a sleep opportunity that does not differ for more than 1 hour from their habitual sleep schedule. Participants were allowed to go about their normal daily activities during the waking interval between nights. The first overnight was used to adapt participants to the sleep laboratory and screen for independent sleep disorders (e.g. apnea, bruxism, restless leg syndrome). Baseline analyses were based on the second overnight, while the third night served as a selective slow-wave disruption (SWD) night.

Participants performed an emotional word encoding task (described below) approximately 1-2 hours prior to bed time on both baseline and disruption nights, utilizing distinct word lists for

each night. Both word lists were controlled for valence, arousal, frequency, and length.

Following completion of task, participants obtained a full night sleep opportunity, monitored

using polysomnography (PSG). In the mornings, after baseline and disruption nights, participants

performed a recognition task (described below) approximately 1 hour after waking. Following

completion of the recognition task, participants completed a word ratings task (described below).

Verbal stimuli were taken from the Affective Norms for English Words (ANEW; Bradley &

Lang, 1999) and an additional set of verbal materials normed in a large sample (Shestyuk et al.,

2005), with words normed on a scale from 1-9 for both valence (1=negative, 9=positive) and

arousal (1=unarousing, 9=arousing). Our stimuli sample set included 100 positive (mean Valence

= 7.25, mean Arousal = 5.52), 100 neutral (meanV = 4.93, meanA = 3.66), and 100 negative

(meanV = 2.61, meanA = 5.35). Positive and negative words did not differ on normed arousal.

All visual stimuli, including fixation crosses, and emotional adjectives and nouns, were

presented in white font on a uniform black background, centered on a 19" computer monitor,

located approximately 80 cm from the participant, utilizing E-prime software.

Emotional Word Encoding Task. Each trial consisted of the presentation of a fixation mark for

1000 ms followed by the presentation of an emotional stimulus (positive, negative or neutral

word) for 1000 ms. Stimuli were equally divided among positive (e.g. happy, delighted, ecstatic),

negative (e.g. sad, gloomy, hostile) and neutral (e.g. OK, neutral, swift) words. Participants were

asked to try to remember the words and to make a button press if the word, more than not,

"describes you in the last two weeks," after which they viewed the fixation mark again for the

remainder of the 1000 ms. The task consisted of 150 trials (75 words, 2 times each) divided into

10 separate runs of 15 words with 30 second breaks between runs. Each run lasted approximately 5 minutes. Trial presentation was pseudo-randomized, with care being taken to ensure that each stimulus category (positive, negative, or neutral) occurred an equal number of times after another stimulus category. Actual training took place between 8:01pm and 11:57pm for both administrations.

Emotional Word Recognition Task. Each trial consisted of the presentation of an emotional or neutral word, half of which appeared during the previous memorizing session, for 500 ms. Participants were required to decide if they had previously seen each word during the encoding session the previous evening, using a Remember-Familiar-New judgment, with a right-hand button press during an inter-stimulus interval (ISI) of 4500 ms. Responses were only permitted and recorded during this ISI, 'Remember' judgments corresponded to words that participants had seen in the previous memorizing session, whereas 'New' judgments were words that had not appeared, and 'Familiar' judgments were words that the participants felt *may* have appeared. The task consisted of 150 trials (50 of each stimulus category) divided into 5 separate runs, with 30 second breaks. Each run lasted 3 minutes, for a total task time of approximately 15 minutes. Trial presentation was pseudo-randomized. Actual testing took place between 6:16am and 9:37am for both administrations of the task.

Emotional Word Rating Task. Following completion of the Emotional Word Recognition Task, participants completed an Emotional Word Rating Task where they were asked to rate the valence and arousal of each word presented during the Emotional Word Recognition Task based on their subjective experience, on a scale ranging from 1 ('most negative') to 9 ('most positive')

for valence; and 1 ('not arousing') to 9 ('most arousing) for arousal, using a standard computer keyboard. Participants were acquainted with the range of options by having the anchored Likert scale appear on the screen during the emotional rating.

Sleep Recording

PSG recording were collected in accordance with standardized techniques using digital electroencephalography (EEG), electromyogram (EMG), and electrooculogram (EOG) signals acquired with a Vitaport^{TM} III digital data acquisition system, with an equivalent sensitivity of 5 (50 µV, 0.5-s duration calibration) corresponding to a gain of 50,000. Filter settings were set at 0.3 and 70 Hz for EEG and 30 and 100 Hz for EOG. All data were digitized at 256 Hz (Armitage et al., 2012).

A PSG electrode montage was utilized and composed of left and right frontal central, parietal, and occipital electrode sites (F3 & F4; C3 & C4; P3 & P4; O1 & O2) according to the International 10-20 System. EMG was recorded from a bipolar chin-cheek montage. EOG recordings were made from the supraorbital and infraorbital ridges of the eyes. A reference electrode, comprised of linked earlobes and passed through a 10 KΩ resistor, was utilized to minimize potential artifact. Respiration was recorded using a nasal oral thermistor and respiratory belt across the abdomen.

Selective Slow-Wave Disruption Procedure

The selective SWD procedure has been previously validated (Ferrara et al., 1999). Sleep technicians continuously inspected left (C3) and right central (C4) EEG over the course of the

full night of sleep and delivered acoustic stimuli (tones) (frequency = 1000 Hz; intensity = 20–100 dB) whenever two delta waves (1–4 Hz; >75 µV) appeared within 15 seconds. Tones were administered, through an earphone insert earpiece taped into the participant's ears, beginning with the lowest intensity (20 dB) and increased by 5 dB intervals if no response occurred (sleep stage shift, K complex, EEG desynchronization, mixed and fast frequency, alpha burst, muscle tone increase, slow eye movements). This methodology allowed for the type and incidence of tones played to be tailored to each individual to suppress slow waves without arousing participants.

Data Analysis

EEG data were visually scored according to standard criteria (Rechtschaffen & Kales, 1968). Each of the digital PSG records was scored, blind to participants' behavioral task performance or diagnostic status, in 30-second epochs, as non-rapid eye movement (NREM) sleep stages 1, 2, 3, or 4, REM sleep, wake, or movement time. Slow-wave sleep (SWS) consisted of stage 3 plus stage 4 NREM sleep combined. These data were then used as a manipulation check of the SWD paradigm.

First, subjective ratings from the Emotional Word Rating Task were used to organize stimuli into valence categories (neutral, negative or positive), and arousal categories (neutral, arousing or unarousing) for each participant. Utilizing subjective ratings may offer a more accurate indication of the individual perception of each stimulus than normed ratings. This is especially true because the present sample included depressed individuals, for whom the normed ratings may not be as representative due to negative biases (Shestyuk et al., 2005).

Second, statistical analyses on accuracy and reaction time during the Emotional Word Recognition Task were conducted using repeated measures analysis of variance (ANOVA), with condition (Baseline and Disruption) and emotion (Negative and Positive) as within-subjects factors and group (HC and MDD) as between-subjects factor. Both hits (old words rated as "Remember") and correct rejections (new words rated as "New") were included in the analyses; familiar judgments were considered incorrect.

Secondary analyses were also conducted because current theories of emotion suggest that stimuli can be evaluated along two dimensions, valence, and arousal. We examined the effects of arousal on reaction time with condition (Baseline and Disruption) and arousal (Arousing and Unarousing) as within-subjects factors and group (HC and MDD) as between-subjects factor. Additionally, post hoc analyses were conducted for both within and between-group comparisons using two-tailed t-tests. All analyses were performed using the software program IBM SPSS v20.0, with $p < 0.05$ considered significant.

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Results

Descriptive Variables

Both demographic and sleep variables were analyzed between the HC group and participants with MDD in order to identify any group differences. As expected, the MDD group had higher levels of depression as measured by the BDI, Group, $F(1,24)=208.83$, $p<0.01$, and had lower levels of restedness during the study protocol, Group, $F(1,21) = 7.60$, $p= 0.01$. Further, as a group, those with MDD took longer to fall asleep (SOL), Group, $F(1,22) = 7.95$, $p= 0.01$. (Table 3.1). No other baseline differences emerged.

Slow-Wave Disruption Manipulation

In order to verify that the SWD paradigm was successfully implemented, the macroarchitectural sleep variables of both the baseline and disruption condition were analyzed. Visually scored sleep data was incomplete for two participants, and thus were not included. As desired, both percent of SWS, and minutes of SWS in the 1st NREM period were reduced by the disruption paradigm, Condition Main Effect, $F(1,12) = 31.56$, $p< 0.01$; $F(1,14) = 42.23$, $p< 0.01$ for those in the HC and MDD groups, respectively (Table 3.2). However, total sleep time was also reduced in those with MDD.

Slow-Wave Disruption effects on Accuracy

Accuracy was examined utilizing two different metrics. First, accuracy was defined as the ratio between the number of words correctly identified as 'old' or 'new' over the total number of words presented. The SWD paradigm appeared to have no effect on accuracy according to the non-significant three-way interaction, Condition x Valence x Group, $F(1,24)=0.001$, $p=0.98$.

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For HC and MDD, both main effects of condition, HC, $F(1,11) = 0.117$, p=0.739; MDD, $F(1,13)$ = 0.086, p=0.774, and valence, HC, $F(1,11) = 1.367$, p=0.267; MDD, $F(1,13) = 0.105$, p=0.751, and interactions were non-significant, HC, $F(1,11) = 0.371$, p=0.555; MDD, $F(1,13) = 0.655$, p=0.433. Means indicated that both positive and negative words were recognized equally as well following baseline and following SWD. Second, accuracy was additionally defined as d'. The three-way interaction was not significant, Condition x Valence x Group, $F(1,24)=0.953$, p=0.34

For HC only, a main effect of valence was found for d', such that positive words were remembered more accurately when collapsed across both conditions, $F(1,11)=13.859$, p=.003 . The main effect of condition, $F(1,11)=0.343$, p=0.57, and the interaction, Condition x Valence, $F(1,11)=0.219$, p=0.649, did not reach significance.. No significant main effects or interactions were found for the MDD group, Condition, $F(1,13)=2.462$, p=0.141; Valence, $F(1,13)=0.188$, p=0.671; Condition x Valence, $F(1,13)=2.124$, p=0.169.

Slow-Wave Disruption effects on Reaction Time (ms) of Positive and Negative Words

Hits & Correct Rejections (Accurate). Reaction time for valence was then examined for old words correctly identified as 'old' and new words correctly identified as 'new.' RT was dependent on group membership, valence, and condition, as evidenced by a Condition x Valence x Group interaction, Condition x Valence x Group, $F(1,24)=4.823$, p=0.038.

For the HC group, a Condition x Valence interaction was also found for accurate words, Valence x Condition, $F(1,11) = 5.674$, p=0.036. Post-hoc means indicated that positive words were recognized faster than negative words after SWD. The main effects of condition $F(1,11) = 1.109$,

p=0.315, and valence, $F_{(1,11)} = 1.671$, p=0.223 were not significant for HC. The MDD group recognized positive and negative words equally fast at baseline and following disrupted sleep, with no significant main effects, Condition, $F_{(1,13)} = 0.296$, p=0.595; Valence, $F_{(1,13)} = 0.156$, p=.699 or interaction, Valence x Condition, $F_{(1,13)} = 0.405$, p=0.536.

Hits only (Hits). Reaction time for valence of only old words correctly identified as 'old' was also dependent on group membership, valence, and condition, as evidenced by a Condition x Valence x Group interaction, Condition x Valence x Group, $F_{(1,23)}=7.01$, p=0.014.

For the HC group, a Condition x Valence interaction was also found for hits, Valence x Condition, $F_{(1,11)} = 12.24$, p<0.01. Post-hoc means indicated that positive words were recognized faster than negative words after SWD. The main effects of condition, $F_{(1,11)} = 0.462$, p=0.511, and valence, $F_{(1,11)} = 2.034$, p=0.182, were not significant for HC. The MDD group showed no significant main effects, Condition, $F_{(1,12)} = 0.008$, p=0.931; Valence, $F_{(1,12)} = 1.619$, p=0.227, or interaction, Valence x Condition, $F_{(1,12)} = 0.18$, p=0.68.

Slow-Wave Disruption effects on Reaction Time (ms) of Arousing Words

Hits & Correct Rejections (Accurate). Reaction time for arousal was likewise examined , and was not different by condition and group, as evidenced by a non-significant Condition x Arousal x Group interaction for accurate words, Condition x Valence x Group, $F_{(1,23)}=0.601$, p=0.446.

In the HC group, a main effect for arousal was found for accurate words, such that arousing words were recognized faster than unarousing words only when collapsed across both conditions, $F_{(1,10)}=36.929$, p<0.01. The main effect for condition, $F_{(1,10)} = 0.911$, p=0.362

and interaction, Condition x Valence, $F(1,10)=1.824$, $p=0.207$, were not significant. The MDD group showed no significant main effects, Condition, $F(1,13) = 0.300$, $p=0.593$; Valence, $F(1,13) = 1.573$, $p=0.232$,or interaction, $F(1,13) = 0.229$, $p=0.640$.

Hits only (Hits). Reaction time for arousal was also examined for hits only, and was also not different by condition and group, as evidenced by a non-significant Condition x Arousal x Group interaction, Condition x Valence x Group, $F(1,22)=0.028$, $p=0.868$.

For both groups, HC and MDD, no main effects were found for condition, HC, $F(1,9) = 3.787$, $p= 0.083$; MDD, $F(1,13) = 0.00$, $p=0.983$, or arousal, HC, $F(1,9) = 1.284$, $p=0.286$; MDD, $F(1,13) = 1.028$, $p=0.329$, and the interactions did not reach significance, HC, $F(1,9)=1.192$, $p=0.303$; MDD, $F(1,13) = 2.308$, $p=0.153$. Means indicated that both arousing and unarousing words were recognized as fast at baseline and following SWD

Discussion

The present study demonstrated that following one night of SWD, HC recognized positive words faster than after baseline sleep, while accuracy for emotional words remained equal. Additionally, individuals with MDD were both equally fast and equally accurate at recognizing both positive and negative words at baseline and following SWD.

That HC recognized positive stimuli faster than negative stimuli indicates that it is easier to access positive or rewarding memories as compared to negative memories following SWD. These results are in line with research showing a hedonic response to decrements in sleep, including those of Gujar and colleagues (2011) who showed heightened reactivity in reward areas of the brain in response to viewing pleasurable stimuli. This may suggest that sleep loss may indeed result in both a behavioral and cognitive bias towards rewarding experiences, perhaps as an evolutionary strategy to increase approach behaviors during periods of insufficient resources, such as sleep deprivation. Cognitive biases towards positive memory traces, specifically, would result in individuals accessing positive memories faster than negative memories, which may impair an individual's perspective on the past. Because decision-making can be biased based on the type of information that is more easily accessed, it will be important to further understand the effects of sleep loss on memory accessibility.

As evidenced by equal rates of accuracy for positive and negative words following baseline and SWD, the present results suggest that disrupting slow-wave sleep does not negatively affect memory accuracy while it does impact reaction time. This finding adds to the body of literature demonstrating that memory can be measured along multiple dimensions, including accuracy,

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which reflects the successful encoding of the stimuli, and reaction time which reflects the accessibility of those memories for recall and recognition (Sternberg,1969; Wattenbarger & Pachellat, 1972). Moreover, equal rates of accuracy also suggest that the present findings were not merely due to practice effects, where participants learn how to complete the task more efficiently following successive administrations. If this were the case, one would expect to observe increased accuracy on the second administration as compared to the first. These findings also add to the increasing body of literature that suggests that it is not one aspect of sleep, like REM (Morgenthaler et al., 2014) or SWS that exclusively supports emotional memory. Indeed, a recent study by Cairney and colleagues (2014) indicates that SWS and REM may actually play distinct, but complimentary roles in emotional memory consolidation. Moreover, Morgenthaler (2014) suggests that spindles occurring in S2 may play a crucial role in emotional memory consolidation, and they would occur despite REM-deprivation or SW-deprivation.

Furthermore, it is important to note that the present results were also found despite negative and positive word stimuli being equally arousing, as evidenced by normed ratings, and self-ratings following baseline and SWD. This indicates that it is not arousal, but valence that is affected by the disruption paradigm. Additionally, a separate analysis examining the difference in RT between arousing and unarousing words revealed that following SWD, self-rated arousing words were recognized equally as fast as self-rated unarousing words. It is also significant that slow-wave disruption specifically altered the accessibility of the memory traces for positive stimuli and did not affect arousal or accuracy. Chapman and Chapman (1973) suggest that specific alterations in behavior, such as decreased reaction time, as opposed to generalized changes, such

as a study paradigm that impacts all measures of memory, more strongly suggest a genuine effect of the manipulation of interest.

With regard to the participants with MDD, the present results revealed that SWD did not affect accuracy or reaction time of emotional words. In contrast to HC, positive words were recognized equally as fast following SWD as following BL. Additionally, although the mean reaction time in the MDD group appears lower than the HC group, the difference between HC and MDD at baseline was not statistically significant due to a large variance in reaction time in the MDD group. Because MDD has often been described as a disorder of the reward network, or mesolimbic dopaminergic system (Perogamvros & Schwartz, 2012; Tremblay et. al, 2002), it is possible that this reward system dysfunction prevents the enhanced reactivity to positive stimuli following SWD observed in healthy individuals. Alternatively, these results could also indicate that because an individual with MDD typically exhibits SWS dysfunction associated with the disorder, they may require a fairly severe challenge of the sleep system to provoke an additional response, and demonstrate increased dysregulation. Specifically, a 40% reduction in slow-wave sleep found here, as opposed to total sleep deprivation, may not be sufficient to result in changes to emotional processing. This interpretation is supported by studies that have used different methods of sleep deprivation in MDD which have concluded that it is a disruption in total sleep time and not a decrement in a specific component of sleep, slow-wave activity or REM, which results in improved mood (Bonnet, 1985; Giedke et al., 2003).

It was expected that the MDD participants would display significant differences in SWS at baseline than HC, as it has been shown that slow-wave sleep abnormalities are trait-like features

of MDD (Pillai et al., 2011). Our results, however, did not reveal any statistically significant differences between HC participants and individuals with MDD with respect to both minutes of slow-wave sleep in the first NREM period, or percent of SWS throughout the course of the night. This discrepancy may be related to symptom severity, as although our participants with MDD had a mean BDI score of 27.86, indicating moderate to severe depression, as mentioned in Horne (1993) SWS abnormalities may be most commonly found in only the most severe cases of depression (Kupfer et al., 1985; Hawkins et al., 1985). Alternatively, it is also possible that group differences may only be found when examining microarchitecture such as delta power (slow-wave activity) based on power spectral analysis.

These results, however, should be interpreted in light of some limitations. First, the present SWD paradigm was able to reduce SWS by approximately 40%. Whereas some previous studies utilizing the SWD paradigm have nearly eliminated SWS (Ferrara et al., 1999), others have also showed a decrease of approximately 40% (Landsness et al., 2011). This difference may be attributed to methodological differences in the study design including the use of one technician in the present study, as opposed to two, to administer the acoustic tones, or the use of headphones as compared to a loudspeaker. Because of the presence of residual SWS, however, we cannot be certain that complete suppression of SWS would not have resulted in additional differences other than the reaction time results found here. Second, this study included a small sample of participants with a relatively large range in subject age. This may have contributed to the high variability with regard to sleep parameters and other outcome measures. Further, the generalizability of the current sample may be limited by our participant inclusion criteria. Depressed individuals who exhibited diagnostic criteria for any other Axis I disorder,

other than anxiety, were excluded, resulting in a fairly homogenous clinical group. Research has shown that many individuals with MDD also have other comorbid Axis I disorders (Kessler et al., 1996) and as such, our results may not apply to the general population of those with MDD.

Additionally, although the SWD paradigm was designed to decrease slow-wave sleep without decreasing total sleep time, the present results indicated that total sleep time was reduced in those with MDD, while the percentage of stage 1 sleep, and stage 2 sleep increased, while REM sleep significantly decreased for both HC and MDD. Consequently, it is possible that the present findings may not be a result of decreased SWS, but may be due to either decreased REM, or increased stage 2 sleep. Indeed, as previously mentioned, Morgenthaler and colleagues (2014) suggest that spindles occurring in stage 2 sleep may play a critical role in emotional memory. This issue could be further addressed by analyzing spindles and spindle activity before and after SWD.   Additionally, it is also possible that sleep fragmentation, more broadly, may have contributed to the present results. As can be noted in Appendix 1, the percent of stage 1 sleep following SWD correlated very highly with the difference score (SWD minus BL) of reaction time of accurate positive words, lending support to this possibility. These alternative explanations could be evaluated with direct experimental manipulation of sleep fragmentation and spindle activity.

Finally, the study protocol was completed in the same order for all participants, with the SWD night following the baseline sleep night in order to prevent SW rebound on the BL night, and to circumvent SWD effects from disturbing BL measures. It is possible that the standardized order may have contributed to certain learning effects for participants on day two as a consequence of

previously completing the task on day one. The pattern of results found presently, however, provides some evidence suggesting that this may not be the case. If learning had occurred, one might expect to find improvement in accuracy following SWD (night 2), which was not observed. Although the lack of counterbalancing may not have resulted in specific learning effects, it does not preclude that it did not contribute to order effects that may have resulted in the findings found presently. Counterbalancing baseline and SWD nights is the only way to assure that this was not the case. In future studies, this limitation should be addressed by counterbalancing the baseline and SWD conditions. However, counterbalancing BL and SWD nights can be a study design challenge. Because the SWD manipulation can have effects which carry over into the next night, a baseline on the second night would be at risk of being contaminated by those effects. Therefore, in order to counterbalance conditions, the best design may be one in which a week separates the BL and SWD recordings.

In summary, this study examined the effects of decreasing slow-wave sleep on the process of word recognition, and found that the healthy control participants, but not those with MDD, recognized positive words faster than after baseline sleep. This suggests that disrupted slow-wave sleep, which can occur due to a disorder like obstructive sleep apnea, may result in a memory bias where positive memories are accessed faster than negative or neutral memories. Understanding this bias is of great importance as memory accessibility influences decision-making and other behaviors.

Table 3.1 Demographic Variables

|	Healthy Control	Major Depressive Disorder
N (No. female)	12 (8)	14 (9)
Age (SD)	24.5 (6.8)	25(7.68)
Years of Education (SD)	15.75(1.29)	15.36(1.50)
Beck Depression Inventory Score	2.0 (2.02)*	27.86 (6.0)*
Sleep Diary Restedness (1-5)	4.1 (0.88)*	3 (1.0)*
Means, standard deviations (within parenthesis) and ANOVA results. Sleep Diary Restedness Scale: 1=very tired, 2=tired, 3=somewhat rested, 4=rested, 5=very rested.		

*indicates group difference

Table 3.2 Macroarchitectural Sleep Variables

Group	Healthy Control		MDD	
Condition	Baseline	Disruption	Baseline	Disruption
TIB	428.04 (28.09)	422.13 (29.57)	429.92 (30.94)	425.17 (32.26)
TST	409.38 (34.44)	390.63 (38.68)	406.75 (27.70)	375.75 (42.34) †
Sleep Efficiency	95.32 (3.13)	92.30 (5.94)	94.48 (2.43)	90.27 (6.31) †
SOL	4.5 (2.24) *	11.04 (10.69)	11.25 (7.50) *	17.25 (15.12)
REM Latency	82 (33.66)	90.5 (42.19)	73.54 (35.74)	105.54 (81.73)
% Stage 1	4.59 (3.2)	6.23 (2.5) †	3.88 (3.27	5.28 (4.53) †
% Stage 2	53.03 (5.57)	59.23 (7.69) †	51.71(6.63)	57.39 (12.21) †
% SWS	17.36 (6.98)	10.29 (9.49) †	16.30 (7.38)	9.54 (10.20) †
Min. SWS in 1st NREM	39.92 (24.12)	16.00 (15.75) †	26.54 (18.96)	14.92 (15.18) †
% REM	21.61 (6.26)	19.27 (5.51) †	25.27 (5.13)	21.62 (8.63) †
% A&M	3.40 (3.28)	4.98 (5.43)	2.84 (1.45)	6.17 (5.21) †
Means, standard deviations (within parenthesis) and ANOVA results.				
TIB = time in bed; TST = total sleep time; SOL = sleep onset latency; SWS = slow-wave sleep (stages 3 and 4); A&M = Awake and Movement. TIB, TST, SOL are expressed in minutes				

*indicates group difference at baseline
†indicates condition difference

Figure 3.1 Reaction time (ms) to recognize emotional words
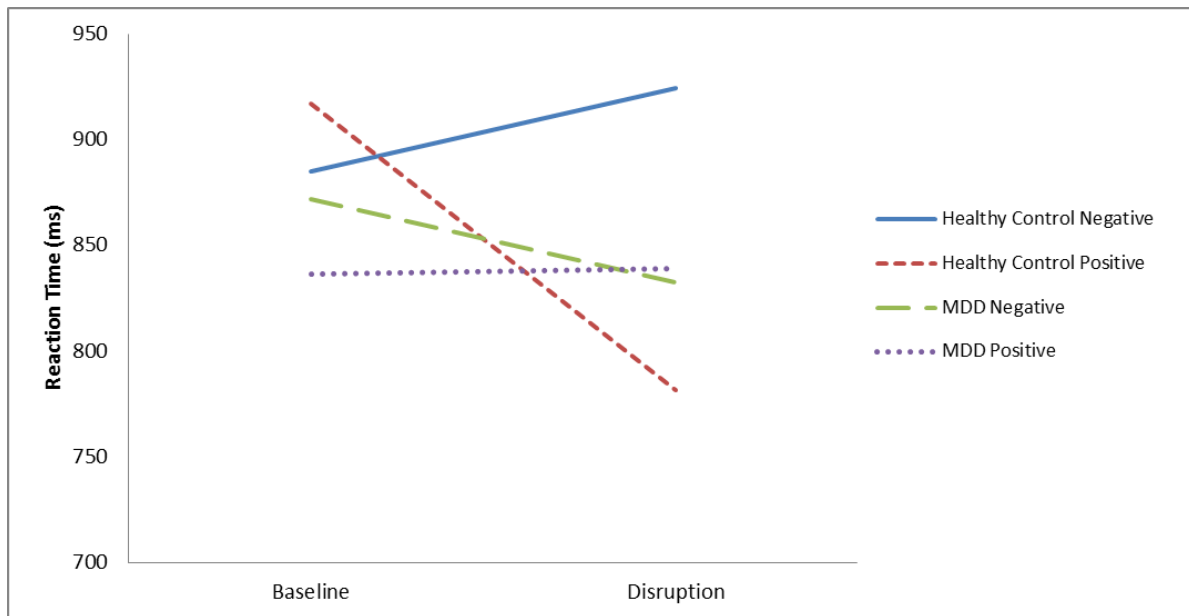
(Please note that means and standard errors are noted in Table 3.3)

Table 3.3   Means and Standard Error for RT, Accuracy, and Self-Ratings for Negative, Positive, Neutral Arousing and Unarousing words at Baseline and following Disruption

Group	HC		MDD	
Condition	Baseline	Disruption	Baseline	Disruption
Negative				
RT (Hits & Correct Rej.; msec)	884.97 (73.59)	924.13(70.40)	871.77 (130.65)	832.23(129.20)
RT (Hits only; msec)	722.15 (79.16)	821.35 (85.93)	760.23 (125.32)	779.87 (112.99)
Accuracy (percent)	0.65 (0.04)	0.61 (0.07)	0.71 (0.06)	0.66 (0.06)
D' (proportion)	0.27 (0.08)	0.22 (0.11)	0.36(0.07)	0.13(0.13)
Average Self-Rating	2.05 (0.12)	2.09 (0.15)	2.22(0.09)	2.16(0.10)
Neutral (Valence)				
RT (Hits & Correct Rej.; msec)	924.67 (72.19)	887.11 (92.09)	899.91(161.81)	867.77 (127.54)
RT (Hits only; msec)	791.65 (77.11)	786.8 (101.94)	830.34 (165.0)	791.25 (118.73)
Accuracy (percent)	0.72 (0.03)	0.70 (0.06)	0.71 (0.06)	0.73 (0.04)
D' (proportion)	0.28 (0.07)*	0.30(0.12)	0.05(0.07)*	0.13(0.09)
Average Self-Rating	4.98 (0.03)	5.08 (0.04) †	5.01(0.04)	5.03(0.03)
Positive				
RT (Hits & Correct Rej.; msec)	917.08(73.42)	781.70(66.22)	836.24(108.57)	838.93(117.71)
RT (Hits only; msec)	791.4 (82.7)	618.12 (72.04) †	721.03 (101.79)	740.59 (100.1)
Accuracy (percent)	0.67 (0.05)	0.68 (0.05)	0.69 (0.06)	0.70 (0.04)
D' (proportion)	0.47(0.07)	0.41 (0.10)	0.23(0.09)	0.20(0.10)
Average Self-Rating	7.76(0.14)	7.7(0.15)	7.78(0.09)	7.65(0.09) †
Arousing				
RT (Hits & Correct Rej.; msec)	902.48 (71.30)	765.06 (72.123)	839.25 (130.08)	801.38 (129.62)
RT (Hits only; msec)	782.64 (89.27)	614.90 (79.94) †	743.60 (137.04)	703.43 (113.99)
Average Self-Rating	7.71 (0.12)	7.70 (0.14)	7.69 (0.07)	7.68 (0.08)
Neutral (Arousal)				
RT (Hits & Correct Rej.; msec)	883.70 (76.44)	922.62 (91.80)	902.03 (151.34)	871.26 (=126.42)
RT (Hits only; msec)	751.33 (82.40)	806.96 (108.68)	817.80 (153.25)	788.58 (106.83)
Average Self-Rating	5.20 (0.04)	5.12 (0.06)	5.07 (0.04)	5.10 (0.06)

Unarousing				
RT (Hits & Correct Rej.; msec)	978.61 (78.25)	960.11 (62.69)	873.04 (150.81)	865.81 (115.35)
RT (Hits only; msec)	815.02 (84.05)	794.43 (66.12)	759.39 (141.64)	796.51 (105.05)
Average Self-Rating	1.90 (0.18)	2.00 (0.19)	2.15 (0.10)	2.25 (0.10)
Means, standard error (within parenthesis) and One-way ANOVA results.				

*indicates group difference at baseline
†indicates condition difference

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Chapter 4[4]

Napping to modulate frustration and impulsivity: A pilot study

Introduction

Understanding the benefits of napping for those who regularly experience prolonged wakefulness is crucial as the number of individuals who experience sleep loss or sleep disturbance is widespread. Currently, at least 28% of Americans get insufficient sleep (Centers for Disease Control, 2008) while approximately 14% perform shift work which can significantly affect sleep quality (Drake et al., 2005), and extend prior wakefulness. The literature has consistently demonstrated that sleep deprivation impairs cognitive functioning, decreasing cognitive speed and impairing attention and memory (Goel et al., 2013).

Sleep deprivation has also been shown to preferentially affect executive functioning (Durmer & Dinges, 1997). This may indicate that complex behaviors such as emotional control, which plays an important protective role in psychological functioning, may also be at risk. For example, sleep deprivation has been associated with a decreased ability to inhibit impulsive responses to a frustrating obstacle (Kahn-Greene et al., 2006). Similarly, increased impulsivity related to sleep deprivation also reduces one's ability to delay gratification (Killgore et al., 2008), which is generally related to more negative outcomes. Taken together, these studies provide evidence that

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[4] Chapter 4 corresponds to the publication Goldschmied et al., 2015

one's ability to inhibit or regulate negative emotional responses deteriorate with prolonged

wakefuless. What is not currently known, however, is how napping during the course of typical

waking hours may affect emotional control.

Presently, the cognitive consequences of sleep deprivation are well understood (Durmer &

Dinges, 1997; Goel et al., 2013). As a result, research on effective ways to decrease prolonged

wakefulness and resultant fatigue is crucial in order to find ways to help those who are required

to maintain high levels of accuracy and attention without attaining a full night of sleep, such as

physicians and pilots, to perform properly. Napping has been identified as one of the most

effective countermeasures to sleepiness and fatigue (Horne & Reyner, 1996).

Very recent research has also shown that a 30-minute nap can improve immune health that may

have been compromised by prior sleep deprivation, indicating that napping provides benefits

beyond reducing sleepiness and fatigue (Faraut et al., 2015). Indeed, studies that have examined

the direct effects of napping on emotional functioning have generally found that napping

increases positive emotions including energy (Taub et al., 1976), motivation (Hayashi et al.,

1999), and joy (Luo & Inoue, 2000). There has been limited research, however, into how

napping affects emotional control, specifically with regard to controlling negative emotional

responses. One study recently showed that toddlers who were not permitted to nap showed more

negative responses to an unsolvable task than did toddlers who napped (Berger et al., 2011),

which may provide preliminary evidence that napping can facilitate this kind of emotional

control. There is little research, however, on the direct effects of napping on controlling negative

emotional responses, including frustration and impulsivity, in adults.

The aim of the present study was to investigate the effects of napping on the regulation of frustration tolerance and impulsivity in a sample of healthy participants. Given that previous research has shown that sleep deprivation decreases the ability to inhibit impulses, we hypothesized that those who did not nap would show decreased tolerance for frustration and increased self-reported impulsivity. On the other hand, napping would increase frustration tolerance and decrease feelings of impulsivity.

Methods

Participants

Participants were recruited by fliers, newspaper ads, and internet recruitment sites in a

Midwestern college town. Inclusion criteria included being between the ages of 18-50, the ability

to speak and understand English fluently, and the ability to keep a consistent sleep schedule.

Exclusion criteria included any history of serious medical disorders, sleep disorders, or

pregnancy. All participants gave informed consent prior to the beginning of study. This study

was approved by the relevant Institutional Review Board.

Procedures

This study was part of a larger project designed to examine napping on (i) emotional processing,

(ii) attention, and (iii) decision-making. Only the tasks and questionnaires relevant to the present,

emotional processing study will be discussed. All participants were instructed to refrain from

alcohol and caffeine on the day of participation and were required to keep a consistent sleep

schedule for three nights prior to the study, verified by sleep diary and calls to a time-stamped

voicemail. On the day of the study, all participants presented at the laboratory at 1pm.

Participants completed computer-based behavioral tasks including the Frustration Tolerance

Task. Upon completion of the tasks, participants completed a battery of questionnaires

examining state characteristics such as sleepiness, mood, and impulsivity. All participants were

then randomly assigned to a 60-minute nap opportunity condition or no-nap condition, where

they watched a 60-minute emotionally neutral nature documentary. Research assistants were

present to monitor all participants, via two-way mirror, to ensure that participant were awake

during the no-nap period or to monitor the sleep EEG to ensure proper recording. Following the

nap or no-nap period, all participants completed the battery of state questionnaires, followed by the behavioral tasks.

Epworth Sleepiness Scale. The Epworth Sleepiness Scale (Johns, 1991) measures chronic daytime sleepiness. Participants are asked to rate the likelihood that they would fall asleep in eight situations on a scale from 0 (would never doze) to 3 (High chance of dozing). Total Epworth scores fall in the range of 0-24, where <10 is considered normal, 10-15 indicates moderate sleepiness, and 16-24 indicates severe sleepiness.

Stanford Sleepiness Scale. The Stanford sleepiness scale (Hoddes et al., 1973) is a one-item scale designed to measure present levels of sleepiness. Participants select one of seven statements that most closely describe their immediate level of alertness. Increasing scores indicate increasing sleepiness.

State-Impulsivity Questionnaire. The State Impulsivity Questionnaire, or STIMP (Wingrove & Bond, 1997) assesses state impulsivity using a set of fourteen statements pertaining to impulsivity measured on a visual analogue scale. Each item is presented to the participant beginning with the statement "Right now…" to emphasize that participants should respond with regard to the present state. Each item of the visual analogue scale is scored from 0-100, and the total STIMP score is the sum of all 14 visual analogue scale item scores.

Frustration Tolerance Task (FTol). Participants completed a computer-based adaptation of Feather's (1961) frustration tolerance task. Four geometric designs are presented successively on

a computer screen. Participants are directed to recopy the diagram on a piece of paper, without tracing over any line twice and without lifting the pencil from the paper. Half of each set of designs was unsolvable. Participants were allowed to make as many attempts on each design as they wished. The total time spent on the impossible puzzles is interpreted as a measure of persistence, namely the less time spent, the less the persistence and the lower the subject's frustration tolerance.

Data Analysis

Statistical analyses were conducted on the STIMP and Ftol scores using repeated measures analysis of variance (ANOVA), with condition (Pre and Post-nap) as within-subjects factors and group (Nap and No-nap participants) as between-subjects factor. Additionally, post hoc analyses were conducted for the correlation between these variables, and difference scores, defined as the scores (STIMP or Ftol) at baseline subtracted from the scores (STIMP or Ftol) following the nap/no-nap period. All analyses were performed using the software program IBM SPSS v20.0, with $p < 0.05$ considered significant.

Results

In order to determine if the groups were appropriately randomized, age, self-reported total sleep time, habitual sleepiness, and present sleepiness were examined. Results revealed no significant differences on all demographic variable scores between groups. Table 4.1 displays key demographic variables. Nappers were confirmed to have fallen asleep as indicated by self-report, and at least three successive 30-sec epochs of any stage of sleep.

Frustration Tolerance Task

Two extreme outliers were identified according to the Grubbs Test, and were thus excluded from this analysis. Before the nap period, nappers and no-nappers spent equal time on the unsolvable task. The main effect of group was significant, F (1, 36) = 7.41, p = 0.01. The main effect of time, however, was not significant, F (1, 36) = 0.10, p = 0.76. After the nap period, however, nappers increased the time spent on the second unsolvable task, while non-nappers decreased time spent, revealed by significant interaction, F (1, 36) = 5.04, p = 0.03, η^2 = 0.12. Post-hoc analyses revealed a large effect for the between-group comparison at post, F (1, 36) = 9.51, p < 0.01, η^2 = 0.46. (Figure 4.1)

The State Impulsivity Questionnaire (STIMP)

One extreme outlier was identified according to the Grubbs Test, and was thus excluded from this analysis. The main effects of time, F (1, 36) = 0.23, p = 0.64, and group were not significant, F (1, 36) = 0.18, p = 0.68. STIMP scores in the nap group showed decreased self-reported impulsivity, while the no-nap group showed increased total scores from pre-nap to post-nap, as indicated by a significant interaction, F (1, 36) = 6.78, p = 0.01, η^2 = 0.16.

There was a significant relationship between frustration tolerance scores and difference scores in total STIMP scores, $r = -.36$, $p < .05$.

Discussion

Consistent with our hypotheses, our results demonstrated that participants who did not have the opportunity to nap were less willing to endure frustration due to an unsolvable task, and reported feeling more impulsive. On the other hand, participants who napped showed increased tolerance for frustration on the unsolvable task compared to baseline, and reported feeling less impulsive on a self-report measure. Moreover, the results do not seem to be due to differences in either habitual total sleep time or chronic sleepiness as indicated by non-significant group differences in baseline measures. These findings provide preliminary evidence that napping may decrease both feelings of impulsivity and impulsive behaviors.

Although very few studies to date have directly examined the direct relationship between sleep and impulsivity, our results are consistent with the existing literature examining the effects of sleep deprivation on response inhibition, a related construct. For example, research using the go/no-go task has shown that sleep deprivation significantly decreases response inhibition (Drummond et al., 2006; Anderson & Platten, 2011; Cedernaes et al., 2014). Our results are also in line with research demonstrating that sleep deprivation decreases tolerance for negative emotional experiences including pain (Onen et al., 2001) and physical exertion during exercise (Martin, 1981). Additionally, with regard to self-reported feelings of impulsivity, Perkinson-Gloor and colleagues (2013) found that sleeping less than 8 hours was associated with less self-reported persistence than sleeping more than 8 hours. Collectively, the present results indicate that prolonged wakefulness contributes to emotional dysregulation by impairing one's ability to inhibit negative emotional responses.

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Our results also suggest that napping may be a beneficial intervention for individuals who may be required to remain awake for long periods of time by enhancing the ability to persevere through difficult or frustrating tasks, and decreasing impulsive decision making. In contrast to many other interventions, napping can be viewed as a relatively cost-efficient, safe and easy to implement strategy to increase workplace safety. Emerging research has suggested that successful regulation of impulsivity is crucial for interpersonal and professional functioning (Franken et al., 2008). To this end, employers may promote napping as a relatively inexpensive strategy to regulate negative emotional responses during compulsory prolonged wakefulness, with the use of nap pods or prolonged break time. Additionally, approaches that regulate sleep/wake processes like napping could ultimately be incorporated into treatment for impulse-related disorders associated with sleep disturbance including substance abuse, and addiction.

The present results, however, should also be interpreted in light of several limitations. First, this study was a preliminary examination of napping on impulsivity, using a smaller sample size of mostly college-aged individuals, thereby limiting generalizability. Second, while habitual sleep was verified using sleep diary and calls to a time-stamped voice mail, use of more continuous and objective measures of sleep, such as actigraphy was not included. Future studies may consider the aforementioned in order to further investigate the effects of napping on impulsivity. Additionally, it may be useful to also investigate the effects of naps following greater periods of sleep debt to determine if naps in those types of circumstance would result in a similar pattern of findings.

In summary, the present study provides novel evidence that a brief, midday nap can moderate impulsive feelings and behavior. Results indicated that those who napped demonstrated

decreased feelings of impulsivity, and increased tolerance for frustration. In contrast, those who

did not nap showed decreased tolerance for frustration and increased feelings of impulsivity.

These findings suggest that napping may be an effective strategy to counteract negative

emotional consequences, including increased impulsivity and decreased ability to tolerate

frustration, that may occur as wakefulness increases throughout the day.

Table 4.1 Demographic Variables and Behavioral Results of the Sample

	No Nap	Nap	Sig.
N (female)	18 (9)	22 (11)	NS
Age	21.31 (1.78)	20.05 (1.79)	NS
Self-reported Total Sleep Time	8:01 (0.03)	7:42 (0.03)	NS
Habitual Sleepiness – Epworth Sleepiness Scale Score	14.67 (3.96)	14.95 (3.46)	NS
Present Sleepiness – Stanford Sleepiness Scale Score	2.94 (1.21)	2.73 (1.08)	NS
Frustration Tolerance - Pre (milliseconds)	69255.13 (29246.75)	68622.05 (40213.99)	NS
Frustration Tolerance - Post (milliseconds)	48558.75 (16036.66)	95924.73 (59674.31)	$p<0.01$
STIMP Score - Pre	29.67 (9.90)	31.11 (14.06)	NS
STIMP Score - Post	33.41 (13.75)	28.53 (14.38)	NS
Means, standard deviations (within parenthesis) and ANOVA results.			

Figure 4.1 Frustration Tolerance scores
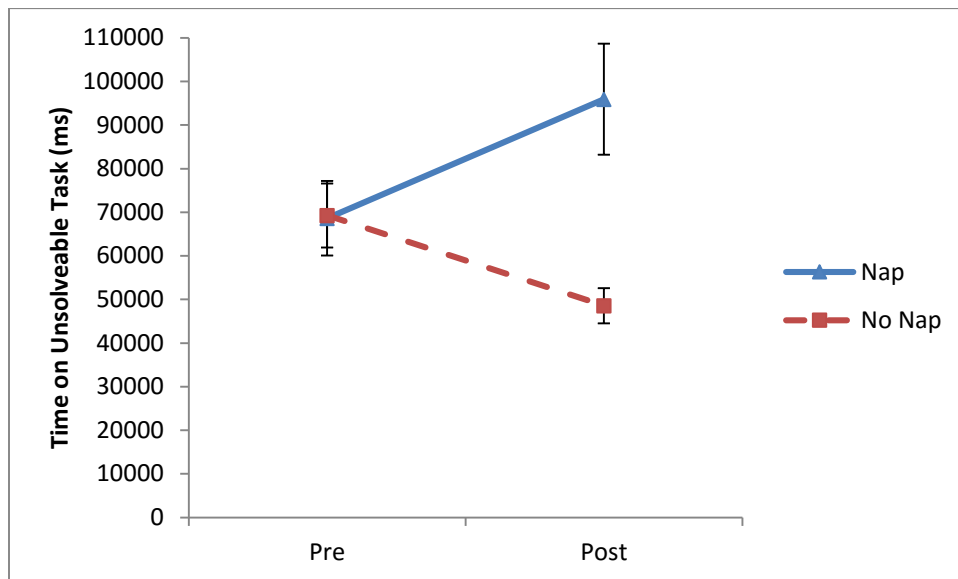
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Chapter 5: General Discussion

This dissertation aimed to further understand the impact of sleep on mood and emotional processing by examining three independent sleep manipulations, sleep delay, slow-wave disruption, and napping. The investigation of distinctive sleep manipulations, in addition to the examination of both healthy and depressed individuals, further allowed us recognize the specific contribution of certain components of sleep to emotional processing, and to understand if these components have a direct relationship to healthy emotional functioning. The methods and findings of each of the three studies are summarized below.

Study 1

Healthy controls and individuals with MDD spent three consecutive nights in the laboratory. The first night served as an adaptation to the laboratory environment, the second served as the baseline night, and on the third night, sleep was delayed by three hours in order to increase the homeostatic drive for sleep. The Profile of Mood States was administered in the morning following both the baseline night and delay night in order to assess subjective mood changes. Following sleep delay, while healthy control participants exhibited increased slow-wave activity in both the first NREM period, and across the night, those in the MDD group did not. Regression analyses revealed that increased normalized SWA during the second NREM period following sleep delay predicted increased mood disturbance in those with MDD. Increases in SWA as a result of sleep delay did not predict mood disturbance in healthy control participants.

Additionally, as has been previously demonstrated, approximately 50% of individuals with MDD responded to the sleep manipulation, by exhibiting increased mood disturbance following sleep delay.

Study 2

Healthy controls and individuals with MDD spent three consecutive nights in the laboratory. The first night served as an adaptation to the laboratory environment, the second served as the baseline night, and on the third night, slow-wave sleep was disrupted utilizing auditory tones. Each night, prior to sleep, participants were directed to memorize a word list of emotional (positive and negative) and neutral words. Each morning, participants completed a recognition memory task utilizing words from the previous night's word list, and new words. Following slow-wave disruption, both healthy control participants and those with MDD demonstrated significantly less slow-wave activity across the night. Subsequently, healthy control participants recognized positive words significantly faster than negative words, and significantly faster than following baseline sleep, demonstrating enhanced accessibility of positive information. In contrast, individuals with MDD recognized positive and negative words equally fast following baseline and slow-wave disruption. Slow-wave disruption did not alter rates of accuracy in either healthy participants or those with MDD, and these findings could not be accounted for by differences in arousal.

Study 3

Before being randomized into a nap or no-nap condition, healthy control participants completed a battery of questionnaires assessing sleepiness, mood and state impulsivity and a task that included an unsolvable puzzle designed to assess tolerance for frustration. Following the nap, or

viewing of an emotionally neutral nature video, participants once again completed the questionnaires and task. Following the nap, behavioral analyses revealed that nappers reported feeling less impulsive, while non-nappers reported feeling more impulsive. Nappers also spent a significantly longer amount of time working on the unsolvable puzzle than before the nap, and significantly longer than those in the non-nap group, demonstrating enhanced control of negative emotional responses following a nap.

Taken together, this dissertation research has shown that manipulations to sleep can alter both the processing of emotional information, in addition to the subjective experience of emotion, including mood, and how one controls negative emotional responses. Research has previously demonstrated that altering sleep can affect emotional functioning, establishing that sleep loss, in the form of total sleep deprivation (Penetar et al., 1993), and chronic sleep restriction (Dinges et al., 1997), both disturbs subjective mood in healthy individuals, and can result in behavioral biases toward rewarding stimuli (Brondel et al., 2010; Mullin et al., 2013; Gujar et al., 2011). The present research extends this literature by demonstrating that wakefulness across the day can likewise contribute to increasing emotional dysregulation, and that napping may counteract this behavior. The present work has additionally indicated that emotional biases do not only occur following total sleep deprivation, but may also occur following the disruption of slow-wave sleep, alone.

Furthermore, research has also begun to establish the relationship between altering slow-wave activity and subsequent changes in mood in individuals with MDD, demonstrating that a reduction in slow-wave activity reduces symptoms of depression (Landsness et al., 2011) and

negative affect (Cheng et al., 2015). The present research extends this work, as well, by demonstrating that increases in slow-wave activity following a homeostatic sleep challenge are related to subsequent increases in mood disturbance, including feelings of depression and anxiety. Future directions will include extending this work in understanding the role of slow-wave activity in addition to the benefits of napping, to adolescent samples, as this group has been shown to exhibit both sleep loss (Carskadon, Acebo, & Jenni, 2004) and emotional dysregulation (Steinberg, 2008).

To conclude, the results of this dissertation have extended previous research which has established the intimate relationship between sleep and emotional functioning by not only showing that brief naps can alter how one experiences and subsequently controls negative emotions, but also by demonstrating the importance of slow-wave activity to healthy emotional functioning and unbiased emotional processing. This work may help inform treatment strategies for psychiatric disorders with concomitant sleep problems such as major depressive disorder, or help in the development of intervention approaches for vulnerable populations who have been shown to be prone to emotional dysregulation, including adolescents, who may also be at risk for sleep disturbance.

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