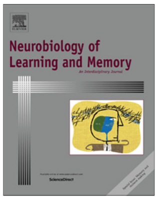
Neurobiology of Learning and Memory 125 (2015) 168–175

Contents lists available at ScienceDirect

Neurobiology of Learning and Memory

journal homepage: www.elsevier.com/locate/ynlme



# Slow-wave disruption enhances the accessibility of positive memory traces ☆

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ARTICLE INFO

*Article history:*
Received 11 March 2015
Revised 4 September 2015
Accepted 8 September 2015
Available online 26 September 2015

*Keywords:*
Slow-wave
Reward
Recognition
Memory

ABSTRACT

The purpose of this study was to explore the effects of slow-wave disruption on positive and negative word recognition in a sample of healthy control participants and those with major depressive disorder. Prior to sleep, participants learned a set of emotional and neutral words during an encoding task by responding whether or not the word described them. Following baseline sleep, participants underwent one night of selective slow-wave disruption by auditory stimuli. Accuracy and reaction time to a recognition word set, including both positive and negative words, was assessed in the morning. Repeated-measures ANOVA revealed a significant interaction between word valence and condition, with positive words recognized significantly faster than negative words after disruption, in only healthy control participants. There were no significant results in those with major depressive disorder, or with regard to accuracy. These results may add to the increasing body of literature suggesting a hedonic bias to positive stimuli following sleep disruption.

## 1. Introduction

Over the last several years, research has begun to show that decrements in sleep may provoke a hedonic response that results in approach behavior toward 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, Fang, and Grigson (2009) showed that rats increased self-administration of cocaine, while Hanlon, Andrzejewski, Harder, Kelley, and Benca (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, Romer, Nougues, Touyarou, & Davenne, 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, Chuah, Huettel, & Chee, 2007). Similarly, Gujar, Yoo, Hu, and Walker (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.

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, Gulec, Agargun, & Besiroglu, 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 (Daurat, Terrier, Foret, & Tiberge, 2007; Plihal & Born, 1997;

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☆ This study was partially funded by RO1-MH61515 (Armitage).

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[1] Retired.

http://dx.doi.org/10.1016/j.nlm.2015.09.006
1074-7427/

Stickgold, 2005) such that sleep following encoding has been shown to improve memory in contrast to a period without sleep (Baran, Pace-Schott, Ericson, & Spencer, 2012). Moreover, sleep is also thought to preferentially consolidate emotional memory (Payne, Stickgold, Swanberg, & Kensinger, 2008), especially when containing REM sleep (Groch, Wilhelm, Diekelmann, & Born, 2013; Nishida, Pearsall, Buckner, & Walker, 2009; Wagner, Gais, & Born, 2001). 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 and 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, 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, Heller, Pack, & Abel, 2003; Kumar & Jha, 2012; Menz et al., 2013) which may suggest a bias toward 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 and 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, De Gennaro, and Bertini (1999) and others (Lentz, Landis, Rothermel, & Shaver, 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, Goldstein, Peterson, Tononi, and Benca (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 toward 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, Kalmbach, & Ciesla, 2011), we expected the effect to be attenuated as compared to HC.

## 2. Methods

### 2.1. 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 and 8 h, with a habitual bed time between 10 pm and 12 am, 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.

#### 2.1.1. 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).

#### 2.1.2. 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.