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Premenstrual Distress Predicts Panic-Relevant Responding to a CO₂ Challenge Among Young Adult Females

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Abstract

The current study examined the incremental validity of self-reported premenstrual distress in predicting panic responsivity (self-reported panic symptoms and skin conductance response frequency; SCR) following inhalation of 10% CO₂-enriched air. A community sample of young adult women ($n = 46$) completed questionnaires assessing substance use patterns, premenstrual symptoms and distress, and anxiety sensitivity and underwent a laboratory biological challenge procedure (4-min 10% CO₂-enriched air inhalation). As hypothesized, higher premenstrual distress scores significantly predicted greater self-reported panic symptoms following the CO₂ challenge above and beyond other theoretically relevant variables (anxiety sensitivity, cigarette use, and alcohol consumption). In predicting SCR, premenstrual distress exhibited only a trend towards statistical significance. These findings provide preliminary evidence that premenstrual symptoms may serve as a potential risk factor to experience more intense panic symptoms in response to perturbations in bodily sensations.

Keywords

premenstrual distress; CO₂ challenge; panic

1. Introduction

Panic Disorder (PD) occurs at a 2:1 female-to-male ratio in the general population (Dick, Bland, & Newman, 1994). The distress and symptoms experienced during the premenstrual phase have been associated with PD and Anxiety Sensitivity (AS; fear of anxiety and anxious arousal symptoms; Bernstein & Zvolensky, 2007; McNally, 2002) in women. AS, or the tendency to respond fearfully to anxiety symptoms, is a cognitive risk factor for the development of PD (Donnell & McNally, 1989; Maller & Reiss, 1992; McNally & Lorenz, 1987). Additionally, women high on AS or who have PD report more severe premenstrual symptoms on the Menstrual Distress Questionnaire (MDQ; Moos, 1968) than women low on AS or women without PD when asked retrospectively to report on their general premenstrual distress and when asked prospectively to report on their current premenstrual phase (Sigmon, Fink, Rohan,

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& Hotovy, 1996; Sigmon, Dorhofer, Rohan, & Boulard, 2000a; Sigmon, Dorhofer, Rohan, Hotovy, Boulard, & Fink, 2000b; Sigmon, Rohan, Boulard, Dorhofer, & Whitcomb, 2000c). These data suggests that women at risk for fearful responding to anxiety symptoms (high AS) experience and/or interpret their premenstrual symptoms differently from women at lower risk for fearful responding to anxiety symptoms (low AS), which indicates a potential shared vulnerability and/or mechanism between premenstrual symptoms and cognitive vulnerability to PD and anxiety. Previous researches have hypothesized similar connections between these variables. Specifically, that women high on AS have repeated, cyclical opportunities to potentially misinterpret bodily sensations that occur in the premenstrual phase, which could result in an expectation of more severe premenstrual symptoms and, therefore, greater premenstrual symptom reporting, particularly retrospectively (Sigmon et al., 2000b). These data indirectly suggest a possible linkage between the premenstrual distress and vulnerability for panic psychopathology.

To our knowledge, no previous research has examined the effect of premenstrual distress and symptoms on panic response and there is only limited research on the association between anxiety vulnerability (high AS) and premenstrual symptoms and distress. Therefore, we review the existing literature on the role of menstrual cycle phase on panic response in order to demonstrate our theoretical rationale for examining premenstrual distress on panic response.

Research addressing the association between menstrual cycle phase and panic attacks and anxiety symptoms has been mixed. One study examining symptom history of individuals with agoraphobia and unexpected panic attacks revealed that 51% of women reported experiencing increased anxiety symptoms and 33% reported increased frequency of panic attacks premenstrually (Breier, Charney, & Heninger, 1986). A prospective study of women with PD across two menstrual cycles revealed an exacerbation of anxiety symptoms and increased panic attacks during the premenstrual phase (Kaspi, Otto, Pollack, Eppinger, & Rosenbaum, 1994). However, another prospective study did not find any menstrual cycle phase differences in anxiety ratings and panic attack frequency among women with PD or in controls (Stein, Schmidt, Rubirow, & Uhde, 1989). The Breier and colleagues (1986) findings were based solely on participant's retrospective report of the relationship between panic attacks and anxiety and their menstrual cycle phase. A direct comparison of retrospective and prospective reports among the same women found no significant relationship between the prospective and retrospective reports (Stein et al., 1989), while Kaspi and colleagues (1994) found that women prospectively reported more panic attack frequency than initially reported retrospectively, suggesting that women may actually under-report premenstrual panic symptoms retrospectively. Further analysis of this finding revealed that women who demonstrated the most consistent report between panic symptoms retrospectively and prospectively also reported more depressed mood premenstrually (Kaspi et al., 1994). It is unclear why the two prospective studies described above (Kaspi et al., 1994; Stein et al., 1989) differed in their findings. Women tend to over-report premenstrual symptoms in retrospective versus prospective questionnaires (Marvan & Cortes-Iniestra, 2001), and future research would benefit from prospectively examining premenstrual symptom distress.

Other work has documented that premenstrual phase and level of AS interact to predict psychophysiological reactivity to an external stressor (Sigmon et al., 1996). Specifically, women higher on AS measured in their premenstrual phase displayed greater skin conductance response frequency and magnitude, but not differences in self-reported anxiety and mood, in response to listening to anxiety-relevant scenes (e.g., *"You are sitting down to relax after a hectic day. Suddenly, you can't breathe, your chest feels tight, and you think, this is it, I am going to die."*) in comparison to women higher on AS assessed in the intermenstrual phase and women lower on AS assessed in either cycle phase, above and beyond baseline level of state

anxiety or panic history (Sigmon et al., 1996). These findings were replicated in a comparison of women with PD vs. nonanxious controls (Sigmon et al., 2000b).

One study examined menstrual cycle phase differences in response to inhalation of CO₂-enriched air— a laboratory physical challenge paradigm used to elicit anxious arousal (Perna, Brambilla, Arancio, & Bellodi, 1995). Specifically, women with PD rated significantly greater anxiety and panic symptoms in response to taking one breath of 35% CO₂-enriched air during the menstrual phase as compared to the midluteal phase (Perna et al., 1995). Premenstrual Dysphoric Disorder (PMDD) is an extreme variant along the continuum of premenstrual symptoms, requiring the presence of 5 or more psychological (e.g., anxiety) and physical symptoms (e.g., headache), which occur regularly during the last week of the luteal phase; diminish with the onset of menses; and are absent the week following menses; and significantly impairs interpersonal relationships, school or work functioning, or other activities (APA, 2000; Halbreich, Borenstein, Pearlstein, & Kahn, 2003). A greater proportion of women with PMDD, who had no other anxiety disorder diagnosis, experience a panic attack during a 20-minute 5% CO₂ challenge and a single breath 35% CO₂ challenge as compared to controls (Harrison et al., 1989; Kent et al., 2001), regardless of cycle phase (Vickers & McNally, 2004), and display similar rates of CO₂ challenge-induced panic attacks as PD patients (Gorman et al., 2001; Kent et al., 2001). These studies collectively suggest that menstrual cycle phase may play an important role in the experience of anxiety and panic among women already at high risk for anxiety. Given that assessment of PMDD requires two months of prospective tracking of symptoms, and because the original study was not designed to assess PMDD, these data were not collected in the current study. No study has examined premenstrual distress in the prediction of panic-relevant self-reported and psychophysiological symptoms following direct exposure to perturbation in bodily sensations.

Research on the role of anxiety vulnerability and symptoms on premenstrual symptoms and distress is limited. There are several competing theories regarding premenstrual symptom reporting. The body sensations hypothesis posits that women accurately report bodily changes during their premenstrual phase (Klebanov & Jemmet, 1992). The expectations hypothesis proposes that women are impacted by cultural beliefs and stereotypes, which influence them to over-report premenstrual symptoms (Klebanov & Jemmet, 1992). A third hypothesis, the menstrual reactivity hypothesis, combines and applies the previous hypotheses to high AS women, specifically. It posits that high AS women are hypervigilant to physical sensations they experience during their menstrual cycle and, consequently, develop a negative expectation bias about these bodily sensations that affects their symptom reports (Sigmon, Whitcomb-Smith, Rohan, and Kendrew, 2004). Women high on AS or who have PD report more severe premenstrual symptoms on the MDQ than women low on AS or women without PD when asked retrospectively to report on their general premenstrual distress and prospectively to report on their current premenstrual phase (Sigmon, Dorhofer, Rohan, & Boulard, 2000a; Sigmon et al., 2000b; Sigmon et al., 1996; Sigmon et al., 2000c). These data suggest that women high in AS or with panic psychopathology may endorse greater premenstrual symptoms. Therefore, in order to understand whether premenstrual distress indeed predicts anxious responding to bodily sensations, premenstrual distress must demonstrate a unique (incremental) effect above and beyond AS.

The prevalence of PD is two times higher in females relative to males (Dick et al., 1994). Additionally, there is a prominent gender difference in AS, whereby women score higher than men on measures of AS (Reiss & McNally, 1985; Schmidt & Koselka, 2000; Stewart, Taylor, & Baker, 1997), an identified cognitive risk factor for panic pathology (Schmidt et al., 2006). Furthermore, reactivity to a 20-second 20% CO₂ challenge also predicts panic vulnerability (Schmidt & Zvolensky, 2007) particularly among women (Kelly, Forsyth, & Karekla, 2006). However, research attempting to explicate this gender difference is limited. Given the small

body of research, which reports a strong relationship between premenstrual symptoms and AS level, experience of symptoms in the premenstrual phase may be an important factor in understanding this gender difference. The current study attempts to understand whether the experience of premenstrual symptoms represents an additional risk to panic vulnerability above and beyond already established risk factors for panic pathology (e.g., AS). Specifically, the present investigation was designed to test the incremental validity of retrospectively reported premenstrual distress, above and beyond other theoretically relevant variables, in predicting panic symptoms and psychophysiological reactivity following administration of 10% CO₂-enriched air among young adult females. The concentration and duration of CO₂ challenge procedures have varied in the literature. CO₂ inhalation procedures range in concentration (5%-35%) and duration (one breath to 20 min). Higher concentrations of CO₂ (35%), typically administered in one breath, produce a sudden and acute response, whereas a lower concentration (2-9%) over a longer duration produces gradual, but increasing arousal (Zvolensky & Eifert, 2000). The current study employed 4-minutes of 10% CO₂-enriched air, which has been used successfully in previous research (Feldner, Zvolensky, & Schmidt, 2004). It was hypothesized that women who reported higher premenstrual distress would report greater panic symptoms and exhibit greater skin conductance response frequency (SCR) following the challenge. These predictions were derived from models of panic psychopathology etiology (Barlow, 2002) and empirical data (Stewart & Pihl, 1994), which suggest that SCR may be related to panic vulnerability. It was expected that these effects would be apparent above and beyond the variance explained by three variables that are known to affect panic and anxious responding to the physical challenge: AS, current average number of cigarettes smoked per day, and level of current alcohol consumption (average frequency-by-quantity per occasion composite score; Zvolensky, Bernstein, Marshall, & Feldner, 2006).

2. Method

2.1. Participants

A community sample of 46 women ($M = 21.2$ year of age, $SD = 6.0$) was recruited via announcements in university classes, flyers placed throughout the greater Burlington, VT community, and advertisements in local newspapers for a study on emotion. The current data are part of a larger study focused on emotional vulnerability among young adults (Bernstein, Zvolensky, Vujanovic, & Moos, 2009), whose main purpose did not include analysis of premenstrual distress or menstrual cycle phase. Therefore, information regarding current menstrual cycle phase was not obtained in the current study, and women in this study were not selected based on currently experiencing premenstrual distress. These data have not been reported previously, and therefore, are a novel contribution. This sample was predominantly white (91%) and exhibited a high percentage of smokers (70%), although the original study did not recruit specifically for smokers. Table 1 summarizes participant demographics. Exclusionary criteria for the current study included: (1) limited mental competency or inability to provide informed, written consent; (2) current suicidal or homicidal ideation; (3) current or past history of psychosis; (4) current (past 6-month) Axis I psychopathology (except for substance use disorders); (5) current major medical problems (e.g., heart disease, cancer); (6) current substance dependence (other than nicotine); and (7) self-reported pregnancy. Participants with a lifetime diagnoses of Axis-I psychopathology were not excluded with the exception of psychosis. These exclusionary criteria ensured the safety of participants during the biological challenge and ruled out alternative explanations related to any observed effects (e.g., effects being due to psychopathology rather than the studied variables). Inclusion criteria included: 1) being female and 2) completed the MDQ.

2.2. Measures

2.2.1. Pre-Challenge Measures—The *Structured Clinical Interview-Non-Patient Version for DSM-IV* (SCID-N/P; First, Spitzer, Gibbon, & Williams, 1994) was administered as a screener to rule out psychopathology and assess for current suicidal ideation (see exclusionary criteria). The SCID was administered by trained research assistants and reviewed by the principal investigator. Although the SCID-N/P has high rates of inter-rater reliability (First et al., 1994), we did not compute such reliability ratings because only the screening module of the measure was employed.

The *Smoking History Questionnaire* (SHQ; Brown, Lejuez, Kahler, & Strong, 2002) is a self-report measure used to assess smoking history and pattern. The SHQ has been successfully used in previous studies as a descriptive measure of smoking history (Brown et al., 2002; Zvolensky, Lejuez, Kahler, & Brown, 2004; Zvolensky, Schmidt et al., 2005). The current study employed an average cigarettes per day variable to ascertain current level of smoking.

The *Alcohol Use Disorders Identification Test* (AUDIT; Babor et al., 1992) is a 10-item self-report screening measure developed by the World Health Organization to identify individuals with alcohol problems (Babor et al., 1992). A large body of literature attest to the sound psychometric properties of the AUDIT (e.g., Saunders, Aasland, Babor, de la Fuente, & Grant, 1993). The current study utilized the frequency and quantity items to index current alcohol consumption (an average frequency-by-quantity per occasion composite score; Stewart, Zvolensky, & Eifert, 2001).

The *Menstrual Distress Questionnaire* (MDQ; Moos, 1968) is a 47-item self-report measure that assesses retrospective premenstrual symptom severity on a 7-point Likert scale (0 = “did not experience” to 7 = “severe or intense experience”). For each symptom, respondents are instructed to select which rating best describes “[their] experience during the week immediately before [their] last menstrual cycle.” Chronbach alphas have varied from .64-.88 (Moos, 1991). In the present study, we employed the MDQ total score as a measure of global premenstrual distress.

The *Anxiety Sensitivity Index* (ASI; Reiss, Peterson, Gursky, & McNally, 1986) is a 16-item measure in which respondents indicate, on a 5-point Likert-type scale (0 = “very little” to 4 = “very much”), the degree to which they are concerned about possible negative consequences of anxiety symptoms (e.g., “It scares me when I feel shaky”). The ASI has high levels of internal consistency for the global score. The ASI is unique from, and demonstrates incremental validity relative to, trait anxiety (Rapee & Medoro, 1994) as well as negative affectivity (Zvolensky, Kotov, Antipova, & Schmidt, 2005). In the present investigation, the total ASI score was used, as it represents the global-order anxiety sensitivity factor, and therefore, takes into consideration fears of anxiety-related somatic, cognitive, and social cues.

2.2.2. Challenge Measures—The *Diagnostic Sensations Questionnaire* (DSQ; Sanderson, Rapee, & Barlow, 1988, 1989) is a measure of DSM-IV panic attack symptoms, which is frequently employed in challenge work (e.g., Zvolensky, Lejuez, & Eifert, 1998). Ratings for the DSQ are made on a 9-point Likert-type scale (0 = “not at all” to 8 = “very strongly felt”). The present study used the DSQ to assess DSM-IV panic attack symptoms immediately post-challenge. The DSQ yields a composite score for mean intensity level of symptoms and composite scores for a mean intensity level for cognitive (e.g., fear of going crazy) and physical (e.g., breathlessness) symptoms. The current study used the mean DSQ composite score to assess global panic symptom severity.

Physiological assessment: A J&J Engineering I-330-C2 system was used to digitally record physiological data on-line at a sample rate of 1024 samples per second across channels using

J&J Engineering Physiolab Software. SCR was examined in the current study (Venables & Christie, 1980). Raw electrocardiogram data were collected with disposable Ag/AgCl electrodes placed in a standard bilateral configuration on the palmar side of each wrist. Data were processed through a 1-100Hz bandpass filter designed to maximize R-wave frequency. SCR converted to microsiemens (μS) were obtained using an RV-5 skin resistance lead connected to SE-35 electrodes placed on the middle segment of the middle finger.

2.3. Materials and Apparatus

Carbon dioxide enriched air (CO_2) was stored in a 24-inch diameter hospital grade latex bag and delivered via 5-centimeter tubing to a positive-pressure C-pap mask worn by the participant. A one-way mirror and video and audio monitoring system allowed the experimenter to observe all session events.

Laboratory sessions were conducted in a 3-meter $\times$ 3-meter experimental room in the Department of Psychology at the University of Vermont. After completing physiological hookup and providing experimental instructions (see Procedure), the experimenter ran and observed study participants from an adjacent control room containing an apparatus designed to provide participants with a mixture of 10% carbon dioxide-enriched air.

2.4. Procedure

Interested persons responding to advertisements who contacted the research team were given a detailed description of the study over the phone. After providing verbal consent, the SCID-NP-screening module was administered by a trained research assistant via telephone. Those meeting inclusionary criteria were scheduled to attend a single laboratory session. Upon arrival, participants: 1) completed a written informed consent, which described the CO_2 procedure, 2) completed the pre-experimental measures, and 3) underwent the challenge procedure. During the session, participants sat alone in a sound attenuated experimental room, which contained a computer, chair, desk, and intercom that allowed participants to communicate freely with the experimenter in the adjacent room. Participants were seated in front of a table, on which a binder with the experimental, paper-pencil self-report measures was placed. Once the electrodes were attached standardized instructions were provided:

“Following the (10 minute) adaptation period, we will start the experimental portion of the study which will last approximately 4 minutes. During this period you will receive several inhalations of CO_2 -enriched air that may produce physical and mental sensations associated with bodily arousal. You may temporarily feel your heart racing, your palms might be sweaty, you might feel dizzy, and you might have some breathing problems.”

The study consisted of two phases: 1) a 10-min baseline adaptation period during which participants sat quietly in the testing room breathing regular room air, and 2) the automated delivery of one 4-min 10% CO_2 -enriched air presentation. Participants completed the DSQ immediately after completing the 4-minute challenge exposure. Participants remained in the experimental room for a 10-minute recovery period. SCR was gathered continuously across both phases. After the study, participants were debriefed and compensated \$20. Given that the definition of AS is fear of anxiety symptoms, knowledge that participants would experience anxiety symptoms (e.g., heart racing) at some point during the procedure, may have lead to anticipatory anxiety prior to the challenge procedure, particularly among individuals high in AS.

2.5. Data Analytic Approach

SPSS 16.0 was used for all analyses with 2-tailed $\alpha < .05$. Hierarchical linear regression analysis was employed to test the study objectives. In the first step of the model, average

number of cigarettes smoked per day and alcohol consumption were entered; anxiety sensitivity level (ASI total) was entered in step 2; and premenstrual distress score (MDQ total) was entered in step 3. Criterion variables included self-report post-challenge panic attack symptoms (mean DSQ score) and SCR (post-challenge SCR controlling for baseline SCR)

3. Results

Zero-order correlations were examined for all predictor and criterion variables (see Table 2). MDQ total score was significantly related to ASI total score, self-reported post-challenge panic attack symptoms, average amount of cigarettes per day, and baseline and post-challenge SCR (range of r 's: .30 - .56). MDQ total score was not related to alcohol consumption ($r = .07$). Mean AS score for women in the current study ($M = 17.5$, $SD = 9.5$, range 1 - 45) is similar to those reported for women in previous research ($M = 19.5$, $SD = 10.6$; Kelly et al., 2006). Paired samples t -tests, examining pre and post challenge anxiety scores via SUDs ratings ($t = -11.9$, $p < .001$) and SCR scores ($t = 8.4$, $p < .001$) revealed that the CO₂ challenge successfully increased anxiety and psychophysiological responses.

Analyses for self-reported panic symptoms experienced during the CO₂ challenge (DSQ mean) revealed that the predictor variables accounted for 22% of the overall variance [$F(4, 45) = 3.0$, $p < .05$]. Step 1 of the model (alcohol consumption and average cigarettes per day) did not account for significant variance in panic responding. Step 2 of the model (ASI total score) accounted for 11% of unique variance ($t = 2.3$, $\beta = .36$, $p < .05$) above and beyond step 1. Step 3 of the model (MDQ total score) accounted for an additional 11% of unique variance above and beyond steps 1 and 2 ($t = 2.38$, $\beta = .40$, $p < .05$; see Table 3).

In regard to SCR, predictor variables accounted for 46% of the overall variance [$F(5, 34) = 4.8$, $p < .01$]. Step 1 of the model accounted for 21% of the variance. Of the variables in step 1, only baseline SCR ($t = 2.5$, $\beta = .41$, $p < .05$) was a significant predictor of SCR at the end of the 4-min CO₂ challenge, and alcohol consumption and average cigarettes per day did not significantly predict post-challenge SCR. At step 2 of the model, ASI total score accounted for an additional 18% of unique variance above and beyond step 1 ($t = 3.0$, $B = .45$, $p < .01$). Step 3 of the model (MDQ total score) demonstrated only a trend towards statistical significance, though accounting for an additional 6% of unique variance above and beyond steps 1 and 2 ($t = 1.83$, $\beta = .31$, $p = .08$; see Table 3).¹ There were no baseline SCR differences between smokers (i.e., participants who reported smoking daily) and nonsmokers ($p = .47$).

4. Discussion

Previous research suggests that menstrual cycle phase may play an important role in the experience of anxiety and panic among women already at high risk for anxiety (high AS) and/or with PD (Perna et al., 1995; Sigmon et al., 1996; 2000b). There is little data, however, regarding the role of premenstrual distress symptoms in panic responding to bodily sensations in real-time, or their unique association, independent of shared variance with AS and other established risk factors. The aim of the present investigation was, therefore, to examine the incremental validity of retrospectively reported premenstrual distress in predicting panic symptoms and psychophysiological reactivity immediately following administration of 10% CO₂-enriched air among young adult females. Specifically, we tested whether premenstrual distress symptoms predict responses to a physical challenge, above and beyond variables that are known to affect these responses and that also may be associated with premenstrual distress (i.e., AS and alcohol and cigarette use). This knowledge may offer one important element to

¹In terms of psychophysiological outcome measures, MDQ total score was not related to baseline ($r = .08$) or post-challenge heart rate ($r = -.05$), and premenstrual distress did not significantly predict differences in heart rate ($t = -.30$, $\beta = -.03$, $\Delta R^2 = .002$, $p = .77$).

explicate gender differences in panic (Dick et al., 1994), and specifically, the role of individual differences in biological processes and responding to them for understanding panic vulnerability.

As a limitation of this study, participants in this study had an increased prevalence of smoking status (70%) as compared to national norms for young adult (age 18-29) women (21%; National Center for Health Statistics Health, 2008). Furthermore, current use of binge drinking (i.e., 5 or more drinks/day) was also elevated in this sample (33%) as compared to national norms for young adult women (9%; National Center for Health Statistics Health, 2008). Therefore, these results may not generalize to samples of adult women who are predominantly nonsmokers or have a lower frequency of binge drinking.

As predicted, women who reported greater premenstrual distress symptoms also reported greater panic symptoms following the CO₂ challenge. This effect, accounting for approximately 11% of unique variance in post-challenge panic symptoms, was evident above and beyond the variance explained by AS, current average number of cigarettes smoked per day, and level of current alcohol consumption. This finding is consistent with the conjecture that premenstrual distress may help to explain self-reported panic symptoms in response to bodily sensations elicited by a physical stressor. Additionally, the size of the premenstrual distress effect on panic responding to the challenge was comparable or larger than that observed for AS ($r = .42$ for MDQ; $r = .32$ for ASI), a well-established risk factor for panic psychopathology (Bernstein & Zvolensky, 2007; McNally, 2002). To our knowledge, all of the combined AS and menstrual distress studies to date have used the MDQ to assess premenstrual distress. Given that many of the symptoms on the MDQ overlap with those on the ASI, it will be important for future research to continue to disentangle shared variance between these two measures. However, currently, they are the most established measures for each of the variables tested. The current study demonstrated 22% shared variance between the MDQ and the ASI.

It is also noteworthy that these findings are consistent with literature on PMDD and CO₂ challenge-induced panic attacks (Harrison et al., 1989; Kent et al., 2001; Vickers & McNally, 2004). The current study is a community sample with MDQ premenstrual distress scores ranging from 26 – 175 ($M = 80.0$, $SD = 33.5$), suggesting that less severe or nonclinical forms of premenstrual distress also may be related to panic response in a similar fashion to those with PMDD. However, we did not assess formally for PMDD in this investigation, and therefore, it is unclear what percentage of the current sample met criteria (current or lifetime) for this diagnosis. In terms of SCR, premenstrual distress exhibited only a trend towards statistical significance. There was more missing data on this variable, owing to sampling error (e.g., participant movement). As a result, there was a slightly smaller sample size ($n = 35$) for this analysis, which may have diminished the power available to detect an effect. Furthermore, it is noteworthy that the zero-order association between MDQ scores and SCR was large in size and statistically significant despite the sample size ($r = .56$, $p < .01$) and moreover, comparable or larger than that observed for all other predictors, including ASI scores and SCR ($r = .34$, $p < .01$). Additionally the regression testing the incremental association between MDQ scores and SCR in response to the challenge was conducted *after* controlling for baseline SCR. This is particularly noteworthy in understanding the potential clinical meaningfulness of the observed, albeit modest, incremental effect of MDQ scores on challenge SCR ($r^2 = .06$), in so far as baseline and challenge SCR were so strongly correlated ($r = .74$, $p < .01$). It also may be important to consider that MDQ scores predicted challenge SCR ($r = .56$, $p < .01$) and baseline SCR ($r = .30$, $p < .05$). Consequently, the observed incremental versus zero-order effect of MDQ scores on challenge SCR also may in part be a function of its association with baseline SCR, reflecting the potentially meaningful association between premenstrual distress levels and psychophysiological levels of anxious apprehension about the biological challenge

procedure that was about to begin. Accordingly, these data indicate that a woman's experience of her premenstrual symptoms may possibly be meaningfully related to SCR, both in (anxious) anticipation of and in response to the physical challenge. Based on these findings, it may be important to further evaluate this issue with the inclusion of a more comprehensive assessment of psychophysiological parameters and with a larger sample size. Furthermore, direct evaluation of the association between MDQ scores and SCR in response to a physical challenge or stressor and psychophysiological processes of anxious apprehension would be important. Future research may also consider the use of skin conductance amplitude to measure the strength of psychophysiological response.

Although these data provide evidence that premenstrual symptoms may serve as a unique risk candidate for more intense panic symptoms in response to perturbation in bodily sensations, the mechanism(s) linking this factor to panic attacks remains unclear. One possibility is that premenstrual symptoms promote more adverse emotional events (e.g., more frequent and intense negative affect), and therefore, leads to learning to fear interoceptive stimuli during this phase of menstruation. It also may be possible that, in some women, elevated levels of premenstrual distress symptoms may promote maladaptive affect regulation strategies (e.g., avoidance, rumination; Zvolensky & Forsyth, 2002) in order to reduce distress that may paradoxically potentiate an increased risk of panic problems, as is prototypical of models of panic etiology and maintenance (Barlow, 2002). Finally, it is possible that greater premenstrual symptoms and distress may result from greater sensitivity to these physiological and affective symptoms (AS) and that repeated negative experiences with menstruation may concurrently potentiate greater sensitivity to anxiety. Thus, premenstrual symptoms and AS may contribute independently as well as interact and impact one another directly over time to predict the development and maintenance of anxiety and panic symptoms. Elucidating the mechanisms linking putative risk factors to panic psychopathology among women will facilitate theoretical refinement of etiological models and thereby guide the development of biologically gender-specific models of panic etiology.

Several important study limitations should be noted. First, this study used only retrospective report of premenstrual symptoms, which may be less accurate than current or prospective reporting (Logue & Moos, 1986; Marvan & Cortes-Iniestra, 2001). Women reported greater premenstrual symptoms when measured retrospectively as compared to when they were measured prospectively on the same premenstrual phase using the MDQ (Marvan & Cortes-Iniestra, 2001). Additionally, women who reported that they believed the majority of women experience PMS were more likely to report more premenstrual symptoms retrospectively as compared to prospectively (Marvan & Cortes-Iniestra, 2001), suggesting that beliefs or cultural stereotypes about the premenstrual phase may influence recall of one's premenstrual symptoms. Therefore, it is likely that the severity and frequency of premenstrual distress reported in this study may be inflated. Thus, future work would benefit by including a prospective assessment (e.g., daily tracking) of menstrual symptoms to evaluate consistency with the results observed here. Second, the present sample was a relatively homogenous (e.g., primarily Caucasian) group of young adults who volunteered to participate in the study for monetary compensation. To rule out potential self-selection bias and to increase the generalizability of these findings, it will be important for future work to draw from other populations (e.g., those with a greater range of clinical issues) and more diverse samples. Specifically, this study did not include a comparison group of individuals with current or past PD or panic attacks. Given data that AS prospectively predicts later panic pathology (Schmidt, Zvolensky, & Maner, 2006), it is likely that the results of the current study would not only be replicated among individuals with PD, but perhaps, exhibit an even stronger association. However, further research examining premenstrual distress and panic response, using individuals with PD, would be needed to fully understand the generalizability of the current findings. Greater variability in the observed data would offer additional empirical insight into the nature of the findings. Third, this study did

not assess current or past clinical forms of premenstrual distress (i.e., PMDD). Future research, comparing nonclinical forms of premenstrual distress to individuals with current or past PMDD, would be needed to further understand if the observed association between premenstrual distress and panic symptoms is unique to individuals with PMDD as compared to individuals with nonclinical levels of premenstrual distress. Fourth, although the advantage of the present design pertains to its ability to isolate theoretically relevant processes as they unfold in “real time” (Zvolensky & Eifert, 2000), these laboratory data will need to be extended to vulnerability processes in naturalistic settings and across larger periods of time. Fifth, the current menstrual cycle phase of the participant is unknown, which might add potentially interesting and important information regarding severity of premenstrual distress and panic response in the challenge. Specifically, participants may experience the challenge differently (e.g., increased anxiety) depending on their current menstrual cycle phase. Finally, all participants knew that they would be receiving CO₂-enriched air, which may have led to anticipatory anxiety and it is not clear how big a role expectancy of breathing CO₂-enriched air may play in the experience of anxiety during the challenge. Additionally, it is possible that participants undergoing a placebo CO₂ challenge (e.g., administered the same procedure but continues to receive room air instead of CO₂) would report similar post challenge anxiety symptoms due to the role of expectancy. Future research would benefit from a blinded pre and post challenge assessment of panic symptoms as well as comparison of panic response between a CO₂ challenge group to a placebo challenge group. The present investigation adds uniquely to the extant empirical literature on premenstrual distress and panic responsivity to bodily perturbation. This type of basic research that guides our understanding of clinically-relevant processes will continue to be an important area of research in the field's translational research efforts focused on understanding, preventing and treating panic and its disorders.

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Table 1
Participant Demographics ($n = 46$)

Age, Mean (<i>SD</i>)	21.2 (6.0)
Race, Number (%)	
White	42 (91%)
African American	2 (4%)
Asian	1 (2%)
Hispanic	1 (2%)
Education, Number (%)	
Some Middle School	1 (2%)
High School Degree	28 (61%)
Some College	14 (30%)
Graduated from 2-yr College	3 (7%)
Current cigarette smoker, Number (%)	32 (70%)
Average cigarettes per day, Number (%)	
6 cigs/day	2 (4%)
10 cigs/day	11 (24%)
15 cigs/day	7 (15%)
20 cigs/day	9 (20%)
30 cigs/day	2 (4%)
40 cigs/day	1 (2%)
Currently Use Alcohol, Number (%)	43 (93%)
Average drinks/day Number (%)	
1-2 drinks/day	6 (13%)
3-4 drinks/day	14 (30%)
5-6 drinks/day	15 (33%)
7-9 drinks/day	5 (11%)
≥ 10 drinks/day	2 (4%)

Table 2
Zero-Order Correlations among Theoretically-Relevant Variables

Variable	1	2	3	4	5	6	7	Observed Range
1. MDQ	1	.46**	.42**	.07	.40**	.30*	.56**	26-175
2. ASI		1	.32**	.12	.24**	.23**	.34**	1-45
3. DSQ mean			1	-.002	-.07	.05	.23*	0-7
4. Alcohol consumption				1	-.13	.09	.20	0-16
5. Cigs/day					1	.05	.23*	0-40
6. Baseline SCR						1	.74**	1-10
7. SCR							1	1-28

* Note: $p < .05$;

** $p < .01$; MDQ = Menstrual Distress Questionnaire - Total Score (Moos, 1968); ASI = Anxiety Sensitivity Index - Total Score (Reiss et al., 1986). DSQ mean = Total number of panic symptoms post-challenge (Sanderson 1988, 1989); Alcohol Consumption = Average frequency-by-quantity per occasion composite score; Stewart et al., 2001; Cigs/Day = Average number of cigarettes smoked per day; Baseline SCR = Baseline skin conductance response; SCR = skin conductance response post-challenge.

Table 3

Summary of Regression Analysis Predicting Panic Symptoms

Variable	ΔR^2	t	β	sr^2	p
DSQ ($n=46$)					
Step 1	.005				ns
Cigs/Day		.45	.07	.00	ns
Alcohol		.05	.01	.00	ns
Step 2	.11				< .05
ASI		2.31	.36	.11	< .05
Step 3	.11				< .05
MDQ		2.4	.40	.11	< .05
SCR ($N=35$)					
Step 1	.21				ns
Cigs/Day		1.5	.25	.06	ns
Alcohol		.81	.13	.02	ns
Baseline SCR		2.5	.41	.16	< .05
Step 2	.18				< .01
ASI		3.0	.45	.18	< .01
Step 3	.06				ns
MDQ		1.8	.31	.06	.08

Note: *MDQ* = Menstrual Distress Questionnaire - Total Score (Moos, 1968); *ASI* = Anxiety Sensitivity Index - Total Score (Reiss et al., 1986); *DSQ* mean = Total number of panic symptoms post-challenge (Sanderson 1988, 1989); *Alcohol Consumption* = Average frequency-by-quantity per occasion composite score; Stewart et al., 2001; *Cigs/Day* = Average number of cigarettes smoked per day; *Baseline SCR* = Baseline skin conductance response; *SCR* = skin conductance response post-challenge.