An Experimental Investigation of the Effects of Acute Sleep Deprivation on Panic-Relevant Biological Challenge Responding

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Prospective research indicates sleep deprivation potentiates anxiety development, yet relatively little research has examined the effects of sleep deprivation in terms of specific types of anxiety. The current study tested the association between acute sleep deprivation and panic-relevant biological challenge responding among nonclinical participants. One hundred and two participants were randomly assigned to either an experimental (acute sleep deprivation) or control (no sleep deprivation) group. The day prior to and following the experimental (sleep) manipulation, participants completed a 5-minute 10% carbon dioxide–enriched air laboratory-based biological challenge. As predicted, sleep deprivation increased anxious and fearful responding to the challenge. Findings suggest sleep deprivation may be an important factor to consider in models of panic development. There are several areas in this general domain that warrant additional investigation.

Sleep deprivation is one of the most common health problems in the United States, with as many as 70 million people reporting sleep deprivation that results in an estimated $65 billion in health care costs and lost productivity (U.S. Surgeon General, 2004). Sleep deprivation is associated with multiple specific sleep disorders. For instance, primary insomnia is defined by problems falling and staying asleep or nonrestorative sleep that persists longer than 1 month and results in functional impairment (American Psychiatric Association [APA], 2000; American Sleep Disorders Association, 1990). Insomnia is the most common sleep problem (cf. hypersomnia), with prevalence rates ranging from 30% to 35% (Breslau, Roth, Rosenthal, & Andreski, 1996). There are high comorbidity rates between chronic (i.e., greater than 6 months) sleep problems and several types of psychopathology, including major depression, anxiety disorders, and substance use disorders (Eaton & Kessler, 1985; Reiger et al., 1984). Specifically, of those with chronic sleep problems, 40% met criteria for at least one psychiatric disorder (Drake, Roehrs, & Roth, 2003). These data have led researchers to focus on the effects of sleep deprivation to better understand its role in the development and maintenance of mental disorders.

Emerging research suggests sleep deprivation potentiates the development of anxiety. Longitudinal evidence indicates that sleep deprivation is associated with an increased probability of developing an anxiety disorder (Ford & Kamerow, 1989). Indeed, sleep problems in childhood and adolescence are related to elevated anxiety symptoms in adulthood (Gregory, Ely, O’Connor, & Plomin,
anxiety (directional relation between sleep problems and patterns. In fact, research has suggested a bi-
nonote, this line of research does not speak to causal problems and adult depression. It is important to
blems developed anxiety disorders by adulthood children with than without persistent sleep pro-
children with than without persistent sleep problems developed anxiety disorders by adulthood (46% and 33%, respectively). There was not a sig-
ificant relation between persistent childhood sleep problems and adult depression. It is important to
ote, this line of research does not speak to causal patterns. In fact, research has suggested a bi-
directional relation between sleep problems and anxiety (Ohayon & Roth, 2003). Although long-
itudinal research has linked sleep deprivation and the development of anxiety broadly, the role of sleep
depprivation in specific types of anxiety remains relatively understudied.

Panic spectrum problems constitute one specific type of anxiety-related psychopathology that may
be affected by sleep deprivation. Indeed, contempor-
ary work on sleep deprivation and panic devel-
lopment suggest at least two possible avenues by which sleep deprivation may potentiate panic deve-
lopment. First, sleep deprivation increases basal
levels of anxiety (Sagaspe, Sanchez-Ortuno, & Charles, 2006) and bodily arousal (Bonnet & Donna, 2006). The co-occurrence of these two factors (even in the absence of a panic attack) likely
results in conditioning of anxious responding to
bodily arousal. Second, elevations in basal anxiety
resulting from sleep deprivation likely potentiate
panic attacks, as such anxiety strongly predicts the
occurrence of a panic attack (Coplan et al., 1998; Eihlers et al., 1986). Sleep-deprived individuals may
be prone to experience panic-related fear along with bodily arousal, further increasing the condi-
tioning of fear and anxiety to bodily arousal. The
pairing of anxiety and fear with bodily arousal likely results in interoceptive cues becoming condi-
tioned stimuli that elicit subsequent anxiety and fear characterized by autonomic arousal, avoid-
ance, and cognitive misinterpretation of bodily arousal (i.e., catastrophic misinterpretation). These
conditioned responses to bodily arousal are of central importance to theories of the development of panic disorder (Barlow, 2002; Bouton, Mineka, & Barlow, 2001; Clark, 1986; Clark & Ehlers, 1993).

Despite the theoretical relevance of sleep depriva-
tion to panic phenomena, the relation between sleep
depression and panic has been the focus of limited
empirical investigation. This is particularly note-
worthy as sleep complaints are elevated among
persons with panic problems (Babson, Feldner, Sachs-Ericsson, Schmidt, & Zvolensky, 2008). As
many as 67% of those with panic disorder (PD) experience clinically significant sleep problems (Mell-
mann & Uhde, 1990) and 59% of persons with PD
without comorbid depression complain of problems sleeping (Overbeek, van Diest, Schruers, Kruizinga, & Griez, 2005). Similarly, 68% of persons with PD
report difficulties falling asleep and 77% report
disturbed and restless sleep (Sheehan, Ballenger, & Jacobson, 1980). Research in this area has primarily focused on the relation between PD and specific parameters of sleep architecture (e.g., durations of rapid eye movement and slow wave sleep; Lauer & Krieg, 1992; Mellman & Uhde, 1989; Stein, Enns, & Kryger, 1993). Generally, this research has suggested there are relatively few reliable differences in sleep
architecture between persons with and without panic
problems (Stein et al., 1993; Uhde, Roy-Byrne, & Gillin, 1984). Little investigation has focused on the
effects of sleep deprivation on panic-relevant respond-
ing. The only study in this domain (Roy-Byrne, Uhde, & Post, 1986) examined the effects of one night of
sleep deprivation on responding to a panic-relevant
biological challenge among 12 patients with PD, 10
patients with major depression, and 10 nonclinical
volunteers. During the night of sleep deprivation,
ratings of anxiety and depression were obtained via
patient self-report and nurse observation ratings.
Researchers then used the means of these ratings to
separate PD patients into two subgroups. Specifically, the “worsening group” showed an increase in mean
self-reported and nurse ratings of anxiety and depres-
sion compared to the control group. In contrast, “improvers” were individuals with PD that
demonstrated at least a 1-point decrease in self-
reported and nurse ratings of anxiety and depression throughout the night of sleep deprivation. Following
acute sleep deprivation, participants completed a 3-
minute voluntary hyperventilation challenge. The
well-established hyperventilation procedure was uti-
lized to index the effects of sleep deprivation on panic-
relevant responding (see Rapee, 1995; Zvolensky & Eifert, 2000). The worsening subgroup of participants
with PD (58%) experienced a significant increase in
overall (self and nurse-rated) anxiety levels compared
to the control group. Moreover, 25% of this PD
subgroup reported experiencing a panic attack
following sleep deprivation. These findings were
specific to this subgroup, as the anxiety ratings and panic attack frequency for the rest of the PD group were not different from that of controls. These initial data suggest that sleep deprivation may potentiate panic. Indeed, acute sleep deprivation (i.e., 36-hour deprivation period) appears to increase anxiety among healthy nonclinical participants (Sagaspe et al., 2006). Thus, given evidence suggesting relatively elevated basal levels of anxiety strongly predict greater anxious and fearful responding to bodily arousal elicited via panic-relevant biological challenges (Coplan et al., 1998; Ehlers et al., 1986; Liebowitz et al., 1984), it is likely that acute sleep deprivation will potentiate anxious and fearful responding to panic-relevant increases in bodily arousal.

The current study extended research focused on the panic-relevant effects of acute sleep deprivation in several novel and significant ways. First, although the study by Roy-Byrne and colleagues (1986) was a commendable first step in this research domain, it may have been insufficiently powered to detect effects of acute sleep deprivation on responding to biological challenge. Second, histories of psychopathology can confound results of laboratory-based studies examining the role of risk-related processes in psychopathology-relevant responding (Zvolensky, Lejuez, Stuart, & Curtin, 2001), and therefore participants were excluded on the basis of such histories in the current study. Third, the absence of a baseline assessment of response to biological challenge makes it difficult to interpret postmanipulation response patterns. Therefore, the current study extended the laboratory design to include a multimodal assessment of panic-relevant responding both pre- and post-sleep manipulation. Fourth, the absence of a no-sleep deprivation control condition did not allow for drawing conclusions regarding differences in anxious and fearful responding specific to the effects of acute sleep deprivation. For this reason, the current study included a no-sleep deprivation control group. Finally, the current study utilized the well-established CO₂ biological challenge procedure (see Rassovsky & Kushner, 2003), which elicits greater panic-relevant responding than the hyperventilation procedure (Rapee, Brown, Antony, & Barlow, 1992) and therefore likely increases variability in elicited anxiety and panic symptoms. There were several other advantages to using a 10% CO₂-enriched air biological challenge, including its ability to reliably produce abrupt increases in psychological and autonomic responses comparable to those that are central to learning theories of panic (Bouton et al., 2001) and the ability to safely (Prenoveau, Forsyth, Kelly, & Barrios, 2006) and carefully control its administration (i.e., onset, timing, dose, and duration) via an automated delivery system (see Lejuez, Forsyth, & Eifert, 1998, for a detailed description). Finally, anxious responding to CO₂-enriched air biological challenge procedures prospectively predicts panic onset among young adults (Schmidt & Zvolensky, 2007), suggesting that such responding may mark vulnerability to the development of panic disorder.

It was hypothesized that acute sleep deprivation, relative to no sleep deprivation, would increase baseline anticipatory anxious arousal (i.e., self-reported anxiety prior to the post-sleep deprivation CO₂ challenge). Furthermore, it was hypothesized that sleep deprivation, as compared to no sleep deprivation, would increase panic-relevant responding (i.e., greater self-reported anxiety and more intense panic symptoms) elicited by the CO₂ challenge procedure.

Method

Participants

One hundred and two (44 females) adults (\(M_{\text{age}} = 23.19\ \text{years}, SD = 8.2\)) were recruited via fliers and announcements within the University of Arkansas and the local Northwest Arkansas community. Of this original sample, 91 completed all portions of the protocol. Of this sample of 91, four were removed due to lost data. Overall, a final sample of 87 (36 female) adults (\(M_{\text{age}} = 23.41\ \text{years}, SD = 8.5\)) completed all portions of the experimental protocol and was utilized in all analyses. Participants lost to attrition did not differ from those retained in the study on any of the variables examined in the current study, including group assignment. Please see Table 1 for group demographic information.

Inclusion criteria included age of at least 18 years. Participants were excluded based on evidence of: (a) a lifetime history of Axis I psychopathology, including panic attacks or psychotropic medication use; (b) a lifetime history of a sleep disorder; (c) a history of significant medical illness, such as cardiovascular, endocrine, pulmonary (including asthma), and gastrointestinal illness; (d) limited mental competency and the inability to give informed, voluntary, written consent to participate; (e) pregnancy; and (f) suicidality. Participants reporting current Axis I psychopathology, sleep disorder, or suicidality were given referral information as legally and clinically indicated. Histories of Axis I diagnoses, past and present treatment history, and medication use were identified with the Structured Clinical Interview for DSM-IV-Non-Patient Version (First, Spitzer, Gibbon, & Williams, 1995). Medical screening was conducted using a structured medical screening interview used successfully in our prior biological challenge work (e.g., Feldner, Zvolensky, Eifert, & Spira, 2003; Feldner, Zvolensky, Stickle, Bonn-Miller, & Lean-
Table 1
Descriptive Data for Demographic Variables and Day 1 and Day 2 Responding as a Function of Group

<table>
<thead>
<tr>
<th>Group</th>
<th>Experimental M or n (SD or %)</th>
<th>Control M or n (SD or %)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>19 (43.2%)</td>
<td>17 (39.5%)</td>
</tr>
<tr>
<td>Age</td>
<td>21.75 (6.44)</td>
<td>25.11 (9.99)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>34 (77.3%)</td>
<td>33 (76.7%)</td>
</tr>
<tr>
<td>African-American</td>
<td>1 (2.3%)</td>
<td>1 (2.3%)</td>
</tr>
<tr>
<td>Asian</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (20.5%)</td>
<td>9 (20.9%)</td>
</tr>
<tr>
<td>Education Completed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>2 (4.5%)</td>
<td>3 (7%)</td>
</tr>
<tr>
<td>Two-year college</td>
<td>1 (2.3%)</td>
<td>1 (2.3%)</td>
</tr>
<tr>
<td>Partial four-year college</td>
<td>40 (90.9%)</td>
<td>34 (79.1%)</td>
</tr>
<tr>
<td>Four-year college</td>
<td>0 (0%)</td>
<td>2 (4.7%)</td>
</tr>
<tr>
<td>Partial graduate</td>
<td>0 (0%)</td>
<td>2 (4.7%)</td>
</tr>
<tr>
<td>Complete graduate</td>
<td>1 (2.3%)</td>
<td>1 (2.3%)</td>
</tr>
<tr>
<td>Smoking Status</td>
<td>7 (15.9%)</td>
<td>11 (24.4%)</td>
</tr>
<tr>
<td><strong>Manipulation Checks</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep between day 1 and day 2</td>
<td>0.14 (0.78)</td>
<td>7.74 (1.1)*</td>
</tr>
<tr>
<td>Change in stimulant use</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nicotine use</td>
<td>1.1 (2.64)</td>
<td>0.86 (2.74)</td>
</tr>
<tr>
<td><strong>Day 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline SUDS</td>
<td>0.77 (1.30)</td>
<td>0.74 (1.65)</td>
</tr>
<tr>
<td>Post-challenge SUDS</td>
<td>2.04 (1.77)</td>
<td>2.09 (2.30)</td>
</tr>
<tr>
<td>Panic Attack Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td>1.52 (1.54)</td>
<td>1.25 (1.32)</td>
</tr>
<tr>
<td>Physical</td>
<td>2.96 (1.93)</td>
<td>2.76 (1.92)</td>
</tr>
<tr>
<td><strong>Day 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline SUDS</td>
<td>1.18 (1.87)</td>
<td>.44 (1.31)*</td>
</tr>
<tr>
<td>Post-challenge SUDS</td>
<td>2.93 (2.12)</td>
<td>1.74 (1.94)*</td>
</tr>
<tr>
<td>Panic Attack Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td>2.05 (1.94)</td>
<td>1.01 (1.30)*</td>
</tr>
<tr>
<td>Physical</td>
<td>3.27 (2.02)</td>
<td>2.38 (1.63)*</td>
</tr>
</tbody>
</table>

Note: N=87; n for gender reflects women and for smoking status reflects smokers; SUDS=Subjective Units of Distress Scale (Wolpe, 1958); sleep between day 1 and day 2 measured in hours; nicotine use measured via cigarettes smoked.
* = significant difference between group means.

Feldner, 2006) to identify current and/or past history of chronic physical health conditions. Thirteen individuals responding to recruitment efforts were excluded due to positive histories of a medical condition, 14 were excluded due to current sleep problems, including the use of prescription sleep medications, and 54 individuals were excluded on the basis of other exclusionary criteria.

**MEASURES**

Structured Clinical Interview for DSM-IV-Non-Patient Version (SCID-IV). Lifetime and current axis I psychopathology and psychotropic medica-
.83 to .90 and .85 to .93, respectively). A large body of literature supports the validity of the PANAS (see Watson, 2000). In the current study, the negative affect subscale, which evidenced good internal consistency (alpha = .75), was utilized to compare groups on baseline negative affectivity.

Sleep Anticipatory Anxiety Questionnaire (SAAQ). The SAAQ (Kuo, Racioppo, Bootzin, & Shoham, 1994) is a 10-item questionnaire on which respondents indicate their anxiety about sleep on a 4-point Likert-type scale (1 = strongly disagree to 4 = strongly agree). Example questions include: “My muscles are tense,” “My heart is beating rapidly,” and “I worry I will not be able to sleep” (Bootzin, Shoham, & Kuo, 1994). Two scores are obtained in the administration of the SAAQ: a total score measuring overall anxiety about sleep and a subscore measuring self-reports of cognitive and physical arousal while trying to fall asleep at night. The SAAQ has demonstrated adequate internal consistency (Cronbach’s alpha = .83 in a student sample and .85 for individuals with sleep problems; Bootzin et al., 1994). In line with these data, within the current study good internal consistency was demonstrated (alpha = .86). Moreover, scores on the SAAQ are negatively correlated with self-efficacy about sleep (Kuo et al., 1994), and it reliably differentiates between those with and without sleep problems (Bootzin et al., 1994). The SAAQ was used in the current study to compare groups in terms of sleep anticipatory anxiety as a check on random assignment.

Subjective Units of Distress Scale (SUDS). The SUDS (Wolpe, 1958) was used to measure self-reported anxiety elicited by the CO2 challenge. Ratings were made on an 8-point Likert-type scale (0 = no anxiety to 8 = extreme anxiety). This measure is well-established in biological challenge studies (e.g., Forsyth, Eifert, & Canna, 2000; Karekla, Forsyth, & Kelly, 2004; Kelly, Forsyth, & Karekla, 2006; Rapee et al., 1992; Schmidt & Zvolensky, 2007).

Diagnostic Symptom Questionnaire (DSQ). The DSQ (Sanderson, Rapee, & Barlow, 1988, 1989) is a common measure used in challenge experiments (Zinbarg, Brown, Barlow, & Rapee, 2001; Zvolensky, Lejuez, & Eifert, 1998) to index panic attack symptoms elicited by a biological challenge procedure. Participants rate each of 13 panic symptoms on a 9-point Likert-type scale (0 = not at all to 8 = very strongly felt). Although the DSQ was developed based on the DSM-III-R (APA, 1987) diagnostic criteria for panic attacks, these criteria have not been substantially altered for DSM-IV. Consistent with past biological challenge studies (Feldner, Vujanovic, Gibson, & Zvolensky, 2008; Forsyth et al., 2000; Schmidt, Forsyth, Santiago, & Trajkowski, 2002; Zvolensky, Feldner, Leen-Feldner, & McLeish, 2005), two composite scores were created which indexed the intensity of cognitive (e.g., fear of going crazy) and physical (e.g., breathlessness or smothering sensations) panic symptoms elicited by the challenge. The DSQ demonstrated good internal consistency within the current sample for both the cognitive (alpha = .82) and physical (alpha = .93) symptom scales.

Physiologic Stimulus and Gas Delivery

A physiologic stimulus of 10% CO2-enriched air (10% CO2, 21% O2, 69% N2) was used. Participants were equipped with a continuous positive pressure Downs C-Pap Mask (Vital Signs Inc., Model No. 9000). For a comprehensive description of the automated apparatus, see Lejuez and colleagues (1998). Consistent with prior research (Feldner et al., 2006), participants were administered a single 5-min CO2 presentation.

Apparatus

Laboratory procedures were conducted in a 12-by-14-foot experimental room in the Intervention Sciences Laboratory, housed in the Department of Psychology at the University of Arkansas. This room contained a chair, desk, and computer. A two-way mirror, intercom system, and surveillance video allowed for continuous monitoring and communication between the participant and the experimenter located in an adjacent room. The experimenter room contained a 40-cylinder CO2 tank filled with 10% CO2 compressed air and a J &J Engineering recording device transferring information onto a personal computer.

Procedure

Participants were recruited from the Northwest Arkansas community, including from the University of Arkansas. Announcements were made in psychology classes and via flyers announcing the study placed at various locations in the community (e.g., local market place, community bulletin boards). Interested participants contacted the Intervention Sciences Laboratory, at which time the SDQ and the screening portion of the SCID were administered to initially assess exclusion criteria. Potentially eligible participants were then invited to attend a laboratory-based individual baseline assessment session (Day 1). At this session, participants provided written informed consent and were told that the purpose of the study was to investigate the effect of sleep on different health behaviors. All participants were aware there were two conditions in the
experiment, a sleep deprivation and sleep-as-normal group. Importantly, the informed consent procedures described possible effects of acute sleep deprivation (e.g., irritability, difficulty concentrating) but did not include a description of the possible effects of sleep deprivation on anxiety. Participants also were informed about the likely effects of the CO\(_2\) procedure (e.g., trouble breathing, sweating, feeling lightheaded). They were further informed that these bodily effects are harmless and painless and that they disappear quickly after returning to normal breathing. Upon provision of informed consent, the SDQ, SCID, and medical screening interview were administered to further evaluate exclusion criteria. Participants not eligible for participation at this stage were compensated $10 and thanked for their participation. Eligible participants then completed a battery of self-report measures and the baseline biological challenge procedure (Day 1 CO\(_2\) challenge; please see below for procedural details).

After initial screening, informed consent procedures, questionnaire packets, and the biological challenge were completed, participants were randomly assigned to either the acute sleep deprivation (experimental) or no sleep deprivation (control) group. Participants were asked to choose a day and time when losing sleep for an entire night would not interfere in their daily life and when they could attend the second laboratory session the morning after the night of acute sleep deprivation. Those assigned to the control group were instructed to sleep as normal and those in the experimental group were instructed to stay awake through the night. All participants were instructed to not change drug use patterns, including alcohol and cigarette use patterns, relative to normal routines. In an effort to control for possible differences in drug-related withdrawal symptoms, they were not instructed to completely refrain from typical substance use (e.g., smoking) patterns. Participants assigned to the experimental group consented to not drive to the laboratory for their second appointment to protect participants against impaired driving that may result from acute sleep deprivation. Within the sleep deprivation condition, a phone-in digital sleep diary procedure was implemented in order to monitor sleep loss. Specifically, participants were instructed to call the laboratory every hour (calls were digitally time stamped to check participant compliance) between 10:00 P.M. and 8:00 A.M. as a manipulation check.

Upon completion of the randomization procedures and explanation of the instructions for the night, participants scheduled their Day 2 appointment for the next day, and were compensated $20 for completion of Day 1. All participants completed Day 1 between 12:00 P.M. and 5:00 P.M. All participants then returned to the laboratory to complete Day 2 of the protocol the next day between 6:00 A.M. and 10:00 A.M. The 1-hour Day 2 session included a brief semi-structured interview administered to assess the prior night’s sleep level as well as substance use levels (i.e., cigarettes, caffeine, stimulants) during the prior night. Participants who reported changing use of these substances relative to typical use patterns and those who did not follow the protocol for acute sleep deprivation or a full night sleep, were given the option of either (1) refraining from sleep on a separate night and again returning to the laboratory to complete the biological challenge procedure or (2) discontinuing participation in the study and receiving an additional $10 compensation. Participants who followed the experimental directions completed a brief questionnaire packet and the second challenge procedure. Then, participants were debriefed and compensated an additional $60 for completion of Day 2.

Biological challenge procedures. During both laboratory challenges (Day 1 and Day 2), individual participants sat in front of a computer in the experimental room. The researcher then fitted the participant with a C-PAP mask. At this point, the researcher left the room and began the procedure. Participants sat alone in the experimental room. The researcher observed the participant via a two-way mirror, a video surveillance system, and a bi-directional intercom. Participants first completed a 10-minute baseline period (baseline), which was immediately followed by a 5-minute 10% CO\(_2\)-enriched air administration. The SUDS was administered via automated computer delivery at the beginning of the baseline period and immediately after the challenge procedure (post-challenge period). Upon completion of the CO\(_2\) administration, the DSQ was administered via automated computer delivery to measure panic attack symptoms experienced during the challenge. After the challenge was completed, the researcher entered the room and removed the mask.

Results

MANIPULATION CHECKS

Random assignment. To check the efficacy of random assignment, differences between groups on key baseline characteristics were examined. Groups (experimental, control) were compared in terms of dichotomous variables (i.e., gender and smoking status) using chi-square analyses. Continuous variables (i.e., negative affect, nonclinical sleep problem levels, and sleep anticipatory anxiety) were
examined using independent samples $t$-tests. Analyses suggested no pre-experimental group differences (all $p$’s > .1). Please see Table 1 for means and standard deviations for each of these baseline measures.

**CO$_2$ challenge.** To examine the efficacy of the CO$_2$ procedure, paired samples $t$-tests were utilized to examine changes in self-reported anxiety (collapsed across group) for both days 1 and 2. Mean levels of SUDS were compared between the baseline and postchallenge periods. Analyses suggested that the CO$_2$ challenge elicited anxiety during both days 1 and 2 [Day 1: $t(86) = 5.54$, $p < .001$; Day 2: $t(86) = 7.17$, $p < .01$].

**Sleep manipulation.** In addition to the methodological checks in place to ensure the efficacy of the experimental acute sleep manipulation (e.g., hourly phone calls made during the night by the sleep deprivation group), participants’ adherence to the experimental instructions (sleep pattern and substance use) was examined using independent samples $t$-tests that compared groups in terms of self-reported hours of sleep, number of cigarettes smoked, and caffeinated beverages consumed the 24 hours prior to the Day 2 laboratory appointment. Results suggested participants followed the experimental directions. Participants in the sleep deprivation group reported greater sleep loss compared to those in the control group, $t(84) = 36.3$, $p < .001$ (see Table 1). Furthermore, all participants in the sleep deprivation group completed the phone-in digital sleep diary every hour during the night of sleep loss. Participants in both the sleep deprivation and control groups reported no change in stimulant use patterns and both groups used comparable amounts of nicotine during the night. There were no significant differences between groups in substance use levels (all $p$’s > .1).

**Primary Hypothesis Tests**

**Self-reported anxiety.** To test the effect of sleep deprivation on anxious responding to the biological challenge procedure, a repeated measures analysis of variance (ANOVA) was conducted. Within-subject variables included day (Day 1, Day 2) and measurement point (baseline and postchallenge SUDS ratings) and the between-group variable was group (sleep deprivation versus control). In the case of significant interactions, simple effects $t$-tests were conducted to analyze the interaction. A Bonferroni correction was employed to control for multiple comparisons yielding a corrected alpha level of .025 for simple effects tests. Effect size was indexed via eta squared ($\eta^2$).

Results suggested no main effect of day. However, there was a main effect of group [$f(1, 85) = 7.79$, $p < .01$; $\eta^2 = .08$] and measurement point [$f(1, 85) = 9.06$, $p < .01$; $\eta^2 = .09$]. A significant interaction between day and group also emerged [$f(1, 85) = 11.04$, $p < .01$; $\eta^2 = .12$]. Simple effects tests suggested there was no difference in SUDS ratings (collapsed across pre- and postchallenge ratings) between groups on Day 1 [$t(85) = .54$, $ns$]. However, there was a significant difference in SUDS ratings between groups on Day 2 [$t(85) = 4.32$, $p < .01$]. Specifically, the sleep deprivation group reported significantly higher anxiety compared to the control group (please see Table 1 for means).

**Panic attack symptoms.** In terms of panic attack symptoms elicited by the CO$_2$ challenge, two separate repeated measures ANOVAs were conducted to test the effects of sleep deprivation on physical and cognitive symptoms of panic. Specifically, the within-subjects variable was day (Day 1, Day 2) and the between-group variable was group (sleep deprivation versus control). A Bonferroni correction was again employed to control for multiple comparisons, yielding a corrected alpha level of .025 for simple effects $t$-tests. Effect size was indexed via eta squared ($\eta^2$).

In terms of physical panic symptoms, there was no main effect of group or day. However, there was a significant interaction between day and group [$f(1, 85) = 4.43$, $p < .05$; $\eta^2 = .05$]. Simple effects tests indicated there were no group differences in physical panic symptoms on Day 1; however, group differences emerged on Day 2 [$t(85) = 2.25$, $p < .02$]. Specifically, the sleep deprivation group experienced more physical panic symptoms than the control group on Day 2 (see Table 1 for group means). In terms of cognitive panic symptoms, a main effect of group was evidenced [$f(1, 85) = 6.50$, $p < .05$; $\eta^2 = .07$] such that the sleep deprivation group reported more intense cognitive panic attack symptoms in response to the challenge procedure than the control group (see Table 1).

**Discussion**

A burgeoning literature documenting that sleep problems occurring during childhood are related to elevated anxiety in adulthood (Gregory & O’Connor, 2002; Gregory et al., 2004; Gregory et al.,...
toward an interaction between group and day as a result of sleep deprivation. Although the means (see symptom intensity increased among this group as a result of sleep deprivation, despite a well-established association between panic and sleep problems. Indeed, only one study has been conducted in this domain (Roy-Byrne et al., 1986), which generally suggested sleep loss may potentiate panic attacks. Although this study was a commendable first step in the area, several limitations (e.g., small sample size, lack of pre- and post-challenge assessments) limited conclusions that could be drawn. The current study uniquely extended this work (e.g., greater methodological power, pre- and post-sleep manipulation assessments, inclusion of a no-sleep deprivation control group, more strict inclusion criteria) to an experimental examination of the role of acute sleep deprivation in responding to a laboratory-based panic-relevant biological challenge. Nonclinical participants were randomly assigned to an acute sleep deprivation or normal night sleep condition and completed a 2-day laboratory-based protocol that included repeated 5-min 10% CO

2-enriched air administrations. Consistent with hypotheses, acute sleep deprivation increased baseline anxiety and self-reported anxious and fearful responding to the challenge procedure.

Results suggested acute sleep deprivation increased various aspects of panic-relevant anxious reactivity. First, a significant interaction between group and day in terms of SUDS ratings suggested that despite a lack of differences in anxious responding to the challenge on Day 1, the acute sleep deprivation group reported greater anxiety both before and after the Day 2 challenge procedure than the control group. These data support the hypothesis that acute sleep deprivation increased baseline anxiety prior to the Day 2 CO

2 challenge. Acute sleep deprivation also increased the reported intensity of panic symptoms elicited by the challenge. Despite a lack of differences between groups in response to the Day 1 challenge, participants in the sleep deprivation condition endorsed greater intensity of physical panic symptoms in response to the Day 2 challenge. In combination with the SUDS results, these findings suggest that acute sleep deprivation increased panic-relevant anxious and fearful responding to the challenge procedures. In contrast to expectation, although cognitive panic symptoms were higher overall in the sleep deprivation group, there was not evidence that cognitive symptom intensity increased among this group as a result of sleep deprivation. Although the means (see Table 1) and a statistically nonsignificant trend toward an interaction between group and day ($p = .07$) were in the expected direction, it did not appear that cognitive panic symptoms (e.g., fear of going crazy, fear of losing control) were affected by the sleep manipulation. Given the healthy sample and consent procedures that informed participants that the effects of the CO

2 challenge are safe and short-lived, it is likely the magnitude of the effect of sleep deprivation on these symptoms was too small to be observed in this study. Nonetheless, these findings generally suggest that acute sleep deprivation increases anticipatory anxiety about abrupt increases in bodily arousal and it increases panic-relevant responding to such arousal. It is important to note that the size of the effects was relatively small ($\eta^2 = .05$ to .12), which may be due, in part, to the conservative nature of the design (e.g., psychologically and physically healthy sample, controlled environment). Given this conservative test of the hypotheses, it is likely these small effects are nonetheless meaningful (Abelson, 1985), demonstrating that, even in a carefully controlled setting, acute sleep deprivation has panic-relevant effects on healthy individuals. Importantly, this is a first step, and future prospective naturalistic research with participants suffering from panic attacks will ultimately be needed to directly test the role of more chronic sleep deprivation in panic development. Moreover, given linkages between elevated anxiety sensitivity (i.e., fear of the consequences of anxiety) and sleep problems (Babson, Trainor, Bunaciu, & Feldner, 2008), extending this work to participants at risk for panic and anxious reactivity to the effects of sleep deprivation would likely amplify the effects of acute sleep deprivation and increase generalizability to models of the development of panic.

Acute sleep deprivation appears to increase anxious and fearful responding to abrupt increases in bodily arousal, which is positively related to panic onset (Schmidt & Zvolensky, 2007). These results may have implications, albeit tentative at this early stage of research, for models of panic development. Scholars in this area have suggested that panic attacks among persons with PD are elicited by conditioned responses to bodily arousal characterized by autonomic arousal, avoidance, and catastrophic misinterpretation of bodily arousal (Barlow, 2002; Bouton et al., 2001; Clark, 1986; Clark & Ehlers, 1993). The current findings suggest acute periods of sleep deprivation increase the risk for anxious and fearful responding to bodily arousal, perhaps by increasing anxiety and activating interpretive biases leading to catastrophic misinterpretation of bodily arousal. Thus, after acute sleep deprivation, abrupt increases in bodily arousal, which can be elicited by various activities (e.g., drug use,
vigorous exercise), may be particularly likely to be paired with anxiety and fear because sleep-deprived individuals are at increased risk for fearfully responding to such arousal. Therefore, acute sleep deprivation may “set the stage” for fear-based conditioning of interoceptive arousal. Importantly, as this is a first step in this domain, this theoretically based speculation requires additional empirical examination in order to draw etiological conclusions. For instance, this model would predict that an individual’s first panic attack is more likely to occur subsequent to sleep deprivation than after a normal night of sleep. Similarly, future research could beneficially extend this work to examination of psychobiological mechanisms (e.g., learning-based mechanisms, catastrophic misinterpretation of bodily arousal, hypersensitivity of neuroanatomical fear circuitry) implicated in panic development. For example, the underlying mechanisms of action discussed in contemporary neuroanatomical accounts of panic (Gorman, Kent, Sullivan, & Coplan, 2000) could be tested as mediators of the acute sleep deprivation–panic-relevant reactivity association. The specificity (or lack thereof) of the influence of sleep deprivation on panic as opposed to other specific anxiety disorders also warrants additional investigation. For example, given well-established associations between posttraumatic stress disorder and sleep deprivation (Spoormaker & Montgomery, 2008), it is possible that acute sleep deprivation amplifies anxious reactivity among persons suffering from this disorder as well.

Interpretation of the current findings requires consideration of a number of limitations. First, this study employed a nonclinical, healthy sample consisting mainly of Caucasian, well-educated, young adults. Although aspects of this approach were important for the (prioritized) internal validity of the study (e.g., screening for histories of psychopathology), our ability to generalize these results to a more heterogeneous population is constrained. For instance, it is possible that the effects of sleep deprivation vary with age as sleep patterns typically vary across the lifespan (Ohayon, Carskadon, & Guilleminault, 2004). Future research would benefit from utilization of a more heterogeneous sample. Furthermore, this constrained variance may have restricted the range of reactivity to the challenge procedure, suppressing effect sizes. Our focus on internal validity, which reduced the external validity of these findings, is reasonable at this early stage of research (Mook, 1983), yet future research would benefit from including more diverse populations that would increase generalizability and variability in responding to the challenge. Second, the laboratory paradigm utilized elicits bodily arousal relevant to panic, which is helpful for examining risk processes (Schmidt & Zvolensky, 2007; Zvolensky et al., 2001). However, this paradigm does not allow for studying naturalistic panic attacks (e.g., those experienced as uncued) or naturally occurring sleep deprivation. Therefore, it will be important to extend this research to the naturalistic examination of these factors. For instance, future research could usefully employ repeated measures of anxiety throughout a naturalistic period of sleep deprivation (among persons with chronic sleep problems, for example). This type of design would allow for drawing conclusions about the pattern of anxiety development during sleep deprivation and may shed light on threshold-type issues, such as the degree of sleep deprivation necessary to potentiate panic responding. Similarly, it remains unclear how the panic-related effects of acute sleep deprivation relate to possible panic-related effects of chronic sleep deprivation. Although the current study offered a novel opportunity to experimentally test the effects of acute sleep deprivation in terms of responding to abrupt increases in bodily arousal elicited in the controlled environment of the laboratory, these conclusions cannot be extended to inferences regarding the role of chronic sleep deprivation in panic development. For this reason, future prospective studies would benefit from examining the relation between chronic sleep deprivation and the development of anxious and fearful responding to bodily arousal. Future research also could beneficially integrate a more detailed (laboratory-based) assessment of sleep parameters to better understand how specific sleep parameters relate to biological challenge responding. For instance, it is possible that reductions in slow wave sleep, in particular, increased anxious and panic-relevant responding. Indeed, extant research suggests slow wave sleep is particularly strongly related to anxiety (Arriaga et al., 1996). Examining continuous indices of this type of sleep parameter would allow for more refined conclusions regarding the mechanism(s) of sleep deprivation that increase anxiety and panic intensity in this paradigm. Relatedly, the current study did not include direct observation of sleep patterns, leaving open the possibility that participants in the sleep deprivation condition were not as deprived of sleep as they reported. Importantly, reliance on self-report is consistent with prior research on the effects of sleep deprivation (e.g., Thatcher, 2008) and the digital sleep diary procedure utilized herein helped to ensure the validity of the sleep manipulation by precluding last-minute completion of a paper-and-pencil diary, a type of “faked compliance” observed in studies using self-monitoring diaries (Litt, Cooney, & Morse, 1998).
Nonetheless, this study would have benefited from direct observation of sleep in both conditions, which would further ensure the internal validity of this type of design. Similarly, we were unable to directly observe substance use patterns throughout the night of sleep loss. The structured clinical interview administered on Day 2 to assess substance use during the previous night is a first step in controlling for the effects of substance use patterns. However, future work would benefit from inclusion of direct observation of substance use patterns throughout a night of sleep loss. Furthermore, participants may have been aware of the primary aims of the current study, which may have affected self-reported responding. Although the current study uniquely added a pre/post-sleep deprivation assessment and control group to this area of research and therefore improved upon previous designs, future research nonetheless needs to control for the possible role of experimental demand characteristics. Finally, although persons lost to attrition in the current study did not appear to differ from those retained, decreasing the attrition rate would lead to greater generalizability of the current results (i.e., decrease the potential role of self-selection biases).

References


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