Sleep deprivation alters pupillary reactivity to emotional stimuli in healthy young adults

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ABSTRACT

The aim of this pilot study was to quantify the impact of sleep deprivation on psychophysiological reactivity to emotional stimuli. Following an adaptation night of sleep in the lab, healthy young adults were randomly assigned to either one night of total sleep deprivation or to a normal sleep control condition. The next afternoon, responses to positive, negative, and neutral picture stimuli were examined with pupillography, an indicator of cognitive and affective information processing. Only the sleep-deprived group displayed significantly larger pupil diameter while viewing negative pictures compared to positive or neutral pictures. The sleep-deprived group also showed anticipatory pupillary reactivity during blocks of negative pictures. These data suggest that sleep deprivation is associated with increased reactions to negative emotional information. Such responses may have important implications for psychiatric disorders, which may be triggered or characterized by sleep disturbances.

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1. Introduction

Effects of sleep deprivation on neurobehavioral function (e.g., vigilance and cognition) are well documented. The prefrontal cortex (PFC) is particularly sensitive to sleep loss (Drummond et al., 1999; Thomas et al., 2000), with corresponding impairments observed in PFC-associated executive functions (Harrison and Horne, 1998, 1999; Jones and Harrison, 2001; Muzur et al., 2002) and vigilance (Belenky et al., 2003; Van Dongen et al., 2003). The adverse impact of sleep deprivation on mood and affective reactivity and regulation has been less thoroughly explored in the experimental literature. This is surprising given the role of prefrontal cortical circuits in regulating mood, particularly by inhibiting brain structures important to the generation and recognition of affect such as the amygdala (Davidson et al., 2000; Phillips et al., 2003; Urry et al., 2006). Recent evidence suggests such processes may be impaired by sleep deprivation. In a recent neuroimaging study (Yoo et al., 2007), sleep deprived individuals demonstrated heightened amygdala reactivity to negative picture stimuli, which was also associated with reduced functional connectivity between the amygdala and the medial PFC.

Mood responses to sleep deprivation are variable and at times labile. Sleep deprivation can induce giddiness, child-like behaviors, and silliness (Bliss et al., 1959; Horne, 1993), as well as more widely recognized negative effects including dysphoria, increased irritability, and lowered frustration tolerance. The increased irritability that frequently accompanies sleep deprivation suggests that sleep-deprived individuals are highly reactive to emotional cues. These effects on mood can lead to negative consequences and impact functioning. For example, an inverse association between sleep duration and interpersonal difficulties and even violence has been observed in medical residents (Baldwin and Daugherty, 2004), and sleeping less than 8 h is associated with increased risk for adolescent suicidal behavior (Liu, 2004). Chronic sleep deprivation/restriction has also been associated with the development of psychopathology, including bipolar disorder (Kasper and Wehr, 1992; Wright, 1993; Frank et al., 1997), pre- and post-partum psychosis (Brockington et al., 1990; Sharma et al., 2004), and depression in both new mothers and fathers (Hiscock and Wake, 2001). However, the relationship between sleep deprivation and mood is not simple. Sleep deprivation transiently improves mood symptoms in 40–60% of individuals with clinical depression, although some patients' symptoms worsen (Naylor et al., 1993; Wirz-Justice and Van den Hoofdakker, 1999; Giedke and Schwarzler, 2002; Giedke et al., 2003).

Previous experimental studies of chronic sleep restriction and acute sleep deprivation in healthy individuals have documented a deterioration of mood, with larger effect sizes than for either cognitive or motor responses (Pilcher and Huffcutt, 1996). However, previous studies almost exclusively used self-report outcomes. The reliability of such self-report data is uncertain due to contextual factors (e.g., reporting bias, demand characteristics,

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and scale interpretation). Objective measures of affective responding may help to characterize and quantify the affective consequences of sleep deprivation. Ultimately, such information may help to uncover pathways by which sleep is related to affective impairments and the development of mood disorders. For instance, sleep deprivation may be associated with disruptions in the dynamic time-course of responses to cognitive and emotional information as seen in depression (Challis and Krane, 1988; Deldin et al., 2001; Siegle et al., 2001, 2002, 2003a,b, 2007; Wagner et al., 2006). Self-report measures cannot capture this information, which occurs on the time-scale of milliseconds or seconds.

In this study, we used pupillary response as an indicator of cognitive and emotional information processing in order to examine the magnitude and time-course of responses to affective picture stimuli in healthy adults following sleep deprivation or normal sleep. We used pupillography for several reasons. First, as there is extensive overlap between cognitive and affective processes (e.g., Davidson, 2003) it is appropriate that pupillary responses reflect each of these phenomena. Many studies have demonstrated pupil dilation to be a reliable correlate of cognitive load. For example, the pupil dilates more under conditions of higher attentional allocation, memory use, or interpretation of more difficult material (see Beatty, 1982; Steinhauer and Hakerem, 1992 for reviews). The pupil has also been shown to dilate in response to emotional information (Janisse, 1974; Bradley et al., 2008). Second, sustained cognitive load leads to sustained pupil dilation (Beatty, 1982). Thus, pupillography is an appropriate measure to examine immediate and sustained processing of emotional information. Third, the pupil is innervated by brain structures involved in cognitive and emotional processing, such as the anterior cingulate cortex (Szabadi and Bradshaw, 1996). Stimulation of limbic regions such as the amygdala increases pupil dilation (Koikegami and Yoshida, 1953; Fernandez De Molina and Hunsperger, 1962), as does stimulation of the midbrain reticular formation (Beatty, 1986), which receives afferent projections from the frontal cortex and sends efferent projections to the ocular motor nuclei. Concurrent pupil dilation/functional magnetic resonance imaging assessment has confirmed that pupil dilation reflects the time-course of activity in brain areas associated with cognitive processing including the dorsolateral prefrontal cortex (Siegle et al., 2003a,b). Urry and colleagues (2006) recently used this method to demonstrate that pupil dilation reflects the time-course of neural responses to affective picture stimuli as well as explicit instructions to regulate emotions. The pupil therefore reflects initial reactivity as well as brain processes associated with subsequent affect regulation, and aspects of arousal (Critchley et al., 2005), even though it may be difficult to distinguish specific cognitive and emotional subprocesses in a given instant.

For this pilot study, we used passive viewing of visual stimuli to examine automatic reactivity to emotional stimuli (e.g., Cuthbert et al., 2000) in healthy adults following either one night of total sleep deprivation or following a night of normal sleep. A passive viewing task was employed to assess naturalistic reactivity outside the context of laboratory-induced explicit cognitive or emotional demands. We expected negative stimuli to induce larger pupillary responses than neutral or positive stimuli in the sleep deprivation condition compared to a non-sleep-deprived control group. Such data would reflect a fundamental tendency towards increased reactivity in the seconds following emotional stimuli in sleep deprivation. That said, our analysis path also allowed for the potential that sleep deprivation was associated more diffusely with increased arousal which would be evidenced by increased pupillary responses to both negative and positive stimuli compared to neutral stimuli.

2. General methods

Following an adaptation night of sleep in the lab, participants were randomly assigned to either one night of total sleep deprivation (SD group) or to a control condition (non-SD group). Emotional reactivity to affective picture stimuli was assessed the next afternoon, after approximately 31–33 h of wakefulness in the SD group.

2.1. Participants

Participants included 30 healthy adult volunteers ages 21–30: 15 female and 15 male (8 females and 7 males assigned to the sleep deprivation group); 20 Caucasian, 4 African–American, 4 Asian, 2 Hispanic; mean age ± standard deviation M = 24.4 ± 2.76 years. Potential participants were excluded if they had any of the following: current or past psychiatric or sleep disorders; presence of significant sleep disordered breathing or leg movements (10 or more events per hour of sleep); significant hearing or vision problems or major medical problems and any medications other than contraception; bedtimes earlier than 10:00 p.m. or later than 2:00 a.m., or an irregular sleep/wake schedule (i.e., 2 or more hours of variability in sleep/wake times based on a week of sleep diary data); tobacco use; or consumption of more than 2 caffeinated beverages daily.

2.2. Procedure

Following an initial telephone screening, interested participants were scheduled for an in-person assessment interview at the Clinical Neuroscience Research Center (CNRC), a satellite of the University of Pittsburgh's General Clinical Research Center. At the screening, the experiment was explained to participants, who signed a consent form approved by the University of Pittsburgh Institutional Review Board. Structured clinical interview assessments for psychiatric (SCID I, First et al., 1995) and sleep disorders were conducted by trained and reliable research nurses. Eligible participants were scheduled for an adaptation night in the CNRC lab, including an overnight diagnostic polysomnogram to rule out clinically significant sleep disordered breathing or leg movements. Participants returned the next evening and stayed at the lab for 24 h. Participants assigned to the non-SD control group went to bed at their habitual bedtime and were allowed 8 h of time in bed from the time of sleep onset. Those assigned to the SD group remained awake all night under continual polysomnographic and frequent behavioral monitoring. During the SD night, participants had access to food, TV, and the internet. Participants were run in pairs when possible to help facilitate wakefulness for the sleep-deprived group. Participants completed emotional information processing and cognitive tasks (the latter to be presented in subsequent reports) in an afternoon test session that started at 2:30–4:30 p.m.; task order was randomized. Multiple self-report and physiological measures of sleepiness were also administered across the day. These measures have been described separately (Franzen et al., 2008). Participants refrained from caffeine and alcohol for 24 h prior to the adaptation night and throughout remainder of their time in the lab.

2.3. Apparatus

Testing occurred with the participant alone in a moderately lit room. Stimuli were presented using E-Prime software (Psychology Software Tools, Pittsburgh, PA). Pupil diameter was recorded with a sampling frequency of 60 Hz using an ISCAN RK726 pupillometer (Burlington, MA), which consisted of a video camera and infrared light source pointed at the participant's left eye to track pupil size. The pupillometer's resolution is typically better than 0.05 mm pupil diameter.

2.4. Preparation of pupil data for analysis

Data were cleaned using our lab's standard methodology, derived from Granholm et al. (1996), including blink and artifact rejection. Eye blinks were removed and then corrected for by linear interpolation. Trials which consisted of over 50% blinks were removed from consideration. Data cleaning procedures resulted in the elimination of median Md = 2, mean ± standard deviation M = 2.4 ± 2.1 trials per subject out of 45 trials presented. Data were smoothed by applying a 3-point flat filter twice. Linear trends in pupil dilation were calculated over blocks of 20 trials and removed from pupil dilation data to eliminate effects of slow drift in pupil diameter unrelated to trial characteristics. Prior to removing these trends, we examined the slopes over blocks of 20 trials (in three blocks). All three slopes were slightly negative. Only block 2 was significantly different from 0 ($t(29) = -2.35$, $p = 0.026$), whereas blocks 1 and 3 did not have a significant slope effect ($t(29) = -1.21$, $p = 0.236$ and $t(29) = -1.40$, $p = 0.173$, respectively); moreover, the three slopes did not differ from one another ($F(2,58) = 1.05$, $p = 0.358$). Thus it is unlikely that results observed in any block were affected by ceiling or floor effects of drift across the block. Data were corrected for baseline by subtracting tonic, baseline pupil diameter (100 ms prior to the warning cue) from waveforms representing pupillary responses. Baseline pupil diameters between the SD and non-SD groups did not significantly differ ($t(28) = 0.46$, $p = 0.65$). As a final data reduction step prior to statistical analysis, the original 60-Hz waveforms were binned into 0.5 s intervals.